



# Quality Control Electronic Records for 21CFR part 11 Compliance

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## Introduction

The FDA's 21CFR part 11 guidance<sup>1</sup> on the use of electronic records for data retention or submission is clear. With manually implemented Standard Operating Procedures for Quality Control testing and manual transcription of the test results still common practices in the pharmaceutical QC world, the resultant opportunities for human error raises concerns over the integrity of the data in the final electronic record, no matter how safely the final record is stored.

This paper describes how Quality Control instruments can be optimised for pharmaceutical use, helping to improve the integrity of the data in the final electronic record.

## Quality Control Manual SOPs

The introduction of the FDA's Guidance for Industry Part 11, Electronic Records; Electronic Signatures prompted the pharmaceutical industry to take a closer look at how it stored and controlled electronic records. One area however still very much remains a concern: the potential for affecting the integrity of Quality Control (QC) test result data by human error through the use of manual Standard Operating Procedures (SOPs). A manual SOP is where the instrument set-up and configuration is performed manually by the user or where the QC test results are manually transcribed into electronic record format. The electronic record may be kept safely and securely, but the data it contains may not be correct, or may simply be missing!

## Electronic SOPs

In an effort to improve data integrity, some manufacturers have optimised their instrumentation specifically for pharmaceutical QC use, building into the instrument design the capability for pre-configured electronic SOPs for:

- a) Instrument set-up and configuration
- b) Automatic pass-fail reports to pharmacopoeial criteria
- c) Generation of electronic records straight from the instrument

The user simply selects the electronic SOP that has been pre-configured in the instrument and hits the 'Go' button and the instrument configures itself correctly according to the SOP, carries out the correct test and produces an electronic test result record, all automatically.

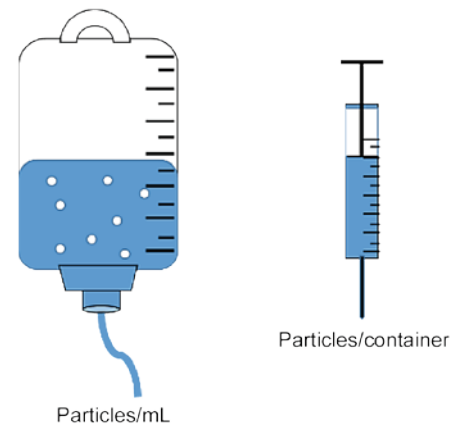


**Figure 1.** Manual SOPs introduce opportunities for human error to impact on the integrity of data in electronic records

## Final Product QC

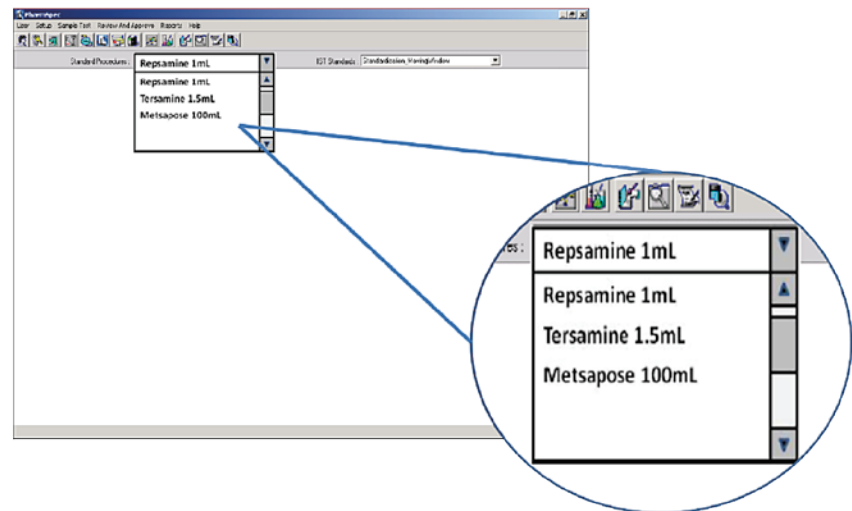
Although largely harmonized, the requirements for parenteral drug particulate testing do vary from country to country and from product to product. The volume of the sample to be analysed and the format that the results are reported varies from product to product, e.g. the sampling requirements for small volume biological parenteral product, such as vaccines<sup>6</sup>, is different for that of a large volume parenteral such as an intravenous drip bag<sup>9</sup>. Results must be calculated and expressed in the correct format, e.g. counts per container, or counts per mL, depending on the product under test.

Whilst general-purpose liquid particle counting instrumentation can be used for the testing of particles in parenteral products, counters that have been optimized for the application are preferable due to the wide range of complexity in the testing. Particle counters that have been optimized for this testing will have the various compendial tests built-in and will calculate a pass/fail result automatically. As QC teams tend to use their product brand name to describe the product sample under test, optimized particle counters will allow the user to select the required test for each sample by selecting the product by name from a drop-down menu.



