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Data Integrity
FDA Regulations

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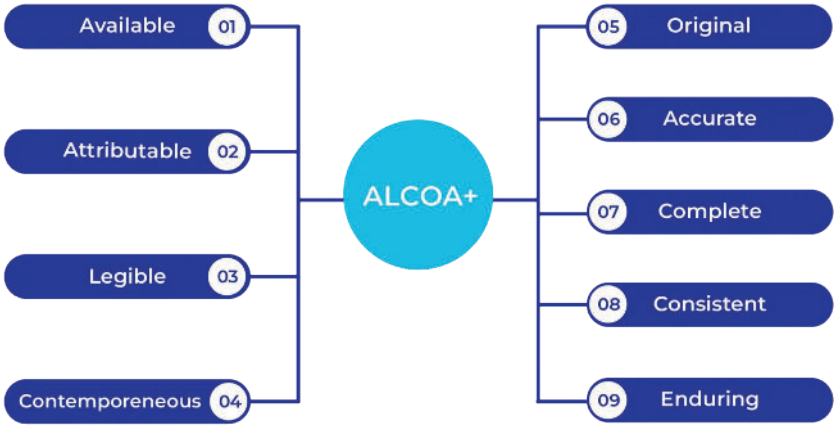
DATA INTEGRITY

Overview

Data integrity is a critical component of current good manufacturing practices (CGMP) as it ensures that data is complete, consistent, and accurate. The U.S. Food and Drug Administration (FDA) has issued guidance to clarify the expectations around data integrity within the pharmaceutical industry.

This paper provides a concise overview of the FDA's "Data Integrity and Compliance with Drug CGMP" guidance.

Particle Counters capture critical data and should be properly designed to meet these requirements and validated to prove the systems meet the applicable regulatory requirements when dealing with electronic data and electronic signatures.



Understanding Key Terminology

Data Integrity:

Refers to the completeness, consistency, and accuracy of data, ensuring it is attributable, legible, contemporaneously recorded, original, and accurate (ALCOA+).

Metadata:

Contextual information that explains or provides meaning to data, making it easier to retrieve, use, or manage. Metadata is structured information that describes, explains, or provides context about other data.

An example of metadata is the date and time stamp and location of a sample on particle counter environmental air samples. The User is also logged onto the system providing an electronic signature attributed to the data collector. This metadata provides context about when the sample was taken, where it was taken and by whom. Without this additional information the data would lack important information about its origin, location and the person collecting the data.

Audit Trail:

A secure, computer-generated, time-stamped record that allows for the reconstruction of events related to the creation, modification, or deletion of an electronic record.

When can a CGMP result be Invalidated?

A CGMP result can only be invalidated if there is a scientifically sound and documented justification. Even invalidated results must be retained and reviewed by the quality unit as part of the complete batch record.

For example, if a particle counter sample probe is knocked over then that sample can be aborted (but the aborted data must be captured and available for review). A new sample can be started once the probe setup is reset.

Computer System Validation

Every CGMP workflow on a computer system must be validated to ensure it performs correctly for its intended use. This includes validating the creation of electronic master production and control records (MPCRs).

Particle Counter data should be validated from its origin right through to how it is transferred ensuring Data Integrity adherence is followed throughout the data lifecycle.

Restricting Access to CGMP Systems

Access to CGMP computer systems must be controlled to ensure only authorized personnel can make changes. This includes assigning system administrator roles to independent personnel and maintaining a list of authorized users.

21CFR11 should be followed and the Particle Counter should be validated to ensure it meets the applicable requirements.

Concerns with Shared Login Accounts

The FDA discourages the use of shared login accounts because it makes it impossible to attribute actions to specific individuals, violating CGMP requirements.

21CFR11 validations should specifically test these issues and the use of SOPs and providing training to users on the accountability effect. Inactivation logout times should be introduced into the Particle Counter.

100% digital ApexZ Portable Particle Counter without onboard printer

Control of Blank Forms

Blank forms, whether electronic or paper, must be controlled by the quality unit or a document control group. This ensures that all forms are accounted for and used appropriately.

