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Διπλωματική Εργασία

Digital Transformation in Pharma: A Strategic Framework for Cloud eQMS Validation and ROI Analysis

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ΠΑΝΕΠΙΣΤΗΜΙΟ ΠΕΙΡΑΙΩΣ

ΣΧΟΛΗ ΟΙΚΟΝΟΜΙΚΩΝ ΕΠΙΧΕΙΡΗΜΑΤΙΚΩΝ & ΔΙΕΘΝΩΝ ΣΠΟΥΔΩΝ ΤΜΗΜΑ ΟΡΓΑΝΩΣΗΣ ΚΑΙ ΔΙΟΙΚΗΣΗΣ ΕΠΙΧΕΙΡΗΣΕΩΝ ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ

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Abstract

Title: Digital Transformation in Pharma: A Strategic Framework for Cloud eQMS Validation and ROI Analysis
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The pharmaceutical industry faces a critical inflection point: the imperative to shift from reactive, paper-based compliance to proactive, digital quality management (Quality 4.0). However, this transition is often stalled by the perceived complexity of validating Cloud Software-as-a-Service (SaaS) systems and the difficulty in quantifying the Return on Investment (ROI) of quality initiatives.

This thesis addresses these barriers by developing a comprehensive strategic framework for the adoption of Cloud Electronic Quality Management Systems (eQMS). First, it establishes a GAMP 5 risk-based validation strategy tailored for SaaS, advocating for a shift from traditional Computer System Validation (CSV) to modern Computer Software Assurance (CSA). This approach leverages the "Shared Responsibility Model" to minimize validation overhead while maintaining strict GxP compliance.

Second, the research moves beyond theoretical cost estimation by developing a proprietary **Stochastic Decision Support System** (Python/Streamlit). This Monte Carlo simulation engine models the variability of quality events to forecast the Total Cost of Ownership (TCO).

Empirical analysis of 5,000 simulated events demonstrates that the digital transition yields a statistically significant administrative efficiency gain of **€391.22 per quality event**, independent of complexity. By integrating this financial proof with a validated functional blueprint (URS), this thesis provides Quality Directors and IT leaders with a data-driven roadmap to justify, implement, and validate digital transformation in a regulated environment.

Keywords: *Pharma 4.0, Cloud eQMS, GAMP 5, Computer Software Assurance (CSA), ROI Analysis, Monte Carlo Simulation.*

Chapter 1: Introduction

1.1 Background: The Imperative for Digital Transformation (DX) [1] in Pharma

The pharmaceutical industry operates within one of the world's most **highly regulated environments**, where product quality, patient safety, and data integrity are non-negotiable legal and ethical mandates. At the core of this compliance structure is the **Quality Management System (QMS)**, a foundational set of processes and documentation governed by global regulatory standards such as Good Manufacturing Practices (GMP), Good Laboratory Practices (GLP), and Good Clinical Practices (GCP)—collectively known as **GxP**—enforced by bodies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) [2]. The traditional QMS, often reliant on paper-based records, manual approvals, and decentralized data archives, served as the historical bedrock of compliance.

However, the pharmaceutical landscape has shifted dramatically, creating unprecedented **pressure points** that legacy QMS models are ill-equipped to handle:

> **Global Supply Chain Complexity:** Modern drug manufacturing involves intricate, multi-national networks of suppliers, contract manufacturers (CMOs), and distributors. [3] Managing quality documents, audits, and deviations across this expansive, fast-moving chain manually introduces significant compliance risk and operational friction.

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1 Mario Miozza et al., "Digital Transformation of the Pharmaceutical Industry: A Future Research Agenda for Management Studies," *Technological Forecasting and Social Change* 207 (October 2024): 123580, https://doi.org/10.1016/j.techfore.2024.123580.

2 Reham M. Haleem et al., "Quality in the Pharmaceutical Industry – A Literature Review," *Saudi Pharmaceutical Journal* 23, no. 5 (2015): 463–69, https://doi.org/10.1016/j.jsps.2013.11.004.

3 Klaus Reinholdt Nyhuus Hansen and Martin Grunow, "Planning Operations before Market Launch for Balancing Time-to-Market and Risks in Pharmaceutical Supply Chains," *International Journal of Production Economics* 161 (March 2015): 129–39, https://doi.org/10.1016/j.ijpe.2014.10.010.

Increasing Regulatory Scrutiny on Data Integrity (DI): [4] Regulators have intensified their focus on the reliability and trustworthiness of quality data, mandating strict adherence to the **ALCOA+** [5]principles (Attributable, Legible, Contemporaneous, Original, Accurate, plus Complete, Consistent, Enduring, and Available). Paper-based and hybrid digital systems inherently struggle to enforce these controls, resulting in a surge of regulatory findings (e.g., FDA Warning Letters citing poor audit trails or data manipulation risk).

Inefficiency and Risk of Legacy Systems: Reliance on paper or fragmented, on-premise solutions results in lengthy cycle times for core processes like batch release, deviation investigation, and change control. This inefficiency contributes directly to the **Cost of Poor Quality (COPQ)**, draining resources through higher administrative overhead and delaying the **Time-to-Market** [6]**(TTM)** for critical therapies. Furthermore, a paper-based system lacks the real-time visibility and analytics needed for **proactive quality management**, turning compliance into a reactive function.

These converging factors establish the **imperative for Digital Transformation (DX)**. The industry can no longer afford to view digitalization merely as an IT project; it is a **strategic necessity** to secure future compliance, drive operational excellence, and sustain scalable growth. This transition positions the **Electronic Quality Management System (eQMS)**, especially modern Cloud-based (SaaS) solutions, as the crucial digital backbone required to enforce GxP requirements in the era of Industry 4.0.[7]

1.2 Problem Statement

Despite the recognized imperative for digital transformation, the pharmaceutical industry continues to face significant strategic challenges due to the reliance on traditional, paper-based, or hybrid Quality Management Systems (QMS).

The core business challenge is that **traditional, legacy QMS models have become a fundamental barrier to achieving scalable compliance, operational efficiency, and sustainable, data-driven growth.**

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[4] Naseem A. Charoo et al., “Data Integrity Issues in Pharmaceutical Industry: Common Observations, Challenges and Mitigations Strategies,” *International Journal of Pharmaceutics* 631 (January 2023): 122503, https://doi.org/10.1016/j.ijpharm.2022.122503.

[5] Preeti Kulkarni and Charmy Kothari, “Documentation and Data Integrity in Pharmaceutical Industry,” in *Modern Aspects of Pharmaceutical Quality Assurance: Developing & Proposing Application Models, SOPs, Practical Audit Systems for Pharma Industry*, ed. Minal Ghante et al. (Springer Nature, 2024), https://doi.org/10.1007/978-981-99-9271-3_11.

[6] Taiwen Feng et al., “Customer Orientation for Decreasing Time-to-Market of New Products: IT Implementation as a Complementary Asset,” *Industrial Marketing Management* 41, no. 6 (2012): 929–39, https://doi.org/10.1016/j.indmarman.2011.11.027.

[7] Attia Hussien Gomaa, *Quality Management Excellence in the Era of Industry 4.0 (Quality 4.0): A Comprehensive Review, Gap Analysis, and Strategic Framework*, 2 (n.d.).

These systems are fundamentally reactive, struggling to provide the **closed-loop integrity** necessary to meet modern regulatory standards, particularly regarding Data Integrity[8] (ALCOA+) and real-time management review (ICH Q10). This systemic deficiency translates directly into a quantifiable financial burden, represented by the **Cost of Poor Quality (COPQ)** [9] and increased regulatory risk.

The **Cost of Inaction** [10]—the continued reliance on outdated QMS methodologies—manifests through several critical metrics:

Elevated Deviation and CAPA Cycle Times: Manual processes for initiating, investigating, reviewing, and closing Quality Events introduce lengthy delays, often leading to average **CAPA cycle times exceeding 90 to 120 days**. This slows down continuous improvement and prevents timely correction of systemic issues.

Increased Operating Costs and Inefficiency: Administrative overhead associated with physically managing, reviewing, storing, and retrieving paper records generates high labor costs. Furthermore, the preparation time and expense for regulatory audits (the "war room" effect) are unnecessarily prolonged and costly.

Risk of Regulatory Action and Delayed Time-to-Market[11] **(TTM):** The inability of legacy systems to enforce real-time audit trails and robust data security increases the probability of critical findings, such as **FDA Form 483 observations or Warning Letters** related to data integrity failures. The financial impact of a regulatory consent decree, a product recall, or delayed batch release due to protracted investigation cycles can reach tens of millions of dollars, directly eroding shareholder value.

Lack of Strategic Visibility: Without centralized, structured data provided by an electronic system, Quality Assurance and executive management cannot perform effective **trend analysis** to identify common causes of failure. This keeps the organization in a reactive, rather than proactive, quality state, directly contradicting TQM principles.

Therefore, a strategic, GxP-compliant transition to an Electronic Quality Management System (eQMS) is not merely an upgrade; it is a **mission-critical investment** required to mitigate systemic compliance risk and unlock the operational efficiency demanded by modern pharmaceutical economics.

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8 Pravin Ullagaddi, "Safeguarding Data Integrity in Pharmaceutical Manufacturing," *Journal of Advances in Medical and Pharmaceutical Sciences* 26 (August 2024): 64–75, https://doi.org/10.9734/jamps/2024/v26i8708.

9 Andrea Schiffauerova and Vince Thomson, "A Review of Research on Cost of Quality Models and Best Practices," *International Journal of Quality & Reliability Management* 23, no. 6 (2006): 647–69, https://doi.org/10.1108/02656710610672470.

10 Evangelos L. Psomas et al., "The Impact of ISO 9001 Effectiveness on the Performance of Service Companies," *Managing Service Quality* 23, no. 2 (2013): 149–64, https://doi.org/10.1108/09604521311303426.

11 Feng et al., "Customer Orientation for Decreasing Time-to-Market of New Products: IT Implementation as a Complementary Asset."

1.3 Research Objectives and Questions (Q)

Based on the urgent need to address systemic compliance risks, mitigate the Cost of Poor Quality (COPQ), and capture operational efficiencies, the primary goal of this research is to move beyond the technical necessity of eQMS adoption and focus on developing a **strategic, financially justifiable, and compliance-driven framework** for successful implementation.