**Figure 2.** Particulate contamination reporting requirements are product-dependent

**Figure 3.** Electronic SOP functionality in Beckman Coulter HIAC PharmSpec software allows pre-configured SOP test routines to be named according to the brand name of the product under test and selected by the technician via drop-down box



## Cleanroom Routine Environmental Monitoring Records

Electronic SOPs are of particular benefit in portable air particle counters used in cleanroom routine environmental monitoring. While the FDA's CGMP<sup>5</sup>, Europe's GMP Annex 1<sup>3</sup>, World Health Organisation<sup>2</sup> and PICS<sup>4</sup> documents specify the maximum concentration of airborne particles in pharmaceutical cleanrooms, it is ISO 14644-1<sup>10</sup> that specifies the method for cleanroom qualification/classification and routine environmental monitoring plans should be created by each factory based on their own risk assessment. Once SOPs for qualification and routine monitoring are in place they are typically carried out manually, with the instrument operator responsible for configuring the particle counter at each sample location according to the requirements of the SOP. Typically teams of people are dedicated to carrying out routine environmental monitoring on a daily basis and thousands of pieces of data are created each month. The manual SOP typically requires the data to be manually transcribed into an electronic record. Manual instrument configuration and data transcription process can be very error-prone. Counters that are optimised for pharmaceutical cleanroom use allow the whole process to be automated using electronic SOPs that are pre-programmed once into the counter and then simply called up by the operator, who selects the correct SOP by choosing the environmental location name from the counter menu.

## Electronic Records Direct From QC Instrumentation

There are three methods for electronic record generation direct from QC instrumentation:

1. export in file format listed in the FDA 21CFR part 11 guidance via wired Ethernet
2. export in file format listed in the FDA 21CFR part 11 guidance via wireless Ethernet
3. totally separate electronic test results record database on a separate, secure server

QC instrumentation is typically a capital expenditure and this, combined the cost of validation, means that instruments tend to be retained for a very long time, sometimes in excess of 15 years. Customers considering the purchase of QC instrumentation should bear in mind that they may wish to move to full electronic records at some time during the lifetime of the QC instrument and require one of these three electronic record generation methods in any new instrument purchases, even if they intend to remain with manual SOP execution in the short-term. The availability of wireless Ethernet capability is of particular significance to portable QC instrumentation, such as portable air particle counters used in cleanroom routine environmental monitoring programs.

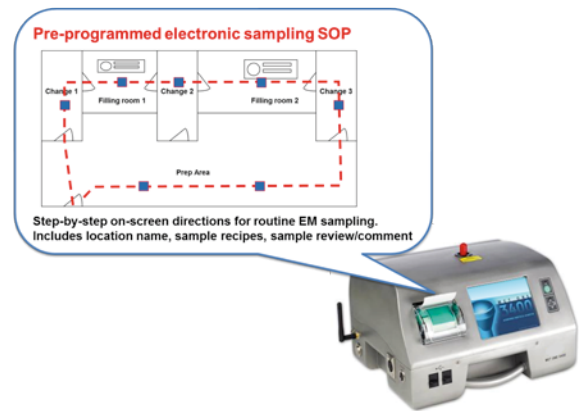
In their guide to 21CFR part 11, the FDA suggests that electronic records may be kept in standard electronic file format and gives PDF, XML and SGML as examples. Many Laboratory Information Management Systems (LIMS) are designed to accept data from QC instrumentation in standard electronic formats including .csv and Excel\*.

## Conclusion

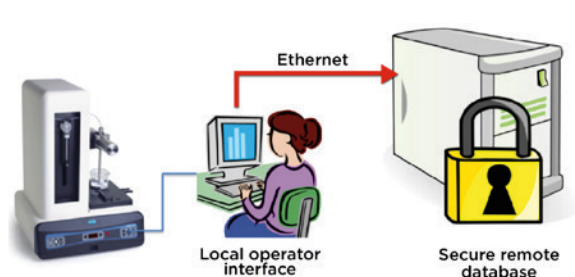
Pharmaceutical QC testing is complex and at the same time absolutely critical to a successful, compliant batch release. When selecting instrumentation, the QC team leader is well advised to look for instrumentation that has been optimized for pharmaceutical QC use, taking into account automated, pre-configured electronic SOPs, built-in compendial tests and secure electronic file transfer, such as File Transfer Protocol (FTP), for 21CFR part 11 electronic record retention.

## References

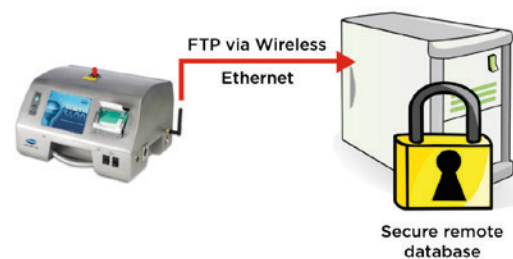
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**Figure 4.** Beckman Coulter MET ONE 3400 air particle counter can have cleanroom sampling SOPs loaded and recalled by simply selecting the location name from the on-screen menu improving 21CFR part 11 compliance



**Figure 5.** Beckman Coulter HIAC PharmSpec software allows the electronic test results database to be kept remotely on a secure server, where the IT department can implement 21CFR part 11 secure controls



**Figure 6.** Wireless Ethernet functionality in Beckman Coulter MET ONE 3400 portable air particle counter allows future implementation of electronic records for cleanroom routine environmental monitoring, sending the electronic records straight from the counter to a secure server, where the IT department can implement 21CFR part 11 secure controls

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## Author Biography



### Tony Harrison

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Tony has spent the last twelve years in applied metrology in the pharmaceutical and healthcare manufacturing industries. Prior to that, he worked for companies providing process control automation solutions for manufacturing industries.

Tony was joint-editor of the ISPE Guide to Ozone Sanitization of Pharmaceutical Water Systems<sup>8</sup> and was also chief editor of the PHSS Best Practice Guide for Cleanroom Monitoring<sup>9</sup>.

Tony is a well-known international speaker and has provided educational seminars on TOC, liquid particle counting, ozone sanitization for water systems and cleanroom monitoring in UK, France, Italy, India, Germany, Malaysia, China, USA, Scandinavia, Ireland, Hungary, Switzerland, Indonesia, Belgium, Greece, Switzerland, Turkey, Egypt and Denmark.



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