With advanced smart Particle Counters switching from paper-based records to digital systems is becoming more popular particularly with adherence to EU GMP Annex1 Contamination Control Strategy and Pharma 4.0 systems which pave the way for continuous manufacturing.

Review of Audit Trails

Audit trails should be reviewed by the personnel responsible for record review under CGMP. The frequency of review should align with the criticality of the data and regulatory requirements.

Administrator access should be setup on a Particle Counter to allow for this high-level data reviews. Compliance reports can be easily generated to provide a snapshot summary of Audit Trails any "Bad Data" should be recorded and marked for attention of the reviewer.

Use of Electronic Copies

Electronic copies can be used as true copies of records as long as they preserve the content, meaning, and metadata of the original records.

Ensure your Particle Counter is validated to prove the ALCOA++ requirements so the data lifecycle is traceable from origin to end user.

Retaining Original Electronic Records

Original electronic records, especially from dynamic systems like chromatographic instruments, must be retained in their original dynamic format to meet CGMP requirements.

Particle Counter EM SOP should have data download requirements for all data to be loaded digitally onto a secure server folder. CIFS is a good option for secure electronic record retention in a secure folder.

Electronic Signatures

Electronic signatures can be used in place of handwritten signatures on CGMP records, provided they meet the security and traceability requirements of 21 CFR Part 11.

Particle Counter IQ/OQ should test and validate the electronic signatures to comply to 21CFR11 requirements. This should be completed before a Particle Counter is put into service.

When Does Electronic Data Become a CGMP Record?

Electronic data becomes a CGMP record when it is generated to fulfill a CGMP requirement. This data must be saved and protected from unauthorized modifications.

Particle Counters should have an internal buffer capable of saving all data records. EM SOPs should have a time interval for uploading buffered data to secure server.

Use of Actual Samples in System Suitability Testing

The use of actual samples in system suitability tests, test preps, or equilibration runs is discouraged as it may lead to testing into compliance, which is against CGMP.

Not Applicable for Particle Counters.

Saving Final Results from Reprocessed Chromatography

All results from reprocessed chromatography, not just the final result, must be saved and reviewed as part of the complete CGMP record.

Not Applicable for Particle Counters.

Handling Quality Issues Informally

Any information regarding potential data integrity issues must be handled formally within the CGMP quality system. Informal handling is not acceptable.

Some particle counters can instantly mark "Bad Data' based on sensor and instrument diagnostics. An action alarm is typically generated if data integrity is an issue. This should trigger the root cause analysis.

Training Personnel on Data Integrity

Training on preventing and detecting data integrity issues should be a part of routine CGMP training programs to ensure personnel are well-informed.

Particle Counter vendors can assist in training on data integrity and how to setup the Particle Counter to ensure data integrity alarms are configured and users are alerted immediately.

FDA Access to Electronic Records

The FDA has the right to access and inspect all CGMP records, including electronic records, during inspections.

Saving Particle Count data securely on server folders enables a location where all Particle Counter data is stored for easy retrieval for FDA auditors. Compliance reports from the raw data can be easily generated based on auditors' requests with a couple of minutes.

Addressing Data Integrity Problems

Companies are encouraged to take a proactive approach to address data integrity problems, including conducting root cause analyses, implementing corrective actions, and possibly engaging third-party auditors.

New smart Particle Counters such as the ApexZ enable users to address Data Integrity issues with ease.

Conclusion

The FDA's guidance on data integrity emphasizes the importance of maintaining accurate, complete, and secure records throughout the lifecycle of CGMP data. By adhering to these guidelines, pharmaceutical companies can ensure compliance, safeguard product quality, and protect patient safety.

Selection of the right Particle Counter and vendor is important. When reviewing options be sure to ask the vendor how their Particle Counter handles Data Integrity. The ApexZ has the most self-diagnostic parameters available on a Particle Counter ensuring data integrity is built into each and every sample record.

References

1. *Data Integrity and Compliance with Drug CGMP Questions and Answers Guidance for Industry (Dec 2018): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers*

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