1.3.1 Primary Objective

To develop and validate a **Strategic Roadmap and Total Cost of Ownership (TCO) model** [12] for the successful adoption, validation, and organizational change management (OCM) of a Cloud-based Electronic Quality Management System (eQMS) within the GxP-regulated pharmaceutical industry.

1.3.2 Secondary Objectives

1. To define the necessary **User Requirement Specification (URS)** functional blueprint[13] for core eQMS modules that enforces Data Integrity (ALCOA+) and closed-loop quality principles.
2. To analyze the **GAMP 5 risk-based validation strategy** [14]for a Cloud (SaaS) deployment, specifically defining the Shared Responsibility Model between the pharmaceutical company and the vendor.
3. To design and code a configurable, algorithmic Decision Support Tool (Python) that allows quality managers to simulate the Total Cost of Ownership (TCO) and ROI. This tool utilizes Monte Carlo simulation methods to model the stochastic nature of quality events (e.g., variation in complexity and linkages), enabling a precise, data-driven financial justification tailored to specific organizational volumes and labor rates.

1.3.3 Key Research Questions (Q)

This study will seek to answer the following research questions:

1. **Operational Performance (Q1):** How does the adoption of an eQMS, based on the defined URS blueprint (Chapter 4), correlate with measurable improvements in key quality system performance indicators, such as **reduced CAPA cycle time, decreased deviation recurrence rate, and streamlined batch disposition cycles**?

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[12] Dara G. Schniederjans and Douglas N. Hales, “Cloud Computing and Its Impact on Economic and Environmental Performance: A Transaction Cost Economics Perspective,” *Decision Support Systems* 86 (June 2016): 73–82, https://doi.org/10.1016/j.dss.2016.03.009.

[13] Issa Atoum et al., “Challenges of Software Requirements Quality Assurance and Validation: A Systematic Literature Review,” *IEEE Access* 9 (2021): 137613–34, https://doi.org/10.1109/ACCESS.2021.3117989.

[14] Francisca Pedro et al., “Impact of GAMP 5, Data Integrity and QbD on Quality Assurance in the Pharmaceutical Industry: How Obvious Is It?,” *Drug Discovery Today* 28, no. 11 (2023): 103759, https://doi.org/10.1016/j.drudis.2023.103759.

2. **Compliance Strategy (Q2):** What is the necessary and auditable **GAMP 5-compliant validation strategy** for a Cloud [15] (SaaS) eQMS, and how should the pharmaceutical organization leverage the supplier's documentation within the defined Shared Responsibility Model?
3. **Strategic Management (Q3):** What are the critical elements of the **Organizational Change Management (OCM)** strategy (e.g., training, communication, stakeholder management) required to successfully drive user adoption and overcome the cultural resistance inherent in transitioning from paper-based to digital assurance processes?
4. **Financial Justification (Q4):** How does the comprehensive **Total Cost of Ownership (TCO)** of a 5-year Cloud eQMS subscription compare against the quantified **Cost of Poor Quality (COPQ)** and operational costs of legacy systems, thereby proving the financial feasibility and ROI of the digitalization investment?

1.4 Scope and Limitations

To ensure a focused and methodologically sound analysis, this research is subject to a defined scope and specific limitations.

1.4.1 Scope of the Research

The research is specifically scoped to maintain relevance to both the strategic and compliance goals of the pharmaceutical industry:

1. **Industry and Focus:** This study is confined to organizations operating within the highly regulated **GxP-environment** (Good Practices: GMP, GCP, GLP). The primary focus is on quality processes directly related to **manufacturing, laboratory operations, and post-market surveillance** (e.g., Document Management, Change Control, CAPA, OOS/OOT, and Complaint Management).
2. **Technology:** The analysis centers exclusively on the strategic adoption and validation of **commercial, off-the-shelf[16] (COTS) Electronic Quality Management Systems (eQMS)**, specifically those utilizing a **Cloud Software-as-a-Service (SaaS)** [17] deployment model. This choice is deliberate, as SaaS introduces unique GxP compliance challenges (e.g., Shared Responsibility Model) that must be addressed strategically.

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[15] Prashant Gupta et al., "The Usage and Adoption of Cloud Computing by Small and Medium Businesses," *International Journal of Information Management* 33, no. 5 (2013): 861–74, https://doi.org/10.1016/j.ijinfomgt.2013.07.001.

[16] Asheesh Singh et al., "Computer System Validation in the Perspective of the Pharmaceutical Industry.," *Journal of Drug Delivery & Therapeutics* 8 (20181102): 359–65, https://doi.org/10.22270/jddt.v8i6-s.2102.

[17] Shengli Li et al., "A Study of Enterprise Software Licensing Models," *Journal of Management Information Systems* 34, no. 1 (2017): 177–205, https://doi.org/10.1080/07421222.2017.1297636.

3. **Organizational Viewpoint:** The developed strategic roadmap and TCO model (Chapter 6) are designed primarily for **mid-to-large-sized pharmaceutical and biotechnology companies** that possess established GxP quality systems but are still reliant on hybrid or legacy paper-based processes.
4. **Compliance Framework:** The validation strategies and functional requirements (URS) presented are framed by major global regulatory requirements, including **FDA 21 CFR Part 11**, **EU Annex 11**, and the **GAMP 5** risk-based approach[18] for computer system validation.

1.4.2 Limitations of the Research

The findings and recommendations of this thesis should be considered within the context of the following limitations:

1. **Data Generalizability:** Due to the complexity and proprietary nature of internal quality data, the quantitative ROI analysis (Chapter 6) relies on **industry benchmarks, secondary data**, and qualitative estimates derived from semi-structured interviews (Chapter 3). The precise financial figures and cycle time reductions may vary based on a specific company's size, organizational maturity, and implementation strategy.
2. **Focus on Core QMS:** The research deliberately restricts its detailed functional specifications to the **core quality modules**. It does not extend into the detailed integration requirements for other critical enterprise systems, such as Enterprise Resource Planning (ERP), Laboratory Information Management Systems (LIMS), or Manufacturing Execution Systems (MES), although the necessary interfaces (APIs) are recognized as non-functional requirements.
3. **Regulatory Jurisdiction:** While the study references major global regulations (FDA, EMA), it does not account for every region-specific GxP variance (e.g., specific requirements in Asia-Pacific or LATAM jurisdictions). The primary focus remains on alignment with internationally harmonized standards (e.g., ICH Q10).
4. **Rapid Technological Change:** The pharmaceutical digital landscape is evolving rapidly. While this thesis addresses current trends like Quality 4.0 and Computer Software Assurance [19] (CSA), the specific feature sets, vendor capabilities, and market segmentation (Chapter 2) are subject to continuous change.

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[18] ISPE, "ISPE GAMP® 5: A Risk-Based Approach to Compliant GxP Computerized Systems (Second Edition)," GAMP, accessed November 15, 2025, https://guidance-docs.ispe.org/doi/book/10.1002/9781946964571.

[19] Jacqueline K. Davidson, "Advancing the Transition to Computer Software Assurance: Responding to the FDA Draft Guidance for Production and Quality System Software," *FDLI Update* 2023, no. 2 (2023): 22–31.

Chapter 2: Literature Review and Theoretical Framework

2.1 Regulatory and Quality Landscape (GxP and Data Integrity)

The digitization of quality processes is fundamentally dictated by a complex, evolving body of international regulatory requirements. The **Quality Management System (QMS)** framework is not voluntary; it is an obligation enforced globally through various Good Practices guidelines e.g. Good Manufacturing Practices (**GMP**)[20] which is prominent in the pharmaceutical industry[21]. The most relevant regulations compelling the adoption of secure, electronic systems are centered on the acceptance of digital records and the mandatory assurance of data integrity.

2.1.1 Core Regulations for Electronic Systems

The acceptance of electronic records and signatures in place of paper is governed by two primary global regulations:

> **FDA 21 CFR Part 11 (Electronic Records; Electronic Signatures):** This U.S. regulation, established in 1997, sets forth the criteria under which the FDA considers electronic records and electronic signatures to be trustworthy, reliable, and equivalent to paper records. It mandates controls such as secure **audit trails** (to record actions, users, and timestamps), **system validation**, and **electronic signature integrity** (requiring two distinct identification components). Compliance with Part 11 is the essential prerequisite for transitioning to an eQMS.[22]
>
> **EU Annex 11 (Computerised Systems):** The European equivalent, this guideline ensures that computerized systems used within GxP-regulated activities are compliant and do not compromise patient safety or product quality. Key requirements include **data security**, **audit trails**, procedures for **data migration**, and provisions for **business continuity and disaster recovery**.[23]

Beyond the rules for electronic systems, the overall quality structure is defined by the International Council for Harmonisation (ICH):

> **ICH Q10 (Pharmaceutical Quality System):** ICH Q10 describes a model for an effective PQS that is to be implemented throughout the product lifecycle. A core expectation is the continuous improvement

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[20] Rashed Ahmed, "The Role of cGMP in the Manufacturing Unit of a Pharmaceutical Industry," *RADINKA JOURNAL OF HEALTH SCIENCE* 2, no. 2 (2024): 242–53, https://doi.org/10.56778/rjhs.v2i2.361.

[21] Olivia McDermott et al., "Pharma Industry 4.0 Deployment and Readiness: A Case Study within a Manufacturer," *The TQM Journal* 36, no. 9 (2024): 456–76, https://doi.org/10.1108/TQM-04-2024-0160.

[22] FDA, "Part 11, Electronic Records; Electronic Signatures - Scope and Application," FDA, October 1, 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/part-11-electronic-records-electronic-signatures-scope-and-application.

[23] "EU GMP Annex 11: Computerised Systems - ECA Academy," accessed November 16, 2025, https://www.gmp-compliance.org/guidelines/gmp-guideline/eu-gmp-annex-11-computerised-systems.

of the quality system and the promotion of innovation. This principle is precisely what an eQMS enables, transforming the quality system from a static repository into a **dynamic, data-driven management tool**[24]Furthermore, ICH Q10 identifies two primary enablers for the Pharmaceutical Quality System: Quality Risk Management (QRM) and **Knowledge Management (KM)**. While QRM is widely adopted, KM often remains the "missing link" in legacy systems. The eQMS must therefore serve as the technological vehicle to capture, analyze, and disseminate product and process knowledge throughout the life cycle.

2.1.2 The Detailed Review of Data Integrity (DI)[25]

Regulatory bodies have intensified their focus on **Data Integrity (DI)**[26] [27], moving beyond procedural compliance to demand assurance that data is accurate, complete, and reliable throughout its lifecycle. DI failures are now the leading cause of regulatory findings globally, establishing DI as the single most critical driver for eQMS adoption[28].

