White Paper

Evolving from ALCOA+ to DYNAMIC+: A Modern Framework for Data Integrity

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Abstract

With the rapid rate of digital change nowadays, ensuring data is secure and intact across complicated systems is the biggest challenge for the pharmaceutical industry. Government agencies such as the FDA, EMA, MHRA, and ICH all emphasize that trustworthy data, being complete, consistent, and accurate, is the foundation of product quality and patient safety. Audit trails are mentioned here as a basis for data integrity to facilitate 'who, what, when, and why' reconstruction of any change to the records. It parallels the evolution of data management development from static paper records to dynamic, real-time electronic streams and parallel regulatory expectation development (e.g., FDA 21 CFR Part 11 audit trail expectations). The ALCOA+ rule has been directing industry practice up to now to ensure that data are Attributable, Legible, Contemporaneous, Original, Accurate, and complete, consistent, lasting, and accessible. Yet, with the onset of the Pharma 4.0 era of IoT, AI, and cloud computing for pharma manufacturing, traditional ALCOA+ regulations have shortcomings in recording the integrity of dynamic high-frequency data. To bridge these gaps, this article presents a novel DYNAMIC+ framework—extending ALCOA+ with Decentralized, Yield-driven, Non-repudiable, Autonomous, Meta-integrated, Interoperable, and Cognitive characteristics incorporated into it, and a particular focus on Cybersecurity and Continuous monitoring. This article is a detailed examination of DYNAMIC+, compared to ALCOA+, and presents actionable recommendations for running future-proofed audit trail strategies compliant with international regulatory guidelines.

Keywords: Data Integrity, Audit Trails, ALCOA+, DYNAMIC+ Framework, Pharma 4.0, Regulatory Compliance

1.Introduction

Data integrity refers to the trustworthiness and reliability of data over its entire lifecycle. In pharmaceutical manufacturing and quality systems, maintaining data integrity is not only a scientific necessity but also a regulatory imperative. Regulators worldwide – including the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), the UK's Medicines and Healthcare products Regulatory Agency (MHRA), and the International Council for Harmonization (ICH) – have established strict expectations to ensure that all GxP data (encompassing manufacturing, laboratory, and clinical data) are complete, consistent, and accurate (Alosert et al., 2022). Central to these expectations is the use of audit trails: secure, computer-generated, time-stamped records that log modifications to data. Audit trails create a forensic history of "who" performed an activity, "what" was performed, "when," and in most cases "why," enabling reconstruction of events in the event of queries. In keeping this chain of custody for electronic records, audit trails facilitate data integrity principles' compliance and empower businesses to detect unauthorized alteration, omission, or error. Data integrity failures have prompted prominent regulatory enforcement actions during the last decade, highlighting the necessity of stringent audit trail controls for good manufacturing practice (GMP), good laboratory practice (GLP), and good clinical practice (GCP) setups (Ronolo, 2023). This introduction sets the context by describing the way in which the industry's approach to data and audit trails has evolved alongside technological advancement, and why systems such as ALCOA+ have been so effective at guiding compliance to date. As we move into a new age of digitalization, often described as Pharma 4.0, new challenges require an evolution of such frameworks, setting the background to the DYNAMIC+ approach outlined in this article.

2. Evolution of Data and Audit Trails in Regulated Environments

Pharmaceutical data management has transitioned from paper to networked computerized systems. Before the 2000s, GMP record keeping existed as predominantly paper-based manual records with partial computer control and higher potential for loss or manipulation of data (Kodumuru et al., 2025). FDA 21 CFR Part 11 in the late 1990s made electronic records and audit trails mandatory, which required secure, date-and-time-stamped records of all changes in any record (FDA, 2018). During the 2010s, data integrity issues necessitated more prescriptive regulatory guidance, such as EMA's Annex 11 (2011) and MHRA's 2018 GxP data integrity guidance, which added emphasis on the requirement for secure, reviewable audit trails for GxP-critical data. International guidelines, such as ICH's Q7, also suggested more frequent review of audit trails and prevention of unauthorized electronic data changes (Austin et al., 2021).

As data management evolved, the nature of data itself in regulated environments shifted from predominantly static to increasingly dynamic (Charoo et al., 2023). Table 1 illustrates key differences between static and dynamic data in this context according to (Kowal et al., 2021):

Table 1: Key differences between static and dynamic data

Feature	Static Data	Dynamic Data
Nature	Fixed and unchangeable once recorded	Continuously evolving with ongoing updates
Storage	Paper records, PDFs, or structured local databases	Cloud-based systems, real-time logs, IoT streams
Modification	Not editable after initial entry (any change creates a new record)	Frequently updated; requires version control and audit trails for changes
Compliance Focus	Traditional ALCOA principles suffice	Requires ALCOA+ plus additional controls for real-time data integrity

Static data are permanent records, like signed batch records or PDFs, that do not change once established. Dynamic data, by contrast, is updated in real time, like laboratory instrument data or live databases. Regulators draw a distinction between the two, with static data needing only single-point authentication and dynamic data needing continuous audit trail entries. With the pharma industry moving towards dynamic data, technologies such as AI, automation, and blockchain are being implemented to handle real-time audit trails and ensure compliance in the emerging Pharma 4.0 environment (Sabale et al., 2024).

