Data integrity based on ALCOA+ principles

In the context of the CA79 TOC analyzer combined with the Viewer analysis software.

Endress+Hauser
People for Process Automation

Contents

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 innovative 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) published good practice guidelines, which also reference the ALCOA/ALCOA+ principles. Together with the ALCOA/ALCOA+ principles, these guidelines lead a globally consistent approach to ensure data integrity.

Authors

Philipp Zumoberhaus, Head of Global Program Management Execution, Endress+Hauser Group Services AG

Sylvia Del Sorbo, Validation Manager Life Sciences Industry Support, Endress+Hauser Group Services AG

Guido Mennicken, Expert Environmental Analytics, Endress+Hauser Liquid Analysis

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 CA79 TOC analyzer software combined with the Viewer 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 TOC analyzer 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 CA79 analyzer and the Viewer 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.

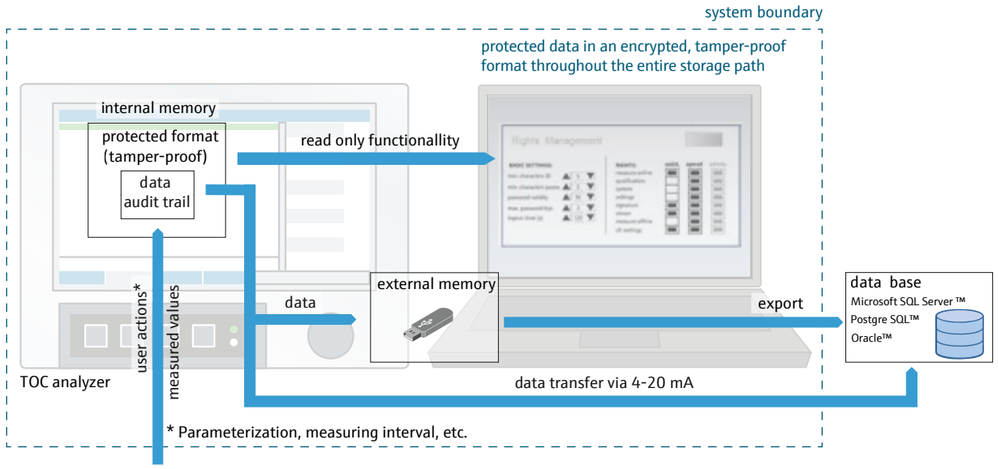

Fig. (1) System architecture and data flow

Application of ALCOA/ALCOA+ principles and how they are supported in the TOC Software

The following table shows the product features and system functions of the TOC analyzer and the Viewer software, that are used to implement the ALCOA/ALCOA+ requirements.

Requirement	Implementation in the system	Note
Attributable	The process data are generated by the TOC analyzer software; the origin of the data and the identity of the analyzer is recorded automatically by the system using the serial number and assigned to the measured values. Integrated user administration functionality (as per FDA 21 CFR Part 11) permits only users logged in with a ID and unique password to enter data into the system in accordance with their access authorization and role. All diagnostic and error messages, are stamped with the date and time. User comments 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) in the form of numeric or graphical displays (line graphs). Information in the audit trail is presented to the user in tabular form. 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 Whitepaper WP01278C – 21 CFR Part 11 section 11.10(b)
Contempora-neous	All measured data is recorded and processed in real time; the value update rate is <2 s. A real-time clock (RTC) is used to stamp all data records and events with the date and time.	Time logging of all data records with the system time
Original	Within the system boundaries, data records are managed in an encrypted binary file format. The audit trail can be visualised by the Viewer software, that has a read-only functionality. A later modification of the audit trail is not possible.	
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 user and a date/time stamp. The encryption guarantees that only valid data are still readable and useable. Corrupted data are not useable for processing.	See Whitepaper WP01278C – 21 CFR Part 11 section 11.10(a)
Complete	All data (measured data, user inputs) is stored together in one file. A later modification of the audit trail is not possible. Each data record is stamped with the date and time, thus ensuring the precise temporal sequence and completeness of the data.	
Consistent	The data are recorded with the TOC analyzer software and are immediately stored in an encrypted, tamper-proof format. The audit trail always runs as an unstoppable system routine, which cannot be reset or switched off. The system time included in the data records guarantees the consistency of the data.	
Enduring	All data is stored in the CA79 TOC on hard drive (non-volatile memory) that meet industrial standards. The system applies a waiting time of 30 seconds for any new parameter, to guarantee that the settings were stored in a safe and permanent way. The saved data would not be affected by a possible power failure.	Permanent hard drive storage
Available	The data is visualized on a display on the TOC or displayed in the Viewer software. For documentation and auditing purposes, the data can be made available at any time in digital exchange formats, such as PDF or CSV. The original data are stored permanently in an encrypted, tamper-proof format. The data is available at any time via secure access by authorized persons with the appropriate access authorization, e.g. for verification.	

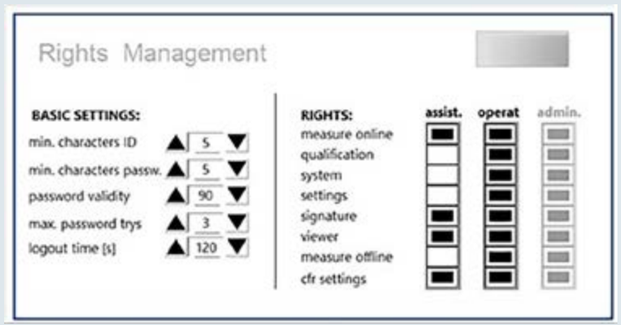

Fig. (2) User administration in accordance with requirements of FDA 21 CFR Part 11

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 CA79 TOC and the Viewer software offer other important product features that increase data security and data integrity.

- Customizable password rules: adjustable password strength (password length, automated password change requirement)
- Blocking of users in case of multiple incorrect entries, which is documented in the audit trail
- Identification of the User by the unique ID + Password combination for any user interaction
- measurement data and parameter settings are stored immediately in an encrypted format and cannot be changed afterwards

Summary

The Endress+Hauser CA79 TOC analyzer and the Viewer software were designed specifically for users in the life sciences industry. With their internal system functions and product features, they fulfill the requirements based on the ALCOA/ALCOA+ principles. Users receive an 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 online TOC analyzer, it is important to consider more than just product features and technical/functional aspects. Certified suppliers of measurement and control technology have already taken 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 and Data Integrity Guide, ALCOA/ALCOA+)
- Certifications in development and production in accordance with international standards, e.g. ISO 9001
- 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 16,000 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

www.adresses.endress.com

WP01279C/07/EN/01.26

Endress+Hauser
People for Process Automation