The industry and regulators rely on the **ALCOA+** principles as the benchmark for data reliability:

Principle	Description	eQMS Enforcement Mechanism
Attributable	Data must show who performed an action and when.	Mandatory **secure login** and **21 CFR Part 11-compliant electronic signatures**.

[24] EMA, *ICH Guideline Q10 on Pharmaceutical Quality System - Step 5*, n.d., https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-guideline-q10-pharmaceutical-quality-system-step-5_en.pdf.

[25] Naseem A. Charoo et al., "Data Integrity Issues in Pharmaceutical Industry: Common Observations, Challenges and Mitigations Strategies," *International Journal of Pharmaceutics* 631 (January 2023): 122503, https://doi.org/10.1016/j.ijpharm.2022.122503.

[26] "Guidance on GxP Data Integrity," GOV.UK, September 27, 2021, https://www.gov.uk/government/publications/guidance-on-gxp-data-integrity.

[27] Yoseok Park and Kyenghee Kwon, "Trends in FDA Data Integrity Enforcement Before and After the COVID-19 Pandemic: An Analysis of 1766 Warning Letters (2016–2023)," *Therapeutic Innovation & Regulatory Science*, ahead of print, October 10, 2025, https://doi.org/10.1007/s43441-025-00870-3.

[28] Divya Gokulakrishnan and Sowmyalakshmi Venkataraman, "Ensuring Data Integrity: Best Practices and Strategies in Pharmaceutical Industry," *Intelligent Pharmacy* 3, no. 4 (2025): 296–303, https://doi.org/10.1016/j.ipha.2024.09.010.

Principle	Description	eQMS Enforcement Mechanism
Legible	Data must be readable and understandable.	Standardized, system-generated, digital records.
Contemporaneous	Data must be recorded at the time the work is performed.	**System-enforced timestamps** locked to actions in the audit trail.
Original	The original record must be preserved.	Secure, non-editable electronic archive protected by **version control**.
Accurate	Data must be correct and truthful.	Automated calculations, system-enforced **business rules**, and validation protocols.
+ (Complete, Consistent, Enduring, Available)	Data must be complete (no missing entries), consistent (in time and sequence), enduring (long-term accessibility), and readily available.	**Centralized database** design, **automated workflows**, and **disaster recovery** protocols.

An eQMS is the digital tool uniquely positioned to **enforce** these ALCOA+ principles. Unlike paper, which relies on procedural controls, a validated eQMS imposes **technical controls** (e.g., locking a record once signed, sequential workflow enforcement) that make compliance the only option, thereby fundamentally mitigating the risk of DI failures.

2.2 Digitalization[29], Industry 4.0[30], and Quality 4.0[31] in Pharma:

The transition to an eQMS is an integral component of the pharmaceutical industry's participation in the global trend of **Digital Transformation (DX)**[32]. DX[33] is defined not merely as the adoption of new technology, but as the comprehensive, strategic change in business models, processes, and culture to leverage digital data for improved performance and value creation. Within the operational context of the industry, this strategic shift is rooted in the concepts of Industry 4.0 and its quality-focused derivative, Quality 4.0.

2.2.1 Industry 4.0[34] and the Pharmaceutical Value Chain

Industry 4.0[35] represents the fourth industrial revolution, characterized by the integration of cyber-physical systems, the Internet of Things (IoT), cloud computing, and advanced analytics into manufacturing and supply chain management. For the pharmaceutical value chain, the strategic impact of Industry 4.0 includes:

Interconnectedness: Linking machines, sensors, and materials across global sites.

Real-time Transparency: Providing immediate data access for decision-making.

Technical Assistance: Aiding human operators through digital tools and augmented reality.

Decentralized Decisions: Enabling smart systems to make autonomous, real-time choices.

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29 Ms, Neha, *Current Trends in Pharmaceutical QA: Digitalization and Automation*, International Research Journal of Education and Technology, November 29, 2024, https://doi.org/10.70127/irjedt.vol.8.issue05.41.

30 "Full Article: Adopting Quality Management Practices in the Industry 4.0 Era: An Investigation into the Challenges," accessed November 16, 2025, https://www.tandfonline.com/doi/full/10.1080/14783363.2024.2354840?src=recsys#d1e193.

31 Rajan Ranjith Kumar et al., "Quality 4.0 – a Review of and Framework for Quality Management in the Digital Era," *International Journal of Quality & Reliability Management* 39, no. 6 (2021): 1385–411, https://doi.org/10.1108/IJQRM-05-2021-0150.

32 Pravin Ullagaddi, "Digital Transformation Strategies to Strengthen Quality and Data Integrity in Pharma," *International Journal of Business and Management* 19, no. 5 (2024): 16, https://doi.org/10.5539/ijbm.v19n5p16.

33 Wan Seon Shin et al., "Open Quality in the Digitalization Era: Concept, Principles, and Implementation Framework," *Total Quality Management & Business Excellence* 36, nos. 7–8 (2025): 675–94, https://doi.org/10.1080/14783363.2025.2472951.

34 Vincent Junior Phiri et al., "Towards Enterprise-Wide Pharma 4.0 Adoption," *Scientific African* 28 (June 2025): e02771, https://doi.org/10.1016/j.sciaf.2025.e02771.

35 Peter Guilfoyle Analytics Northwest, "Pharma 4.0: Industry 4.0 Applied to Pharmaceutical Manufacturing," *Pharmaceutical Processing World*, October 23, 2018, https://www.pharmaceuticalprocessingworld.com/pharma-4-0-industry-4-0-applied-to-pharmaceutical-manufacturing/.

The eQMS serves as the **central nervous system** for these capabilities, providing the trusted, validated platform where the data generated by advanced manufacturing systems (e.g., MES, LIMS) is formally controlled, reviewed, and acted upon under regulatory oversight.

2.2.2 Positioning eQMS as the Digital Backbone for Quality 4.0

Quality 4.0 is the application of Industry 4.0 principles to Quality Management Systems. It represents the move from reactive quality control to a proactive, predictive, and integrated quality culture enabled by digital tools.[36] The eQMS is the foundational digital platform required to shift the quality paradigm by:

1. **Enabling Predictive Quality:** Moving from manual trend analysis to using **embedded Business Intelligence (BI)** tools within the eQMS (e.g., in the CAPA and OOS modules) to analyze aggregated quality data.[37] This allows the system to identify potential issues *before* they become failures, a core tenet of Quality 4.0.
2. **Achieving Systemic Integration:** The eQMS breaks down the informational silos created by paper and fragmented legacy systems by centralizing quality data. This centralization is mandatory for Quality 4.0, which demands that quality data be integrated seamlessly with manufacturing, supply chain, and clinical systems.

2.2.3 eQMS: A Digital Application of TQM Principles

From a theoretical **Total Quality Management (TQM)**[38] standpoint, the eQMS framework is fundamentally an application of TQM principles in the digital age.

> **Deming's System of Profound Knowledge**[39]**:** The eQMS directly supports the principle of **Understanding Variation**. Centralized data in modules like CAPA and OOS/OOT allows for sophisticated **trend analysis** and statistical process control[40] (SPC). This digital visibility helps quality professionals distinguish between **common causes** (systemic issues) and **special causes** (isolated events), leading to more effective, permanent corrective actions.

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[36] Gomaa, *Quality Management Excellence in the Era of Industry 4.0 (Quality 4.0): A Comprehensive Review, Gap Analysis, and Strategic Framework*.

[37] Urszula Balon et al., "KEY PERFORMANCE INDICATORS (KPIs) IN THE QUALITY MANAGEMENT SYSTEM," *International Journal for Quality Researchs*, ahead of print, 2024, https://doi.org/10.24874/IJQR18.02-10.

[38] Andrea Chiarini, "Industry 4.0, Quality Management and TQM World. A Systematic Literature Review and a Proposed Agenda for Further Research," *The TQM Journal* 32, no. 4 (2020): 603–16, https://doi.org/10.1108/TQM-04-2020-0082.

[39] Thomas J. Evans, *Deming's System of Profound Knowledge: An Overview for International Educators* (1996), https://eric.ed.gov/?id=ED401635.

[40] Jiju Antony et al., "The Evolution and Future of Lean Six Sigma 4.0," *The TQM Journal* 35, no. 4 (2022): 1030–47, https://doi.org/10.1108/TQM-04-2022-0135.

Plan-Do-Check-Act (PDCA): The automated workflows within an eQMS digitize and enforce the PDCA cycle.[41] Change management and action plans with defined tasks ensure the “Plan” and “Do” phases. Additionally also modules native enforce some kind of “Do” phase e.g. Document management for document periodic review and Supplier Management for approved suppliers periodic review and Individual retraining needs of the Training module etc . Deviation and CAPA management ensures the "Check" (monitoring and investigating) and "Act" (implementing corrective action) phases are executed in a mandated, closed-loop manner, preventing deviations from closure until effectiveness is verified[42]. Crucially, the "Act" phase in a digital environment extends beyond correction to include **Organizational Learning**. By integrating a Knowledge Management module, the eQMS ensures that the "Lessons Learned" from a failure are not just filed away, but active inputs for future process design, closing the TQM loop.

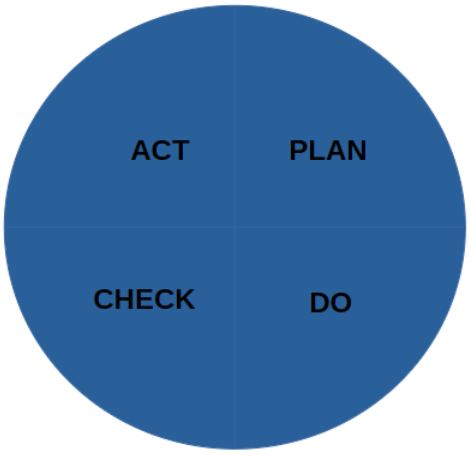

Figure 1: The Plan-Do-Check-Act (PDCA) Cycle. *Source: Author's elaboration, based on Deming (1986).*

[41] Andrea Chiarini and Maneesh Kumar, “What Is Quality 4.0? An Exploratory Sequential Mixed Methods Study of Italian Manufacturing Companies,” *International Journal of Production Research* 60, no. 16 (2022): 4890–910, https://doi.org/10.1080/00207543.2021.1942285.

