Data integrity based on ALCOA+ principles

In the context of the Memograph M RSG45 Data Manager combined with Field Data Manager (FDM) analysis software.

Endress+Hauser
People for Process Automation

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Introduction

Data integrity is an essential part of quality assurance in the life sciences industry. Particularly in pharmaceutical production, processes must adhere to strict requirements in order to guarantee the quality of end products in a consistent and verifiable manner. Only then can the effectiveness of pharmaceuticals be guaranteed and the risk of side-effects and damage to patients' health due to errors in production processes be reduced. Regulatory authorities specify how and to what extent producers must record the data relating to their processes and document these processes in the long term.

Modern measurement and control technology is used to capture large volumes of data along the entire value chain. This data is required not only to enable precision control of plants; it is also particularly important in ensuring that the quality-related parameters of all production batches are fully documented in a traceable manner and can be made available at any time.

This white paper explains the ALCOA/ALCOA+ principles, its application in the life sciences industry and how innovatuve solutions for data logging, data archiving and analysis are helping users to meet data integrity requirements. Global regulatory authorities and associations, such as the International Society for Pharmaceutical Engineering (ISPE), the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have published guidelines on how to guarantee data integrity. These guidelines are based, among other things, on the ALCOA/ALCOA+ principles relating to documentation practice. The Pharmaceutical Inspection Cooperation Scheme (PIC/S) and the World Health Organization (WHO) are drafting good practice guidelines (as of November 2020), which also reference the ALCOA/ALCOA+ principles. Together with the ALCOA/ALCOA+ principles, these guidelines will lead a globally consistent approach to ensure data integrity.

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What do the ALCOA/ALCOA+ principles mean?

ALCOA is an acronym that comprises the following elements:

- **Attributable:** Data must be stored in such a way that it can be uniquely attributed to an individual or computer system.
- **Legible:** Data must be recorded in a form that allows it to be easily traced and reproduced at all times.
- **Contemporaneous:** Data must be recorded and tracked at the time of its creation.
- **Original:** The original record of the data must be logged to ensure the traceability of processes. The data must be saved and preserved in its original form.
- **Accurate:** The data must be stored in such a way that it is true, complete, valid and reliable. This requires suitable process structures and control mechanisms.

The "+" stands for the following additions to the ALCOA acronym:

- **Complete:** The data must be complete (e.g. including data from repeatable tests).
- **Consistent:** All elements, such as the timely based sequence of events, must be in chronological order and stamped with the appropriate date and time.
- **Enduring:** Data should be stored on suitable storage media (hard copy or electronic) to ensure that it is available throughout the entire retention period.
- **Available:** It should be possible to access data throughout the entire life cycle, e.g. for inspection purposes.

Definition of data integrity

Data integrity is defined as the extent to which recorded data is complete, consistent, accurate, truthful and reliable. Data integrity also implies that these attributes are maintained throughout the entire data life cycle, i.e. from the generation of the data to when it is finally deleted. The data should be collected and stored in a secure manner to ensure that it is attributable, legible, contemporaneous, original (or in the form of a certified copy) and correct.
This requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices.

Objective

This white paper describes the ALCOA/ALCOA+ principles in the context of the Endress+Hauser Memograph M RSG45 Data Manager combined with Field Data Manager (FDM) analysis software.
Compliance with the ALCOA/ALCOA+ principles is demonstrated by linking the ALCOA/ALCOA+ attributes to functions and capabilities within the system and describing how data are handled internally throughout the complete data life cycle. This serves as a valuable guidance to users in the life sciences and food and beverage industries* when selecting, evaluating and also validating and verifying this data logging system and its application in customer processes.

*This white paper does not deal specifically with the food and beverage industry. However, the ALCOA/ALCOA+ principles are being applied to an increasing extent in a similar way here.

System architecture and data flow

Data integrity is something that must be considered and guaranteed from the moment raw data is transferred from a process sensor and recorded in the target system to when it is finally stored in a suitable database or, if necessary, in hard-copy documentation. However, data comprises not only measured values but also diagnostic data (identification, status, error and event data), as well as interventions and inputs by users and by other automated systems, allof which is recorded in a secure logbook referred to as the "audit trail". With regard to the latter, see also the Endress+Hauser white paper (WP01028L), which deals specifically with conformity to the requirements of FDA 21 CFR Part 11 in relation to electronic records and electronic signatures.

The system architecture below illustrates the system boundaries, data transfers and data flows within the data logging process with the Memograph M and Field Data Manager software.
The system enables the customer to implement a backup and restore strategy. The data can be exported from the system (CSV, PDF, hard copy). The raw data remain in the system and can be digitally retrieved for verification purposes during inspections.

