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Life Sciences

Optimizing Workflow Efficiency of Cleanroom Routine Environmental Monitoring with Beckman Coulter Life Sciences MET ONE 3400 Portable Air Particle Counters

Biopharmaceutical environmental monitoring is a time-consuming, labor-intensive effort required by major regulatory agencies around the world. Pharmaceutical companies growing their production capacity have experienced an explosion in the monitoring data generated, and the work required to gather, record and interpret them.

Beckman Coulter specializes in manufacturing instruments that optimize workflow efficiencies, including the MET ONE 3400 portable air particle counter. Innovative hardware and software solutions reduce implementation complexity while delivering confidence that required data have been gathered, recorded, and made readily available to the environmental monitoring team.

Failure should never be an option

To ensure quality and safety, biopharmaceutical manufacturing of aseptically produced, parenterally administered products must be performed in an environment free of bacterial or viral contaminants. A thoughtfully designed and well-executed environmental monitoring program tests the controls put in place to maintain the cleanroom to the required Good Manufacturing Practices standards (e.g., CGMP[1] , EU-GMP[2] , and PIC/S[3]). Regulatory agencies will audit these programs to verify they are being executed consistently.

Failure to execute these programs, by missing locations or losing data records, can lead to scrapped product or an audit finding, such as an FDA 483 letter thatcan lead to closure of the manufacturing plant.

Upon discovery of these failures, managers will attempt to find a root cause. An examination of the process will typically illuminate these failure points:

- Failure to execute the defined Standard Operating Procedure (SOP)
- Failure to take samples from all required locations
- Failure to configure the counter to take the required air volume
- Original paper records have faded over time
- Paper records are lost during the process of photocopying or scanning (to avoid fading)
- Manual transcription errors when entering data points into other electronic systems (e.g., Excel or LIMS)

These failures are often attributed to user error. Corrective action for user error typically entails increased training or labor-intensive quality checks; however, neither solution deals with the repetitive and error-prone processes that have been established. Automation and instrument-based software assistance are the only proven ways to reduce the likelihood of user errors in the system.

Following FDA guidelines while using less paper

One of the leading causes for FDA audit findings is data integrity failure. The US FDA has published clarifying guidelines regarding data integrity to help the pharmaceutical industry fully comply with CGMP guidance[4]. In their draft recommendations, the FDA states:

> For the purposes of this guidance, data integrity refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).

When used for environmental monitoring, the Simply Paperless system for the MET ONE 3400 series of portable air particle counters is designed to provide confidence in data integrity.

The MET ONE 3400 has several mechanisms to ensure data are attributable. Once configured, it requires a password-protected login for all operations, meaning all data are attributable to a specific user. Locations with full alphanumeric naming can be configured in the MET ONE 3400, clearly associating a sample with a location. Finally, every sample is recorded with a time and date to clearly identify when the sample was taken.

Use of electronic data recording that generates a text-based PDF inherently improves legibility of records. The MET ONE 3400 includes a comment feature that allows users to add comments to each record, and results can be exported as PDF or XML, which is compatible with SGML. (The FDA recommends submitting copies of electronic records in PDF, XML or SGML formats, among others.[5]) For added assurance, the MET ONE 3400 generates a secure PDF to prevent unauthorized data altering or tampering.

Building the data management and recording system directly into the MET ONE 3400 instrument ensures data are contemporaneously recorded. Immediately following the test, reports are created and available for export via USB thumb drive or to a network via FTP. Using these data transfer mechanisms improves the response time to data by eliminating delays from manually transcribing data into another system.

Using an original, digitally recorded record avoids multiple workflow steps during which data can be lost. Thermally printed paper records fade over time and must be collected and photocopied for long life. The photocopies are then manually entered into other tracking systems. Each step creates opportunities for paper records to be misplaced or mistyped into other databases. Using the MET ONE 3400 Simply Paperless system ensures all records are the originals that were compiled and generated within the instrument itself.

Accuracy is the bottom-line goal of all these data integrity requirements. Workflow efficiencies realized with MET ONE 3400's Simply Paperless system maximize accuracy by reducing the opportunity for human error while eliminating manual configuration, calculation or data entry.