[42] Gautam Dutta et al., “Digitalization Priorities of Quality Control Processes for SMEs: A Conceptual Study in Perspective of Industry 4.0 Adoption,” *Journal of Intelligent Manufacturing* 32, no. 6 (2021): 1679–98, https://doi.org/10.1007/s10845-021-01783-2.

Beyond individual module efficiency, the single greatest strategic advantage of an eQMS[43] is its ability to establish digital traceability and closed-loop integrity across the entire quality system. This means that a single quality event—such as a customer complaint—can be automatically traced and linked to the initiating deviation, the subsequent CAPA and Change Control records, the final document revision (DMS), and the relevant training records (TMS). This cross-referencing capability is critical for Management Review (ICH Q10), as it ensures that actions taken to correct a problem are systematic, documented, and verified across all impacted processes, proving the organization learns and continuously improves from every quality failure.

In summary, the eQMS acts as the **digital backbone**[44] for Quality 4.0[45] , replacing procedural compliance with system-enforced assurance, and moving the organization from a reactive quality gate to a proactive, TQM-aligned engine for continuous improvement.

2.3 Computer System Validation (CSV) and GAMP 5 Framework:

In the GxP environment, any computerized system that affects product quality, patient safety, or data integrity must undergo **Computer System Validation (CSV)**. Validation is the documented process of demonstrating that a system performs its intended functions consistently and reliably. For an eQMS, this is the regulatory gatekeeper ensuring the system meets the functional requirements defined in the User Requirement Specification (URS) and adheres to 21 CFR Part 11 and Annex 11.

2.3.1 GAMP 5[46]: The Risk-Based Approach

The industry standard methodology for CSV is provided by the **Good Automated Manufacturing Practice (GAMP) 5** guide [47], published by the International Society for Pharmaceutical Engineering (ISPE). GAMP 5 enforces a **risk-based approach** to validation, meaning that the effort, documentation, and testing should be proportional to the risk the computerized system poses to patient safety, product quality, and data integrity.

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[43] Kari Miller, “Revitalizing Quality Management Processes through Digitalization | Pharmaceutical Technology,” November 16, 2025, https://www.pharmtech.com/view/revitalizing-quality-management-processes-through-digitalization.

[44] Kashif Ali and Satirenjit Kaur Johl, “Soft and Hard TQM Practices: Future Research Agenda for Industry 4.0,” *Total Quality Management & Business Excellence* 33, nos. 13–14 (2022): 1625–55, https://doi.org/10.1080/14783363.2021.1985448.

[45] Ranjith Kumar et al., “Quality 4.0 – a Review of and Framework for Quality Management in the Digital Era.”

[46] ISPE, “ISPE GAMP® 5.”

[47] Pedro et al., “Impact of GAMP 5, Data Integrity and QbD on Quality Assurance in the Pharmaceutical Industry,” 2023.

System Categorization[48]**:** GAMP 5 classifies software based on its complexity. An eQMS, which is typically a COTS (Commercial Off-The-Shelf) product that is **highly configurable** to match the company's workflows, is usually classified as **Category 4 (Configurable Software)** or occasionally **Category 5 (Custom/Hybrid)** if significant code customization is required. This categorization dictates the required validation activities.

The V-Model: GAMP 5 traditionally relies on the **V-Model**[49] approach, which links user requirements (URS) and functional specifications (FS) to corresponding testing activities:

URS and **FS** define *what* the system must do (Specification phase).

Installation Qualification (IQ), **Operational Qualification (OQ)**, and **Performance Qualification (PQ)** test and document *how* the system works in the operational environment (Testing and Verification phase).

Validation Timing and TQM Alignment: Prospective vs. Retrospective A critical component of the validation strategy is the timing of the assurance activities, which fundamentally differentiates a proactive Quality Management System (QMS) from a reactive one.

Prospective Validation: This approach is conducted *before* the system is released for operational use. It aligns with the TQM principle of "Prevention" and "Right First Time." By defining requirements and testing them beforehand, the organization guarantees that the system is designed to prevent data integrity errors (e.g., preventing a user from deleting an audit trail). For new eQMS implementations, regulatory bodies (FDA, EMA) mandate prospective validation to ensure patient safety is never compromised during live use.

Retrospective Validation: This involves validating a system based on an analysis of historical data *after* it has been in use. This method is often associated with legacy systems or "paper-to-digital" gaps and aligns with the outdated "Inspection" or "Quality Control" mentality.

The transition to a Cloud eQMS represents a strategic shift from reliance on **Retrospective** checks (e.g., auditing paper logbooks for errors at the end of the month) to **Prospective** assurance (e.g., system-enforced workflows that prevent the error from occurring in the first place).

[48] Kailash Athkuri et al., *A Review on Applications of GAMP -5 in Pharmaceutical Industries*, 2013.

[49] Andreas Hoffmann et al., “Computer System Validation: An Overview of Official Requirements and Standards,” *Pharmaceutica Acta Helvetiae*, Quality Assurance in Computer Validation Systems, vol. 72, no. 6 (1998): 317–25, https://doi.org/10.1016/S0031-6865(97)00028-9.

2.3.2 Evolution to Computer Software Assurance (CSA[50])

Recognizing that traditional, document-heavy CSV often creates excessive overhead without significantly reducing risk, the industry is strategically shifting towards **Computer Software Assurance (CSA)**[51], a concept strongly advocated by the FDA. This evolution is a critical strategic consideration.

.Feature	CSV (Traditional)	CSA (Modern/Risk-Focused)
Focus	Document creation and exhaustive formal testing (scripted).	Critical thinking, patient safety risk, and rapid testing (unscripted/exploratory).
Testing Volume	High, often testing low-risk requirements.	Low, focused only on high-risk, unique configurations.
Value Proposition	Proof of compliance through documentation.	Reduction of validation cycle time and cost, directly boosting project ROI.

For a modern Cloud eQMS project[52], the validation strategy should embrace CSA principles by focusing the highest level of testing (PQ) only on the organization's unique workflows (e.g., a specific Change Control approval path), while leveraging the vendor's documentation for lower-risk aspects (IQ/OQ), [53] thereby directly reducing implementation cycle time and cost.

This risk-based strategy is essential for realizing the efficiency gains necessary to justify the eQMS investment outlined in the TCO/ROI analysis (Chapter 6).

2.4 The Cloud (SaaS) Trend and Strategic Vendor Management

The adoption of **Cloud Software-as-a-Service (SaaS)** has become the prevailing trend for new eQMS implementations[54] across the pharmaceutical and life sciences sector. This strategic shift is driven by the

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50 Davidson, “Advancing the Transition to Computer Software Assurance.”

51 FDA, “Computer Software Assurance for Production and Quality System Software,” FDA, September 23, 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/computer-software-assurance-production-and-quality-system-software.

52 Pravin Ullagaddi, “Cloud Validation in Pharma: Compliance and Strategic Value,” *International Journal of Business Marketing and Management (IJBMM)*, 2024.

53 Marius Schönberger and Tatjana Vasiljeva, “Towards Computer System Validation: An Overview and Evaluation of Existing Procedures,” *Journal of Innovation Management in Small and Medium Enterprises* 2018 (November 2018): 1–15, https://doi.org/10.5171/2018.512744.

54 Smritie Sheth et al., “A Systematic Approach for Identifying and Reducing Gaps between the Pharma and Software Industry and Transforming Quality through Digitalization in the Pharma Industry.,” *Current Science (00113891)* 126, no. 11 (2024): 1335–42, 177888062, https://doi.org/10.18520/cs/v126/i11/1335-1342.

significant financial and operational advantages inherent in the SaaS model, though it introduces new complexities related to regulatory oversight and vendor management.

2.4.1 Analysis of Cloud (SaaS) Adoption in GxP Environments

SaaS providers deliver the software application, hosting infrastructure, and maintenance updates remotely via the internet. For GxP-regulated companies, the core advantages of this model include:

Advantage	Strategic Value to Pharma
Scalability	Rapid scaling of user licenses and data storage to accommodate growth without major capital expenditure (CapEx).
Lower TCO	Reduced internal IT infrastructure investment and operational maintenance costs, shifting IT spend from CapEx to a predictable operating expenditure (OpEx).
Continuous Compliance	Vendors are responsible for updating the software to meet new regulations (e.g., EU Annex 11 revisions) and maintain the underlying infrastructure qualification.
Business Continuity	Built-in disaster recovery (DR) and high-availability protocols managed by the vendor, which would be prohibitively expensive to build in-house.

However, this transition requires a fundamental shift in the control paradigm, moving from full ownership to **Shared Responsibility**[55]. The primary challenge is that the regulated company retains ultimate accountability to the FDA/EMA for data integrity and system fitness, while delegating control over the physical and logical security of the platform to the vendor.

2.4.2 Strategic Vendor Management and the Shared Responsibility Model[56]

In a GxP SaaS model, effective **Strategic Vendor Management**[57] is critical and begins with clearly defining the **Shared Responsibility Model**.[58] [59] This model delineates the specific compliance tasks and evidence required from both the pharmaceutical company and the SaaS provider:

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55 Umesh Kumar Singh and Abhishek Sharma, "Cloud Computing Security Framework Based on Shared Responsibility Models: Cloud Computing," in *Cyber-Physical, IoT, and Autonomous Systems in Industry 4.0* (CRC Press, 2021).

56 Ullagaddi, "Cloud Validation in Pharma: Compliance and Strategic Value."

57 Pravin Ullagaddi, "Digital Transformation Strategies to Strengthen Quality and Data Integrity in Pharma," *International Journal of Business and Management* 19, no. 5 (2024): 16, https://doi.org/10.5539/ijbm.v19n5p16.

58 Cristina Reyes and Clarisse Mendoza, *Exploring the Impact of Shared Responsibility Models on Cloud Security Posture and Vulnerability Management*, 8 (2023).

59 Singh and Sharma, "Cloud Computing Security Framework Based on Shared Responsibility Models."

1. **Vendor Responsibility (Security *of* the Cloud):** The eQMS vendor is responsible for the platform's security, including physical data center security, network infrastructure, application security, and system patching/maintenance. The vendor must provide evidence of their GxP-alignment through validated release notes, platform qualification documentation (IQ/OQ), and independent third-party audit reports (e.g., SOC 2, ISO 27001).
2. **User Responsibility (Security *in* the Cloud):** The pharmaceutical company remains fully responsible for defining the **User Requirement Specification (URS)**, configuring the system to match validated workflows, managing user access/roles, controlling the quality of the data entered, and conducting **Performance Qualification (PQ)** testing to ensure the system is fit for its intended GxP use.