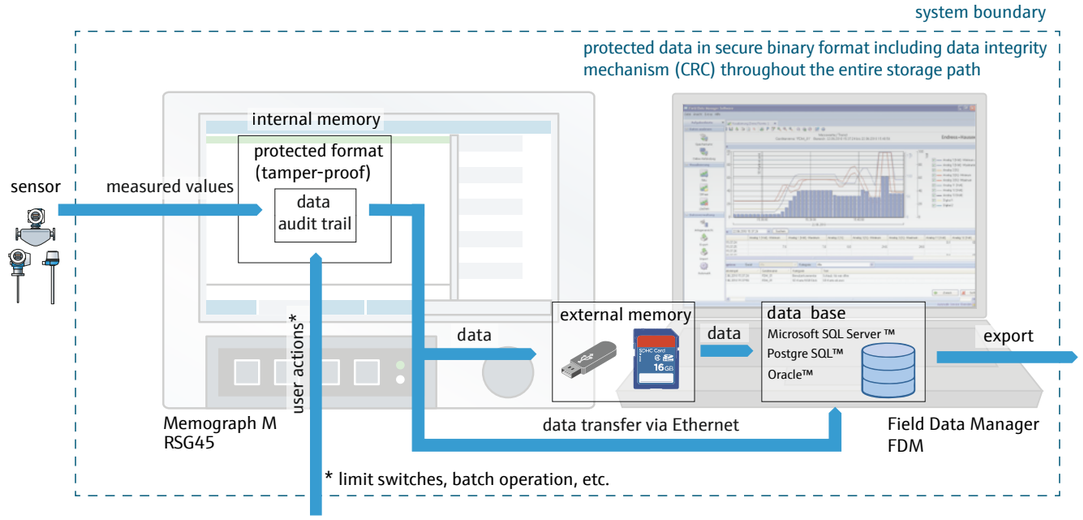

Fig. (1) System architecture and data flow

Application of ALCOA/ALCOA+ principles and how they are supported in the logging system

The following table shows the product features and system functions of the Memograph M and Field Data Manager that are used to implement the ALCOA/ALCOA+ requirements.

Requirement	Implementation in the system	Note
Attributable	The process data is generated via connected sensors; the origin of the data or the identity of the sensors is recorded automatically by the system using the serial number, tag, etc., and assigned to the measured values. Integrated user administration functionality (as per FDA 21 CFR Part 11) permits only users logged in with a name, ID and unique password to enter data into the system in accordance with their access authorization and role. All user inputs, as well as diagnostic and error messages, are stamped with the date and time. The identification data of the actor (user, sensor) and additional information are recorded and saved as plain text in the audit trail.	Automated, tamper-proof allocation and storage of all data For user administration, see Fig. (2)
Legible	Once recorded, measured values are converted to electronic data records and presented by the system (including units on the display) via web server or in FDM in the form of numeric or graphical displays (line graphs, bar graphs or pie charts). Information in the audit trail is presented to the user in tabular form with search and filter functions. Clear printouts in hard copy or in the form of a PDF document ensure legibility for inspections, validation and audits.	All information is presented in easy-to-understand plain text in numeric, tabular or graphical form, see also WP01028L09 FDA 11.10(b) Conformity
Contempora-neous	All measured data is recorded and processed in real time; the minimum scan rate of the Memograph M is 100ms. A real-time clock (RTC) is used to stamp all data records and events with the date and time. If the RSG45 and the FDM software are integrated in a customer network, functions for synchronizing system time can be used (e.g. NTP protocol).	Synchronized real-time logging of all data records
Original	Within the system boundaries, data records are managed in an encrypted binary file format. A cyclic redundancy check (CRC) is performed in the case of all data storage processes and transfers between subsystems. These measures ensure that the data cannot be tampered with and thus guarantee its authenticity.	
Accurate	All measured values and inputs are handled purely digitally from the start of the logging process. A very high resolution (32-bit floating value) is used for logging and storage. Data is stored in encrypted form and includes a reference to the source (sensor), user and a date/time stamp. The CRC procedure used also allows corrupted data records to be detected and marked as corrupted.	See also WP01028L09 FDA 11.10(a) Conformity
Complete	All data (measured data, user inputs, electronic signature) is stored together in one file. Changes and user inputs are stored with the "old value, new value and reason for change". Each data record is stamped with the date and time, thus ensuring the precise temporal sequence and completeness of the data records from when they are first captured to when they are next processed.	
Consistent	The data is recorded with the digital Memograph M RSG45 Data Manager as close to the process as possible and is stored as raw data. The audit trail always runs as an unstoppable system routine, which cannot be reset or switched off. The synchronized system time included in the data records guarantees the consistency of the data from when it is captured and transferred to the database to when it is printed on the graph or chart in hard copy.	
Enduring	All data is stored in the Memograph M on storage media (non-volatile memory, SD cards) that meet industrial standards. Non-volatile memory (RAM) is buffered by a battery; in the event that the power supply is interrupted, an internal emergency routine ensures an additional backup of the memory contents. After the data has been read out by the FDM software, it is stored in certified databases and made available for further use (analysis, reporting, printout, etc.). All databases have secure backup and recovery mechanisms.	FDM-supported databases: PostgreSQL™ Microsoft SQL Server™ Oracle™
Available	The data is visualized on a display on the RSG45 or displayed in the FDM software. For documentation and auditing purposes, the data can be made available at any time in digital exchange formats, such as PDF, XLS, CSV. These files can be generated manually or in an automated, time-controlled batch process. The data is available at any time via secure remote access to authorized persons with the appropriate access authorization, e.g. for verification.	Manual and automated export function

