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Short communication

Mapping a decade of quality failures: longitudinal data trends in European Medicines Agency inspections against the evolution of data integrity frameworks

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Introduction

Pharmaceutical Quality Management Systems (QMS) serve as the foundational architecture ensuring the safety, quality, and efficacy of medicinal products across global supply chains. Over the past decade (January 2015 – December 2025), data integrity has transitioned from a fundamental compliance requirement to the central pillar of regulatory oversight (Pharmaceutical Inspection Co-operation Scheme, 2021). Driven by the increasing complexity of computerized systems, the European Medicines Agency (EMA) and international regulatory bodies enacted a paradigm shift from classic ALCOA principles (Attributable, Legible, Contemporaneous, Original, Accurate) to the expanded ALCOA+ framework (Complete, Consistent, Enduring, Available) (EMA, 2023). Despite comprehensive guidance, systemic compliance vulnerabilities persist globally. Critical data integrity breaches compromise product quality, disrupt supply chains, jeopardize patient safety, and trigger severe enforcement actions. (Sabale et al., 2024). This study evaluates a decade of EMA non-compliance reports to identify structural patterns within failing QMS environments. By mapping historical non-conformities against ALCOA+ milestones, this paper elucidates the critical inflection points where industrial practices diverge from regulatory expectations. (Kodumuru et al., 2025).

Materials and methods

This longitudinal, retrospective study evaluated regulatory enforcement data from 2015–2025. The dataset was aggregated from official inspections conducted by national competent authorities across 25 jurisdictions under the EMA framework.

A total of 146 non-compliance reports were extracted and stratified into Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP) categories (publicly available at http://eudragmp.ema.europa.eu/). From the GMP reports, 1,365 deficiencies were coded according to the standard EMA severity matrix: critical, major, and other.

Quantitative analysis determined regulatory impact rates, focusing on Certificate of Suitability (CEP) suspensions and GMP certificate withdrawals for manufacturing facilities.

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Results and discussion

Distribution of non-compliance reports

The study analyzed 146 non-compliance reports. GMP inspections generated the majority of enforcement actions, accounting for 63.7% (n=93) of the total reports. GDP inspections comprised the remaining 36.3% (n=53). This distribution highlights that while manufacturing sites remain high-risk environments; distribution networks face significant compliance pressures under modern quality management system standards.

Deficiency severity analysis

A total of 1,365 deficiencies were identified across the 93 reports. Critical deficiencies accounted for 9.08% (n=124), major for 38.68% (n=528), and other for 52.24% (n=713). An average of 7.67 ± 5.72 other deficiencies, 5.68 ± 4.08 major deficiencies and an average of 1.33 ± 1.21 critical nonconformities were observed per manufacturer.

Regulatory enforcement and business impact

The consequences of quality management system non-compliance were severe. For API manufacturers, non-compliance directly triggered market restrictions. (publicly available at https://www.edqm.eu/en/databases).

CEP suspensions occurred in 68.9% of API manufacturer cases with the largest concentrations of manufacturers located in India (37) and China (17), effectively halting their legal ability to supply substances to the European market.

Furthermore, more than 33% of all inspected non-compliant facilities suffered a complete withdrawal of their GMP certificates.

Challenges in data integrity and ALCOA+ evolution

The high volume of major and critical deficiencies correlates with the formalization of ALCOA+ standards over the 2015–2025 period. Early in the decade, deficiencies frequently cited basic accuracy and legibility issues. By 2025, regulatory scrutiny shifted heavily toward the "+" components: *consistency* across electronic systems and the *enduring* nature of cloud-hosted audit trails. The data shows that legacy quality management systems relying on hybrid (paper-electronic) workflows struggle to maintain compliance, leading to the high certificate withdrawal rates observed in this study.

To mitigate these systemic vulnerabilities, pharmaceutical organizations must move away from retrospective corrections and incorporate data security directly into system design: decommissioning of hybrid systems, secured audit trail governance and proactive auditing (EMA, 2015).

Conclusion

This longitudinal analysis proves that QMS non-compliance carries severe commercial and operational penalties under EMA regulatory oversight. With nearly half of all deficiencies grading as major or critical, the pharmaceutical supply chain displays systemic vulnerabilities to evolving data integrity standards. As ALCOA+ frameworks integrate tighter electronic controls, manufacturers must move away from hybrid, manual data tracking. Investing in fully automated, data-secure, and audit-ready electronic quality management systems is no longer optional but an imperative for regulatory viability and global market.

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