2.4.2.1 Cybersecurity[60] Governance in the GxP Cloud

While the vendor manages physical security, the pharmaceutical organization must address **Cybersecurity[61] Governance[62]**. In the context of Pharma 4.0, data[63] is the most valuable asset. The strategic risk management framework must address:

Ransomware Resilience[64]: The risk of critical quality data being encrypted by malicious actors. The eQMS must support immutable backups (backups that cannot be altered or deleted) to ensure Business Continuity.

The CIA Triad in GxP[65]:

Confidentiality: Protecting intellectual property (formulas, processes) via encryption at rest and in transit.

Integrity: Ensuring data is not altered (ALCOA+).

Availability: Ensuring the system is accessible during audits or batch release.

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60 P. Ullagaddi, "Leveraging Digital Transformation for Enhanced Risk Mitigation and Compliance in Pharma Manufacturing," *Journal of Advances in Medical and Pharmaceutical Sciences* 26, no. 6 (2024): 75–86, https://doi.org/10.9734/jamps/2024/v26i6697.

61 Ullagaddi, "Digital Transformation Strategies to Strengthen Quality and Data Integrity in Pharma."

62 Marion Toussaint et al., "Industry 4.0 Data Security: A Cybersecurity Frameworks Review," *Journal of Industrial Information Integration* 39 (May 2024): 100604, https://doi.org/10.1016/j.jii.2024.100604.

63 Jayanti Das et al., "Considerations for Big Data Management in Pharmaceutical Manufacturing," *Current Opinion in Chemical Engineering* 46 (December 2024): 101051, https://doi.org/10.1016/j.coche.2024.101051.

64 İsmail İlhan and Mehmet Karaköse, "Requirement Analysis for Cybersecurity Solutions in Industry 4.0 Platforms," *2019 International Artificial Intelligence and Data Processing Symposium (IDAP)*, September 2019, 1–7, https://doi.org/10.1109/IDAP.2019.8875930.

65 Scott Davis et al., "Cloud Solutions for GxP Laboratories: Considerations for Data Storage," *Bioanalysis* 13, no. 17 (2021): 1313–21, https://doi.org/10.4155/bio-2021-0137.

Vendor Surveillance: Cybersecurity is not a "set and forget" task. The organization must review the vendor's SOC 2[66] Type II reports annually to verify their cyber-defenses remain effective.

The relationship must be legally formalized through rigorous contractual agreements:

Service Level Agreements (SLAs): SLAs[67] must define mandatory metrics for the vendor's service delivery, including **guaranteed uptime (e.g., 99.9%)**, documented disaster recovery and business continuity plans with define RPO (Recovery Point Objective) and RTO (Recovery Time Objective) , and protocols for notifying the client of security incidents or planned maintenance.

Quality Agreements (QAs): QAs are mandatory in GxP and specify the vendor's quality management system (QMS) adherence, audit rights for the client, and procedures for managing software releases and changes.

2.4.3 Key Players and Market Segmentation (2.4.4)

The selection of an eQMS provider is a high-stakes decision in the pharmaceutical industry, directly impacting compliance costs, scalability, and long-term Total Cost of Ownership (TCO). The eQMS market is highly competitive and segmented primarily by deployment model (SaaS vs. On-Premise) and industry focus (life sciences vs. general manufacturing).

Established Leaders (Enterprise Focus): Companies such as **Veeva Systems**[68] (known for their cloud-native Vault Quality Suite) and **Honeywell's Sparta Systems TrackWise**[69] (an established legacy player now integrating cloud solutions) have historically dominated the large pharmaceutical and biotech sector. They offer comprehensive integration capabilities and strong regulatory familiarity.

Mid-Market & Specialized Solutions: A growing segment includes agile cloud providers like **MasterControl**[70] and **IQVIA SmartSolve**[71], who offer configurable platforms that appeal to mid-sized pharmaceutical companies and Contract Manufacturing Organizations (CMOs) seeking rapid deployment and lower upfront capital expenditure characteristic of the SaaS model.

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66 Thomas Sommer, "Cloud Computing in Emerging Biotech and Pharmaceutical Companies," *Communications of the IIMA* 13, no. 3 (2014), https://doi.org/10.58729/1941-6687.1218.

67 Ullagaddi, "Cloud Validation in Pharma: Compliance and Strategic Value."

68 *Veeva QMS | Pharma Quality Management System | Veeva*, July 13, 2023, https://www.veeva.com/products/veeva-qms/.

69 "TrackWise QMS Software and Solutions," *Honeywell*, n.d., accessed November 16, 2025, https://www.spartasystems.com/trackwise-qms-software/.

70 "Quality Management System Solutions from Quality Management Experts," MasterControl, accessed November 16, 2025, https://www.mastercontrol.com/quality.

71 "SmartSolve® eQMS for Lifesciences," accessed November 16, 2025, https://www.iqvia.com/solutions/safety-regulatory-compliance/quality-compliance/smartsolve-eqms.

ERP-Attached Solutions: Some large organizations may leverage integrated QMS modules within their existing ERP systems (e.g., SAP QM)[72], though this often requires significant customization to meet stringent GxP and Data Integrity requirements.

The prevailing trend favors specialized, cloud-based vendors whose systems are explicitly designed and continuously maintained for GxP compliance and rapidly evolving regulations, making strategic vendor selection a core component of successful eQMS adoption.

2.5 Strategic Sourcing[73] and Total Cost of Ownership (TCO)

The decision to adopt an eQMS is a significant capital and operational investment, requiring robust strategic sourcing and financial analysis to justify the expenditure. This section introduces the frameworks used to evaluate the commercial viability and long-term financial impact of the eQMS transition.

2.5.1 IT Portfolio Management and the Make vs. Buy Decision

The acquisition of a new eQMS is fundamentally a strategic **Make vs. Buy decision**[74] within the IT Portfolio Management framework.

Make (In-House Development): Historically, some large pharmaceutical firms developed customized, on-premise quality systems. This strategy offers maximum control and customization but involves high initial capital expenditure (CapEx), continuous maintenance and compliance responsibility, longer deployment cycles, and significant risk due to internal IT staffing challenges.

Buy (Cloud SaaS Acquisition): The contemporary preference for SaaS eQMS shifts the cost model to operating expenditure (OpEx), significantly reduces deployment risk, and transfers the burden of platform maintenance and continuous compliance[75] to the vendor. The strategic choice is almost universally "Buy," but the decision then shifts to selecting the right commercial model and vendor.

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[72] "Quality Management (QM) | SAP Help Portal," accessed November 16, 2025, https://help.sap.com/docs/SAP_S4HANA_ON-PREMISE/25a41481f62e469ba0e61015a0d39d20/e2f8f94be737403696eeea0e2be80d87.html?locale=en-US.

[73] E. N. Ntabe et al., "A Systematic Literature Review of the Supply Chain Operations Reference (SCOR) Model Application with Special Attention to Environmental Issues," *International Journal of Production Economics* 169 (November 2015): 310–32, https://doi.org/10.1016/j.ijpe.2015.08.008.

[74] Shengli Li et al., "A Study of Enterprise Software Licensing Models," *Journal of Management Information Systems* 34, no. 1 (2017): 177–205, https://doi.org/10.1080/07421222.2017.1297636.

[75] Li et al., "A Study of Enterprise Software Licensing Models," 2017.

2.5.2 The Principle of Adopting Standard Configuration (Fit-to-Standard)

While COTS (Commercial Off-The-Shelf) eQMS platforms are inherently configurable (GAMP Category 4), a core strategic directive for optimizing TCO and managing long-term compliance risk is the **Fit-to-Standard**[76] [77]principle. This approach dictates that the organization should prioritize adapting existing organizational processes[78] to match the **out-of-the-box** (OOTB)[79] functionality of the eQMS, rather than pursuing extensive customizations to mirror legacy, paper-based workflows. **Customizations significantly increase initial implementation costs** and, more critically, introduce substantial risk during routine vendor software upgrades. Heavily customized systems require complex, costly re-validation efforts with every new software version, which directly negates the continuous compliance and TCO advantages[80] of the SaaS model (2.4). Therefore, the strategic selection process must emphasize leveraging industry best practices embedded in the COTS solution.

This strategic choice requires the analysis to focus on the long-term financial implications—namely, the Total Cost of Ownership (TCO).

The Role of Business Analysis in Process Redesign To successfully execute the Fit-to-Standard strategy, the IT function must evolve from technical support to **Business Analysis (BA)**. The IT team must possess not only technical literacy but also "Process Literacy." Instead of automatically customizing the software to match legacy paper workflows (paving the cow path), the IT Business Analyst challenges the business stakeholders to **Redesign Business Processes (BPR)** to align with the software's industry-standard best practices. This requires a specific skill set: the ability to perform gap analysis between the *As-Is* (Legacy) and *To-Be* (Digital) states and negotiate process changes that preserve compliance while accepting the standard configuration.

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[76] Farhan Aslam, “The Benefits and Challenges of Customization within SaaS Cloud Solutions,” *American Journal of Data, Information and Knowledge Management* 4, no. 1 (2023): 14–22, https://doi.org/10.47672/ajdikm.1543.

[77] Hans Fredrik Hansen et al., “Investigating ERP System Customization: A Focus on Cloud-ERP,” *Procedia Computer Science*, CENTERIS – International Conference on ENTERprise Information Systems / ProjMAN – International Conference on Project MANagement / HCist – International Conference on Health and Social Care Information Systems and Technologies 2022, vol. 219 (January 2023): 915–23, https://doi.org/10.1016/j.procs.2023.01.367.

[78] Thomas H Davenport and James E Short, *The New Industrial Engineering : Information Technology and Business Process Redesign*, June 1990, https://dspace.mit.edu/bitstream/handle/1721.1/48613/newindustrialeng00dave.pdf.

[79] Ajay Prasad, “Transforming Product Development with a Platform-Based Approach to Product Lifecycle Management,” paper presented at Automotive Technical Papers, SAE International, July 17, 2025, https://doi.org/10.4271/2025-01-5051.

[80] Mason Baldwin and Jamal Cromity, “SaaS and Cloud Computing, the Rise of Compartmentalizing Users Online Via Subscription,” *New Review of Information Networking* 17, no. 2 (2012): 120–26, https://doi.org/10.1080/13614576.2012.724302.