3. Role of ALCOA+ Principles

ALCOA+ principles give data integrity for pharmaceutical data management. Attributable, Legible, Contemporaneous, Original, and Accurate constitute the ALCOA, while the addition of ALCOA+ is Complete, Consistent, Enduring, and Available. These regulations give assurance to GxP data by ensuring traceability, readability, error-free, and not altered throughout its life. ALCOA+ is considered the gold standard for data integrity but never directly mentioned in regulations. It is still at the core of compliance, however. Systems are built upon the ALCOA+, influencing training, auditing, and business processes (Durá et al., 2022).

4. Limitations of ALCOA+ in Dynamic Data Contexts

While ALCOA+ provides a strong foundation, it was designed for static data and has limitations in dynamic environments (Miller et al., 2024):

- Static Process Assumption: ALCOA+ assumes linear data flows, making it difficult to apply in non-sequential, real-time data streams like IoT sensors or continuous manufacturing.
- Audit Trail Volume: In dynamic systems, where data changes frequently, audit trails become large and complex. Traditional manual review of these trails becomes impractical.
- Real-Time Monitoring Gaps: ALCOA+ doesn't address automated, real-time monitoring. Dynamic environments require proactive alerts for deviations.
- Multi-Source Data Integrity: ALCOA+ treats each data source independently, which doesn’t address the synchronization and integrity of data across interconnected systems.
- Regulatory Gaps: ALCOA+ doesn’t account for cutting-edge technologies like AI and blockchain, which present new challenges for maintaining data integrity and accountability.

These challenges highlight the need for an enhanced framework like DYNAMIC+, which builds on ALCOA+ to address the dynamic nature of modern data environments while ensuring regulatory compliance.

The Need for the DYNAMIC+ Framework

Pharma 4.0 is transforming data generation, processing, and use in a new technology landscape for life sciences. With connected manufacturing equipment, lab equipment, and information systems, enormous amounts of real-time data are being created in the industry. The industry needs an advanced infrastructure to preserve data integrity with this emerging digital world. DYNAMIC+ expands ALCOA+ to address changing data landscapes as reported in Table 2 . The need for DYNAMIC+ arises from several essential considerations:

- Real-time Data Tracking: Pharma processes, such as continuous manufacturing, require systems that track data changes in real-time, ensuring every update is captured and time-stamped accurately.
- Automation and AI Integration: Strong usage levels of AI and automation in decision-making mean that compliance will be founded on AI-based verification, outlier detection, and predictive testing that go beyond the parameters of standard ALCOA+.
- Version Control and Data Evolution: Dynamic systems may overwrite or update data, so DYNAMIC+ introduces version control to preserve original data and ensure it remains accessible.
- Decentralization and Multi-Site Data: With global operations and cloud-based systems, data integrity must extend across decentralized networks, with technologies like blockchain ensuring tamper-evident records.
- Cybersecurity and Real-Time Monitoring: DYNAMIC+ places emphasis on cybersecurity and real-time monitoring, precluding risks such as ransomware and data breaches, which were not directly encompassed in ALCOA+.
- These points highlight the evolution from ALCOA+ to DYNAMIC+, a framework designed to keep up with the increasing complexity of data in modern pharma.

Table 2: Comparative Framework: ALCOA+ vs. DYNAMIC+ in Pharma 4.0 Data Integrity

Capability/Focus	ALCOA+ (Traditional)	DYNAMIC+ (Pharma 4.0 Era)	Capability/Focus
Handling of Changes	Recorded and reviewed, but the volume is manageable for static records	Emphasizes handling high-frequency, continuous changes with version control and AI analysis	Handling of Changes
Data Sources & Scope	Focus on individual system records (siloed systems)	Focus on integrated, multi-source data streams across platforms (end-to-end integrity)	Data Sources & Scope
Use of Technology	Largely manual processes with basic electronic systems	Leverages advanced tech (AI for monitoring, blockchain for security, cloud connectivity)	Use of Technology
Compliance Approach	Largely reactive (after-the-fact audits, periodic reviews)	Proactive and predictive (real-time monitoring, predictive alerts for potential issues)	Compliance Approach
Security Coverage	Implicit (access controls, audit trails imply security)	Explicit (built-in cybersecurity measures and continuous surveillance of data integrity)	Security Coverage

DYNAMIC+ plays the role of bridging the gap between present data integrity practices and evolving challenges due to digital transformation. It provides a future-oriented framework following present legislation but being adaptable to future legislation, especially with AI, cloud, and blockchain technology setting the fundament of Pharma 4.0 data management.