In summary

A workflow review can reveal numerous touchpoints at which data integrity failures could lead to an audit finding or a production lot rejection. MET ONE 3400's Simply Paperless feature addresses each of these failure points.

- Failure to execute the defined Standard Operating Procedure (SOP)
    - Users see only the SOP(s) and location groups for which they are responsible.
    - Locations are pre-programmed into groups.
- Failure to take samples from all the required locations
    - All locations for each SOP are grouped together in the order in which they should be taken.
    - Users only need to select the Next button to cycle through all locations.
- Failure to configure the counter to take the required air volume
    - Locations are preconfigured with the correct timing to get the required air volume.
- Original paper records have faded over time
    - Secure PDFs of the data are stored on a USB thumb drive or uploaded to a file server.
- Paper records are lost during photocopying or scanning (to avoid fading)
    - No paper records are used, eliminating the possibility of their loss, and avoiding the need for photocopying/scanning.
- Manual transcription errors when entering data points into other electronic systems (e.g., Excel or LIMS)
    - Outside data processing tools can read data directly from a secure PDF, XML or text format. Results can be processed or stored for later analysis, recall or trending.

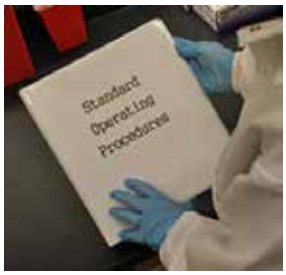
Compliance simplified

The MET ONE 3400 is designed to maximize workflow efficiencies by reducing the possibility of human error and eliminating work steps whenever possible. Using the MET ONE 3400 Simply Paperless portable air particle counter simplifies compliance with global regulatory standards and reduces the chance of an audit finding due to data integrity issues. The result is confidence that the facility and its data are compliant.

Caption: Five manual touchpoints increase the chances of data integrity errors in a typical routine environmental monitoring program.

Touchpoint 1:

- Ensure use of most current SOP
- Read and understand SOP



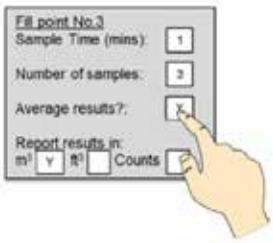
Touchpoint 2:

Manually type each sample location name

Touchpoint 3:

Manually configure counter:

- Sample time
- Number of samples
- Results averaging
- Correct multiplier for m^3



Touchpoint 4:

- Photocopy print-out

Touchpoint 5:

- Manually transcribe results

[1] Food and Drug Administration. Guidance for industry. Sterile drug products produced by aseptic processing – current good manufacturing practice, 2004. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Office of Regulatory affairs (ORA) Division of Drug Information, HFD-240 Center for Drug Evaluation and Research, Food and Drug Administration 5600 Fishers Lane Rockville, MD 20857 USA.

[2] European Commission. EudraLex. The Rules Governing Medicinal Products in the European Union. Volume 4. EU Guidelines to Good Manufacturing Practice. Medicinal products for human and veterinary use, Annex 1: Manufacture of Sterile Medicinal Products, 25th November 2008. European Commission Enterprise and Industry Directorate-General, B-1049 Bruxelles/Europese Commissie, B-1049 Brussel – Belgium.

[3] Pharmaceutical Inspection Co-operation Scheme, PIC/S Guide To Good Manufacturing Practice for Medicinal Products, 1st January 2017, PIC/S Secretariat 14, rue du Roveray CH - 1207 Geneva Switzerland.

[4] U.S. Department of Health and Human Services Food and Drug Administration Data Integrity and Compliance With CGMP Guidance for Industry. April 2016. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), and Center for Veterinary Medicine (CVM).

[5] U.S. Department of Health and Human Services Food and Drug Administration Guidance for Industry, Part 11, Electronic Records; Electronic Signatures — Scope and Application. August 2003. U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Office of Regulatory affairs (ORA) Division of Drug Information, HFD-240 Center for Drug Evaluation and Research, Food and Drug Administration 5600 Fishers Lane Rockville, MD 20857 USA.

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