2.5.3 Total Cost of Ownership (TCO) Framework

The **Total Cost of Ownership (TCO)** [81] framework is an essential management tool used to calculate the comprehensive direct and indirect costs associated with owning, operating, and managing a computerized system over its projected lifespan (typically 5 to 7 years). For a Cloud eQMS, the TCO analysis must contrast the expense of the new system[82] with the often-overlooked, yet substantial, TCO of the legacy/paper-based system.

TCO Component	Description	Strategic Focus for eQMS SaaS
Acquisition Costs	SaaS subscription fees, initial setup, and one-time licensing.	Focus on negotiated discounts and fixed pricing schedules to manage OpEx.
Implementation Costs	Internal labor costs (QA, IT) for URS/PQ development, external CSV consulting fees, and **data migration** costs.	These are the highest one-time capital costs; they must be optimized through the use of CSA (as per 2.3).
Operational Costs	Internal IT support (helpdesk), training curriculum maintenance, and ongoing quality assurance time for **re-validation** after vendor updates.	Low for SaaS, as infrastructure management is outsourced, but internal compliance labor remains.
Hidden Costs	Costs of **vendor lock-in**, potential contract penalties, and the opportunity cost of resources diverted from other projects.	Must be addressed through clear **exit clauses** and the strategic mitigation of vendor lock-in.

2.5.4 Vendor Lock-in and Contract Negotiation

A critical strategic risk in the SaaS environment is **Vendor Lock-in**[83], where the cost and difficulty of switching providers (due to data format dependencies or lack of system interoperability) allow the existing vendor to charge inflated rates upon contract renewal.

Effective contract negotiation for GxP-cloud vendors must therefore focus on:

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[81] Frederik Zachariassen and Jan Stentoft Arlbjørn, “Exploring a Differentiated Approach to Total Cost of Ownership,” *Industrial Management & Data Systems* 111, no. 3 (2011): 448–69, https://doi.org/10.1108/02635571111118305.

[82] Daniel Gull and Alexander Wehrmann, “Optimized Software Licensing – Combining License Types in a License Portfolio,” *Business & Information Systems Engineering* 1, no. 4 (2009): 277–88, https://doi.org/10.1007/s12599-009-0063-2.

[83] Sommer, “Cloud Computing in Emerging Biotech and Pharmaceutical Companies.”

Data Portability: Mandatory contractual clauses ensuring the client can extract all GxP data and associated audit trails in a readily usable, non-proprietary format (e.g., XML, structured CSV) upon contract termination.

Contingency Pricing: Pre-negotiating the cost of data access and archival services in the event of system termination or vendor insolvency.

Service Level Metrics: Structuring contract terms around the performance (SLA[84]) and quality (QA) metrics defined in Section 2.4 to ensure continuous service accountability.

The successful implementation of an eQMS is therefore a function of both technological competence and sophisticated financial and sourcing strategy, requiring a strategic approach to TCO [85] that ultimately underpins the Return on Investment (ROI) analysis in Chapter 6.The definition and quantification of COPQ[86] are based on models like the P-A-F scheme, which categorizes costs into prevention, appraisal, and failure to analyze the total cost impact of quality initiatives.[87]

2.5.5 Strategic Licensing Models: Optimization of Operational Expenditure (OpEx)

A critical factor influencing the long-term Total Cost of Ownership (TCO) of a Cloud eQMS is the vendor's licensing model. In the legacy "Flat Named User" model, organizations often paid a uniform high-cost license fee for every user, regardless of their usage frequency or depth. For a pharmaceutical organization where 80% of staff may only interact with the system passively, this creates massive financial waste.

To maximize ROI, the sourcing strategy must leverage **Tiered (Role-Based) Licensing** and **Concurrent Access** models to match cost to actual utility.

A. The Tiered License Structure (Viewer vs. Full User) Modern SaaS pricing structures allow for granular cost control by segmenting users based on their functional interaction with the system. A strategic allocation typically follows the **80/20 rule**:

Full / Power Users (High Cost): Restricted to Quality Assurance (QA) and System Administrators. These users require full rights to configure workflows, approve validation steps, and manage master data. They typically represent less than 10-15% of the total user base.

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84 Thomas H Davenport, *The Coming Commoditization of Processes*, June 2005.

85 Reza Mohammady Garfamy, "A Data Envelopment Analysis Approach Based on Total Cost of Ownership for Supplier Selection," *Journal of Enterprise Information Management* 19, no. 6 (2006): 662–78, https://doi.org/10.1108/17410390610708526.

86 Johannes Freiesleben, "The Opportunity Costs of Poor Quality," *The Quality Assurance Journal* 9, no. 1 (2005): 3–10, https://doi.org/10.1002/qaj.309.

87 Andrea Schiffauerova and Vince Thomson, "A Review of Research on Cost of Quality Models and Best Practices," *International Journal of Quality & Reliability Management* 23, no. 6 (2006): 647–69, https://doi.org/10.1108/02656710610672470.

Simple / Limited Users (Medium Cost): Assigned to operational staff (e.g., Manufacturing Operators, QC Analysts) who need to execute specific tasks, such as logging a deviation, signing a training record, or approving a specific document step.

Viewer / Read-Only Users (Low Cost): Assigned to the majority of the organization (e.g., Sales, Logistics, HR). These users only require access to "Read and Understand" effective SOPs and view their training dashboards.

Strategic Impact: By shifting the bulk of the organization to "Viewer" licenses (which often cost 70-80% less than Full licenses), the organization can drastically reduce the annual OpEx while maintaining 100% compliance coverage.[88]

B. The Strategic Advantage of Concurrent Licensing Complementing the tiered approach is the **Concurrent (Floating) Licensing** model. This is critical for global organizations operating across multiple time zones. Concurrent licensing limits the number of users who can access the system *simultaneously*, rather than the total number of registered accounts. For instance, an organization with 1,000 registered users may only have 100 logged in at any single peak time. Purchasing 100 concurrent licenses instead of 1,000 named licenses yields a decisive cost saving, often reducing the licensing budget by up to **60-75%**.

C. Organizational Allocation Strategy for ROI [89] To realize these savings, management must perform a strict **User Role Audit** prior to contract negotiation:

1. **Map Roles to Functions:** Analyze job descriptions to confirm which roles *actually* generate data (Simple User) versus those that merely consume it (Viewer).
2. **Strict Allocation Policy:** Implement an IT policy that defaults all new accounts to "Viewer" status, requiring functional justification and budget approval to upgrade to a "Full" license.
3. **Active License Harvesting:** The system administrator must periodically review usage logs (e.g., every 6 months) to identify "Full" users who have not utilized advanced features, downgrading them to lower tiers to optimize the subscription spend.

2.6 Organizational Change Management (OCM) in Digital Transformation

The successful deployment of a GxP-validated eQMS is only 20% technology and 80% effective **Organizational Change Management (OCM)**[90]. Failures in digital transformation projects are rarely due to software

[88] Vidyanand Choudhary and Joseph Vithayathil, "The Impact of Cloud Computing: Should the IT Department Be Organized as a Cost Center or a Profit Center?," *Journal of Management Information Systems* 30, no. 2 (2013): 67–100, https://doi.org/10.2753/MIS0742-1222300203.

[89] Schniederjans and Hales, "Cloud Computing and Its Impact on Economic and Environmental Performance."

[90] Saulo Ferraz Junior and Rodrigo Franco Gonçalves, "Quality 4.0 in Industrial Organizations: Challenges, Benefits, and a Research Agenda," *The TQM Journal*, November 18, 2025, 1–22, https://doi.org/10.1108/TQM-01-2025-0034.

deficiency; they are overwhelmingly caused by user resistance, cultural friction, and inadequate training. This makes OCM[91] a central strategic consideration, particularly within a highly regulated environment where long-standing practices breed deeply entrenched cultural norms.

2.6.1 OCM Models as the Theoretical Lens

OCM provides the theoretical framework for analyzing and guiding the human element of the eQMS implementation. Two widely accepted models serve as valuable lenses for this study:

Kotter's 8-Step Process for Leading Change[92]: This model focuses on the leadership and sequencing required for large-scale organizational transformation. Key steps directly applicable to eQMS adoption include **establishing a sense of urgency** (justified by regulatory risk and COPQ , as per 1.2), **creating a guiding coalition** (QA, IT, and Business leadership), and **generating short-term wins** (e.g., successful validation of one module).

The ADKAR Model (Awareness, Desire, Knowledge, Ability, Reinforcement):[93] This individual-focused model ensures that change is successful one person at a time. For an eQMS, the ADKAR model helps define the necessary interventions:

Awareness: Clear communication of the regulatory mandate and the cost of inaction.

Desire: Proving that the new eQMS makes the user's job safer and easier, not just different.

Knowledge & Ability: Role-based, hands-on training tailored to specific workflows.

Reinforcement: Auditing usage post-Go-Live and celebrating early adopters.

2.6.2 The Cultural Shift: From Paper Control to Digital Assurance

In the pharmaceutical context, the change management challenge is unique and acute, requiring a shift in fundamental work culture:

Addressing the Fear of the Audit Trail: Operators and quality personnel may fear the transparency of the electronic audit trail, believing it will be used for punitive measures. The OCM strategy must focus on creating a **culture of digital assurance and root cause prevention**, emphasizing that the data is used for systemic improvement (TQM/PDCA), not merely blame.

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91 Ullagaddi, "Leveraging Digital Transformation for Enhanced Risk Mitigation and Compliance in Pharma Manufacturing."

92 John P. Kotter, "Leading Change - Book - Faculty & Research - Harvard Business School," accessed November 15, 2025, https://www.hbs.edu/faculty/Pages/item.aspx?num=137.

93 Jeff Hiatt and Jeffrey Hiatt, *ADKAR: A Model for Change in Business, Government and Our Community* (2006).

From Procedural Compliance to Data Visibility: Historically, paper processes provided a measure of control by hiding inefficiency or localized errors. The eQMS, with its secure audit trails and real-time dashboards, instantly provides **unprecedented digital visibility** into every action, delay, and error.

Stakeholder Management[94]**:** Success requires overcoming resistance from critical stakeholders:

QA Leaders: Must transition from being document custodians to **data analysts and strategic process owners**[95].

IT Department: Must transition from managing on-premise hardware to **managing strategic vendor relationships** and **Cloud security** and being **Business Analysts**.

End Users (Manufacturing/QC): Must move from physical sign-offs to **reliable electronic signatures** and adherence to digitally-enforced workflows.