Table 3: The DYNAMIC+ Framework: Key Components of Pharma 4.0 Data Integrity

DYNAMIC+ Component	Focus/Definition
D – Decentralized	Ensures data integrity in distributed systems by leveraging cloud, blockchain, and edge computing. Pharma 4.0 requires multi-site data accessibility and transparency.
Y – Yield-Driven	Aligns data integrity with business and compliance objectives, ensuring that all data contributes to process optimization. Encourages performance-driven (not just compliance-driven) data use.
N – Non-Repudiable	Uses cryptographic security (blockchain, digital signatures) to prevent unauthorized alterations. Makes data tamper-evident, preventing fraud and ensuring accountability.
A – Autonomous	Utilizes AI-driven compliance mechanisms to automate data validation, anomaly detection, and error correction. Minimizes human intervention and enables real-time adherence.
M – Meta-Integrated	Captures rich metadata (context, audit logs, system parameters) alongside data to enhance traceability. Improves visibility across AI-driven systems and digital workflows.

6. DYNAMIC+ Framework Overview

DYNAMIC+ model takes advantage of the data integrity requirements of the present information age and expands on the existing ALCOA+ fundamentals. It contains several significant components to enable effective management of the data. Decentralized (D) concentrates on utilizing blockchain and distributed ledgers for offering evidence-based, worldwide shared data with integrity across sites and systems. Yield-Driven (Y) bridges data integrity and process enhancement since quality and continuous data feed into real-time product quality and yield enhancement. Non-Repudiable (N) enables data authenticity using digital signatures, cryptography methods, and irreversible logs to eliminate deception. Autonomous (A) employs AI for monitoring and confirming data integrity, computerized audit trail verification, and label anomalies to minimize human weakness effects. Meta-Integrated (M) integrates metadata and raw data to ensure context and traceability to enable record completeness and explainability. Interoperable (I) addresses creating systems that ensure data sharing between platforms with a focus on data consistency and accuracy between systems. Cognitive (C) utilizes AI/ML technology to enable predictive compliance by foreseeing issues in advance based on historical trends and data analytics. And finally, Cybersecure & Continuous (+) highlights the importance of enterprise security and vigilant monitoring to protect information from intrusion and uphold real-time integrity.

Conclusion

DYNAMIC+ complements ALCOA+ with new technologies like AI, blockchain, and next-generation cybersecurity and is adapted to the digitalization of the pharmaceutical industry. It enables better data integrity, process efficiency, and compliance in Pharma 4.0. As the industry embraces these technologies, DYNAMIC+ ensures data to be auditable and trustworthy to ensure patient safety and compliance.

Reference:

Alosert, H., Savery, J., Rheaume, J., Cheeks, M., Turner, R., Spencer, C., ... & Goldrick, S. (2022). Data integrity within the biopharmaceutical sector in the era of Industry 4.0. Biotechnology Journal, 17(6), 2100609.

Austin, A. A., Carpenter, T. D., Christ, M. H., & Nielson, C. S. (2021). The data analytics journey: Interactions among auditors, managers, regulation, and technology. Contemporary Accounting Research, 38(3), 1888-1924.

Charoo, N. A., Khan, M. A., & Rahman, Z. (2023). Data integrity issues in pharmaceutical industry: Common observations, challenges and mitigations strategies. International journal of pharmaceutics, 631, 122503.

Durá, M., Sánchez-García, A., Sáez, C., Leal, F., Chis, A. E., González-Vélez, H., & García-Gómez, J. M. (2022). Towards a computational approach for the assessment of compliance of ALCOA+ Principles in pharma industry. In Challenges of Trustable AI and Added-Value on Health (pp. 755-759). IOS Press.

FDA. (2018, August 10). Warning letter Kyowa Hakko Bio Co., Ltd. U.S. FOOD & DRUG ADMINISTRATION. https://www.fda.gov/ inspections-compliance-enforcement-and-criminal-investigations/warning-letters/kyowa-hakko-bio-co-ltd-543924-08102018.

Kodumuru, R., Sarkar, S., Parepally, V., & Chandarana, J. (2025). Artificial Intelligence and Internet of Things Integration in Pharmaceutical Manufacturing: A Smart Synergy. Pharmaceutics, 17(3), 290.

Kowal, M., Siam, M., Islam, M. A., Bruce, N. D., Wildes, R. P., & Derpanis, K. G. (2022). A deeper dive into what deep spatiotemporal networks encode: Quantifying static vs. dynamic information. In Proceedings of the IEEE/CVF Conference on computer vision and pattern recognition (pp. 13999-14009).

Miller, R., Whelan, H., Chrubasik, M., Whittaker, D., Duncan, P., & Gregório, J. (2024). An Overview of Current and New Data Quality Dimensions under a Common Framework.

Ronolo, S. C. (2023). Assuring Data Integrity towards Regulatory Compliance: A Study on Process Improvement in Data Integrity Compliance of Computerized Systems.

Sabale, M. M., Pande, V. A., Tagalpallewar, A. A., Swami, A. G., Pawar, A. T., & Baheti, A. M. (2024). Maintaining data safety and accuracy through data integrity (DI): A comprehensive review. Research Journal of Pharmacy and Technology, 17(5), 2431-2440.