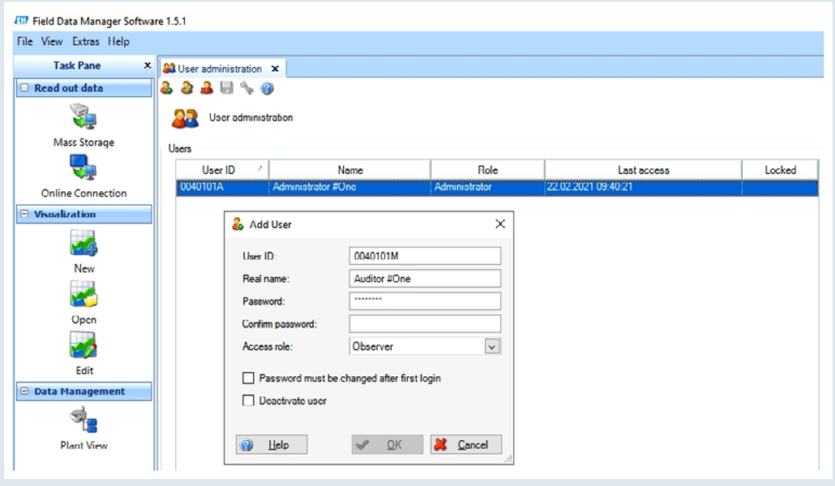

Fig. (2) User administration in accordance with requirements of FDA 21 CFR Part 11

Additional system functionality to protect and ensure data integrity

In addition to the system features described above in the context of the ALCOA/ALCOA+ principles, the Memograph M Data Manager and FDM software offer other important product features that increase data security and data integrity.

- Customizable password rules: adjustable password strength (password length, special characters, automated password change requirement)
- Blocking of users in case of multiple incorrect entries, which is documented in the audit trail
- Auto-logout of users if there has been no user activity within a defined period of time
- Integrated version controls and detection of originality of installed system hardware and firmware
- Additional change and access protection can be achieved via hardware locks (key switch, terminal cover, housing seal, interfaces and memory card slots)

Summary

The Endress+Hauser data logging system, which consists of the Memograph M RSG45 Data Manager and Field Data Manager (FDM) analysis software, was designed specifically for users in the life sciences industry based on the "Quality by Design" (QbD) concept. With Its internal system functions and product features, it can fully meet the requirements based on the ALOCA/ALCOA+ principles. Users receive an innovative, automated system for recording and documenting their quality-related data, which enables them to meet the legal requirements and the requirements of regulatory bodies and associations.

Our competence

When choosing a suitable data logging system, it is important to consider more than just product features and technical/functional aspects. Certified suppliers of measurement and control technology have already taking the necessary measures in their development and production processes to ensure a high degree of product and data security. The relevant certifications, quality guidelines and standards play a key role here. They ensure that any solutions offered are aligned with the specific requirements and principles of users in the life sciences industry. These criteria include:

- Certified products and services in compliance with regulatory requirements (e.g. 21 CFR Part 11, ISPE Records and Data Integrity Guide, ALCOA/ALCOA+)
- Certifications in development and production in accordance with international standards, e.g. ISO 9001, ISO 27001 or IEC 62443 (industrial cybersecurity)
- Employees in development, sales and support who are specially trained to meet the requirements
- Implementation of validation projects, external training and consulting for projects
- Commissioning, service and calibration management onsite at customer premises

As a long-standing partner with more than 14,000 qualified employees in over 120 countries worldwide, Endress+Hauser offers its customers a comprehensive package of products and services for the implementation of legal requirements and requirements of regulatory bodies and associations.

Further information relating to the topic of data integrity in the life sciences industry is available on the websites of the regulatory bodies and associations:

https://picscheme.org
https://www.who.int/
https://www.fda.gov/
https://ispe.org/
https://www.ema.europa.eu

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