By strategically applying OCM principles, the pharmaceutical organization can ensure that the eQMS is not just validated (compliant), but also **fully adopted** (effective), thereby realizing the full ROI potential[96] defined in the business case.

Chapter 3: Research Methodology

3.1 Research Design: Mixed-Methods Approach

The complexity of the research questions—spanning technical compliance (GAMP 5), strategic management (OCM), and financial justification (ROI)—necessitates a **Mixed-Methods Research Design**. This approach combines the depth and context provided by qualitative data with the empirical verification and generalizability offered by quantitative data, ensuring a holistic and robust conclusion.

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94 Milena Ališ, "Integration of the ISO 9001 QMS with the Company's IT Business System," *Total Quality Management & Business Excellence* 29, nos. 9–10 (2018): 1143–60, https://doi.org/10.1080/14783363.2018.1487216.

95 Diska Prini Fadilasari et al., "Adopting Quality Management Practices in the Industry 4.0 Era: An Investigation into the Challenges," *Total Quality Management & Business Excellence* 35, nos. 9–10 (2024): 1098–123, https://doi.org/10.1080/14783363.2024.2354840.

96 E.A.M. Mjema et al., "Analysis of Roles of IT on Quality Management," *The TQM Magazine* 17, no. 4 (2005): 364–74, https://doi.org/10.1108/09544780510603206.

3.1.1 Justification for a Mixed-Methods Approach

The study's primary objective is to develop a *strategic framework* (the artifact) and then *financially justify*[97] its adoption.

Qualitative Data: Required to address the "Why" and "How" of the problem. This includes understanding the specific challenges of Data Integrity failures, capturing expert opinions on vendor selection, and analyzing the nuances of cultural resistance and OCM strategies (Q2, Q3).

Quantitative Data: Required to address the "What" and "How Much." This involves collecting operational metrics (e.g., cycle times, backlog size) to quantify the Cost of Poor Quality (COPQ)[98] and calculate the projected Return on Investment[99] (ROI) and efficiency gains[100] (Q1, Q4).

3.1.2 Research Model: Explanatory Sequential Design

This research will utilize an **Explanatory Sequential Design** (often referred to as QUANT\QUAL).

1. **Phase I (Quantitative Basis):** Initial analysis of secondary data (industry reports, vendor white papers, and public regulatory findings like FDA Warning Letters) will establish the current operational benchmarks (e.g., average CAPA cycle times, TCO components[101]). This phase provides the **statistical foundation** for the problem statement and the ROI[102] model.
2. **Phase II (Qualitative Exploration):** Semi-structured interviews will be conducted with key industry experts (e.g., Head of QA, CSV Specialists) to **enrich and contextualize** the quantitative findings. These interviews will explore the "gaps" in the data, validate the feasibility of the proposed URS and workflows, and provide depth on the OCM strategies and the Shared Responsibility Model.

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97 Robert Joppen et al., "Evaluation of Investments in the Digitalization of a Production," *Procedia CIRP*, 52nd CIRP Conference on Manufacturing Systems (CMS), Ljubljana, Slovenia, June 12-14, 2019, vol. 81 (January 2019): 411–16, https://doi.org/10.1016/j.procir.2019.03.071.

98 Panu Laukkanen, "Quality 4.0 Enabling Cost of Poor Quality Measurement," *LAPPEENRANTA-LAHTI UNIVERSITY OF TECHNOLOGY LUT School of Engineering Science Industrial Engineering and Management*, 2021.

99 Mohamad Abou-foul et al., "The Impact of Digitalization and Servitization on the Financial Performance of a Firm: An Empirical Analysis," *Production Planning & Control* 32, no. 12 (2021): 975–89, https://doi.org/10.1080/09537287.2020.1780508.

100 Chooi-Leng Ang et al., "Measures to Assess the Impact of Information Technology on Quality Management," *International Journal of Quality & Reliability Management* 17, no. 1 (2000): 42–66, https://doi.org/10.1108/02656710010300135.

101 Zachariassen and Stentoft Arlbjørn, "Exploring a Differentiated Approach to Total Cost of Ownership."

102 Paul Pfister and Claudia Lehmann, "Digital Value Creation in German SMEs – a Return-on-Investment Analysis," *Journal of Small Business & Entrepreneurship* 36, no. 4 (2024): 548–73, https://doi.org/10.1080/08276331.2022.2037065.

This sequential structure ensures that the qualitative phase is highly focused, targeting expert insights that directly validate or refine the financial and technical models developed in the quantitative phase.

Research Component	Design Approach	Data Source
Strategic Framework/URS Blueprint	Qualitative/Design	Expert interviews, GAMP 5, Regulatory Literature (21 CFR Part 11)
TCO/ROI Quantification	Quantitative/Analytical	Industry benchmarks, financial modeling, public operational metrics
OCM Challenges & Strategies	Qualitative/Exploratory	Semi-structured interviews with QA/IT Leaders

3.2 Primary Data Collection (Qualitative Validation)

This data provides expert insight to interpret the secondary data, validate the feasibility of the strategic framework, and capture the nuances of OCM challenges (Q3).

Semi-Structured Interviews: The primary qualitative data will be collected through one-on-one, semi-structured interviews. This method allows for a pre-defined set of core questions (ensuring coverage of all research objectives) while maintaining flexibility for in-depth exploration of expert insights, context, and unexpected findings.

Interview Focus Areas: The interview script will be organized around three core themes:

URS/Functional Requirements: Validating the criticality and completeness of the proposed eQMS functional requirements (Chapter 4).

Validation and Vendor Management: Confirming the practical application of the GAMP 5 Shared Responsibility Model for SaaS vendors (Q2).

Organizational Change Management: Capturing real-world examples of resistance[103], successful OCM tactics, and the necessary cultural shifts.

3.3 Sample Selection: Purposive Sampling

Given the highly specialized nature of the research, a **Purposive (or Judgmental) Sampling** method will be used for primary data collection. This non-probability technique selects participants based on their specific knowledge, experience, and authority relevant to the research objectives, ensuring the collected data is maximally informative.

[103] Marjo Kauppinen et al., "Implementing Requirements Engineering Processes throughout Organizations: Success Factors and Challenges," *Information and Software Technology* 46, no. 14 (2004): 937–53, https://doi.org/10.1016/j.infsof.2004.04.002.

3.3.1 Target Population and Criteria

The target population consists of individuals with direct, recent experience in managing or implementing GxP computerized systems, eQMS platforms, or quality system transformation.

Role/Title	Experience Focus	Relevance to Research Questions
Head of Quality Assurance (QA) / Quality Director	Decision-maker on QMS strategy, budget, and regulatory response.	Provides the executive perspective on COPQ and strategic ROI (Q4).
CSV Specialist / GxP IT Lead	Technical owner of system validation and data integrity assurance.	Validates the GAMP 5 approach and Shared Responsibility Model (Q2).
Organizational Change Manager (OCM) / Training Lead	Responsible for user adoption, training development, and cultural shift.	Provides critical data on the feasibility and success factors of OCM (Q3).
External GxP Consultant / System Integrator	Experience with multiple eQMS implementations across various companies/vendors.	Provides objective, broad insight into industry benchmarks and best practices.

3.3.2 Sample Size and Data Saturation

A target sample size of **8–12 highly qualified professionals** is deemed appropriate for a specialized qualitative study of this scope. Data collection will cease once **thematic saturation** is achieved—the point where new interviews no longer yield significant new information or perspectives regarding the strategic framework or OCM challenges.

3.4 Data Analysis

The data collected through the mixed-methods approach will be analyzed using distinct techniques tailored to the nature of the data and the specific research questions they address.

3.4.1. Analysis of Quantitative Data (Q1, Q4)

Quantitative data, derived from secondary sources (industry reports[104], public regulatory findings, and financial benchmarks), will be analyzed to establish the financial and operational justification for eQMS adoption.

> Due to the proprietary and highly sensitive nature of internal pharmaceutical financial logs, obtaining a direct "Paper vs. Digital" dataset from a live operating environment was not feasible. To overcome this limitation and provide a reusable management artifact, a configurable **Monte Carlo**

[104] Andreas Felsberger et al., "The Impact of Industry 4.0 on the Reconciliation of Dynamic Capabilities: Evidence from the European Manufacturing Industries," *Production Planning & Control* 33, nos. 2–3 (2022): 277–300, https://doi.org/10.1080/09537287.2020.1810765.

simulation engine was developed (Appendix C). Unlike static Excel models, this Python-based tool generates a synthetic dataset of **N=10,000 quality events** (scaled from a representative sample of 1,000 matched-pair observations). The model incorporates stochastic variables for 'Complexity' (Log-Normal distribution) and 'Departmental Involvement' (Poisson distribution) to mirror real-world variability. It tests the hypothesis that the **System State** (Digital vs. Paper) is the primary driver of cost, while controlling for event complexity and cross-functional linkages.

Financial Modeling and Ratio Analysis (TCO/ROI):

Total Cost of Ownership (TCO) Calculation: A standardized TCO model (as introduced in 2.5 and detailed in 6.1) will be constructed, aggregating and contrasting the 5-year costs of a legacy system (including COPQ) versus the proposed Cloud SaaS eQMS (including subscription, validation, and OCM costs).

Return on Investment (ROI) Calculation:[105] The financial benefits (value of efficiency gains[106], revenue from faster TTM, and regulatory cost avoidance) will be calculated and compared against the TCO to derive the formal ROI percentage using the formula:

ROI = { (Total Financial Benefits - Total Costs) \over Total Costs } * 100

Variables Defined:

-Total Financial Benefits: The sum of all quantifiable gains (Hard Savings, Value Creation, Cost Avoidance) over the 5-year period.

-Total Costs (TCO): The Total Cost of Ownership (Acquisition, Implementation, and Operational Costs) over the 5-year period

Sensitivity Analysis: Key variables (e.g., labor rates, estimated cycle time reduction, consulting fees) will be varied to test the robustness and financial risk of the calculated ROI.

To validate the financial assumptions, a **synthetic dataset of N=5000 quality events (10,000 matched-pair observations)** was generated based on the industry benchmarks identified in the Literature Review (Phase I). This theoretical simulation allowed for a Multivariate Regression analysis to isolate variables (System State vs. Complexity) that would otherwise be impossible to isolate in a real-world setting without access to proprietary financial logs.

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[105] Guoxu Wang et al., "Quantitative Analysis of the QMS for Pharmaceutical Manufacturing," *Journal of Pharmaceutical Innovation* 17, no. 4 (2022): 1091–108, https://doi.org/10.1007/s12247-021-09579-w.

[106] Ullagaddi, "Leveraging Digital Transformation for Enhanced Risk Mitigation and Compliance in Pharma Manufacturing."

3.4.2. Analysis of Qualitative Data (Q2, Q3, Strategic Framework)

Qualitative data, collected through semi-structured interviews with GxP experts, will be analyzed using systematic coding to extract themes and validate the strategic framework.

Thematic Analysis: This systematic approach will be used to analyze transcribed interview data to identify recurring patterns, concepts, and relationships across the responses. The process involves:

1. **Familiarization:** Reading and re-reading the transcripts.
2. **Coding:** Assigning descriptive codes to text segments related to validation challenges, OCM resistance, vendor management, and specific URS needs.
3. **Theme Development:** Grouping related codes into broader, overarching themes (e.g., "Fear of the Audit Trail," "Importance of Shared Responsibility Definition," "GAMP 5 to CSA Transition").

Content Analysis: Specifically, for the URS (Chapter 4) and GAMP 5 validation strategy (Q2), the interview content will be analyzed to confirm or refute the criticality of proposed functional requirements and the feasibility of the risk-based validation approach in a real-world setting.

Triangulation: The final stage of analysis involves **triangulating** the qualitative themes with the quantitative findings[107]. For example, expert qualitative feedback on "excessive paper-based approval steps" will be linked directly to the quantitative metric showing a high average document approval cycle time. This linkage provides robust validation for the strategic recommendations.

This systematic analytical approach ensures that the thesis conclusions are grounded in both empirical evidence (the numbers) and expert validation (the context), thereby addressing all four research questions comprehensively.

Chapter 4: Core eQMS Components: URS and Module Specifications

The purpose of this chapter is to develop the **functional blueprint** for the eQMS system—the key technical artifact of this thesis. This blueprint ensures that the strategic goals (Digital Transformation, ROI) and compliance mandates (GxP, Data Integrity) are translated into specific, testable system functions.

4.1 User Requirement Specification (URS) Structure and Criticality

The **User Requirement Specification (URS)** is the foundational document in any GxP computer system validation effort. It serves as the formal statement of the needs and expectations that the business stakeholders—in this case, Quality Assurance, Manufacturing, and IT—have for the new eQMS.

[107] Jiju Antony et al., "Quality 4.0 Conceptualisation and Theoretical Understanding: A Global Exploratory Qualitative Study," *The TQM Journal* 34, no. 5 (2021): 1169–88, https://doi.org/10.1108/TQM-07-2021-0215.

The subsequent sections of this chapter will detail the Functional Requirements for the critical eQMS modules, translating these strategic and regulatory needs into a ready-to-use blueprint, while strictly adhering to the Fit-to-Standard principle to minimize long-term maintenance overhead.

4.1.1 The URS as the Critical Starting Point

The URS is the **critical starting point**[108] and the central hub of the entire GAMP 5 V-Model, establishing the **traceability** required by regulators. Every subsequent validation document and test case must link directly back to a requirement defined in the URS.

Defines Scope: It locks the project scope, preventing uncontrolled changes (scope creep) and ensuring the final system addresses the problems identified in Section 1.2.

Regulatory Bridge: It translates high-level regulatory mandates (e.g., "Data must be attributable" from 21 CFR Part 11) into specific, testable **Functional Requirements** (e.g., "The system shall require unique, non-reusable login credentials for all e-signatures").[109]

Vendor Selection Tool: The URS acts as the basis for vendor evaluation, allowing the pharmaceutical company to score potential SaaS providers based on their ability to meet the mandatory GxP and business needs.

4.1.2 Key Sections of a GxP-Compliant eQMS URS

A comprehensive URS for a GxP Cloud eQMS must be structured into several distinct sections to capture all business, regulatory, functional, and operational needs[110]:

URS Section	Focus	Criticality to GxP Compliance
1. Business Requirements	High-level needs and strategic justification (e.g., "The system must reduce the average CAPA cycle time by 50%").	Links the project to the financial justification (ROI).
2. Regulatory Requirements	Specific mandates from 21 CFR Part 11, EU Annex 11, and Data Integrity guidelines.	**Mandatory:** The non-negotiable legal basis for system control (e.g., audit trail requirements).
3. Functional	Detailed, granular actions the system must perform (e.g., "The system shall automatically	These requirements form the basis of the **Operational**

[108] Tetsuo Tamai and Mayumi Itakura Kamata, “Impact of Requirements Quality on Project Success or Failure,” in *Design Requirements Engineering: A Ten-Year Perspective*, ed. Kalle Lyytinen et al. (Springer, 2009), https://doi.org/10.1007/978-3-540-92966-6_15.

[109] Hoffmann et al., “Computer System Validation.”

[110] Stefan Biffl et al., “Software Process Improvement in Europe: Potential of the New V-Modell XT and Research Issues,” *Software Process: Improvement and Practice* 11, no. 3 (2006): 229–38, https://doi.org/10.1002/spip.266.

URS Section	Focus	Criticality to GxP Compliance
Requirements (FRS)	route a Major Change Control request to the Quality Review Board").System must support multiple and configurable workflows and record types for each module which can be created and/or changed by the end-user administrator. System shall support template style elements at each module to reduce repetitive tasks e.g. sets of criteria in Audit module, specific teams by role in workflow types. End-User Administrator can perform User Management e.g. create, activate, deactivate users and assign roles.	**Qualification (OQ)** testing.
4. Non-Functional Requirements (NFR)	System quality attributes related to performance, security, and scalability.	Critical for **Cloud/SaaS** viability (e.g., guaranteed 99.9\% availability, security protocols).
5. Data Migration Requirements	Defining the data to be migrated from the legacy system (e.g., all closed CAPAs from the last 5 years) and the process controls for verifying data integrity during transfer.	Ensures the historical GxP record is maintained in a compliant, accessible state.

The requirements must be written using clear, unambiguous language (e.g., "The system **shall**..." for mandatory requirements) and be **testable**. The subsequent sections of this chapter will detail the **Functional Requirements** for the critical eQMS modules, translating these strategic and regulatory needs into a ready-to-use blueprint.

4.2 Functional Specification and Design for Core eQMS Modules

The Functional Requirement Specification (FRS) details the "how-to" of the system, transforming the strategic objectives and regulatory mandates into specific functions.[111] The following tables define the necessary FRS for the nine core eQMS modules, categorized by their GxP function.

The central design principle governing the FRS is cross-functional traceability. The system must be configured to automatically enforce linkages between related records. This digital closed-loop ensures that a quality event originating from any module (e.g., Complaint, Audit Finding, OOS) is automatically linked to the ensuing CAPA and Change Control record, guaranteeing that corrective actions are executed, validated, and documented in a continuous, auditable chain.

[111] Kauppinen et al., “Implementing Requirements Engineering Processes throughout Organizations.”

4.2.1. Core GxP Modules (Enforcement of 21 CFR Part 11 and ICH Q10)

This section focuses on the modules that manage documentation and control systemic changes.

4.2.1.1 Document Management System[112] [113]

eQMS Module	Regulatory Basis	Key Functional Requirements (FRS)	Data Integrity & Part 11 Controls
Document Management System (DMS)	21 CFR Part 11, EU Annex 11, GMP	**Version Control:** Automatic major/minor versioning with full, secured revision history retention. **Review/Approval Workflow:** Configurable multi-stage, sequential, and parallel approval routes based on document type and user role. **Read Access Control:** Role-based security to restrict viewing of draft, expired, or sensitive documents. **Distribution Control:** Automated notification and electronic delivery of released documents to targeted personnel.	**Electronic Signatures (e-Sign):** Must meet Part 11 requirements (unique, non-reusable, and tied to user credentials). **Audit Trail:** Every action (creation, edit, view, approval, print, status change) must be recorded with user ID, date, time, and reason.

[112] FDA, "Part 11, Electronic Records; Electronic Signatures - Scope and Application," FDA, October 1, 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/part-11-electronic-records-electronic-signatures-scope-and-application.

[113] "The Rules Governing Medicinal Products in the European Union," in *GMP/ISO Quality Audit Manual for Healthcare Manufacturers and Their Suppliers, (Volume 2 - Regulations, Standards, and Guidelines)*, 0 ed., by Leonard Steinborn (CRC Press, 2004), https://doi.org/10.3109/9780203026656-14.

4.2.1.2 Change Control Management[114] [115]

eQMS Module	Regulatory Basis	Key Functional Requirements (FRS)	Data Integrity & Part 11 Controls
2. Change Control	ICH Q10, GMP	**Risk Assessment Integration:** Mandatory linkage to a Risk Management module for preliminary and detailed risk evaluation of the proposed change (Impact on product quality, validation status). **Classification:** Ability to classify changes (Major, Minor, Administrative) to trigger corresponding approval and testing workflows. **Effectiveness Check:** Mandatory scheduling and tracking of post-implementation effectiveness reviews with closure dependent on successful results.	**Non-Repudiation:** Once a change request is submitted and approved, the record must be immutable (locked by e-signature). **Traceability:** Automatic linking to all affected downstream GxP documents (SOPs), CAPAs, and validation protocols.

4.2.1.3 CAPA & Deviation Management[116] [117]

eQMS Module	Regulatory Basis	Key Functional Requirements (FRS)	Data Integrity & Part 11 Controls
3. CAPA & Deviation Management	ICH Q10, GMP	**Deviation Intake:** Structured, standardized forms for logging non-conformances, deviations, and complaints, auto-assigning unique IDs. **Root Cause Analysis (RCA):** Integrated tools (e.g., 5 Whys, Fishbone Diagram) to	**Sequential Workflow Enforcement:** System must enforce the logical closed-loop flow (Investigation --> Action Plan --> Implementation --> Verification). **Security:** Only

[114] "EudraLex - Volume 4 - Public Health - European Commission," November 25, 2025, https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en.

[115] "ICH Q10 Pharmaceutical Quality System - Scientific Guideline | European Medicines Agency (EMA)," June 1, 2008, https://www.ema.europa.eu/en/ich-q10-pharmaceutical-quality-system-scientific-guideline.

[116] Office of Regulatory Affairs, "Corrective and Preventive Actions (CAPA)," *FDA*, FDA, March 28, 2023, https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-guides/corrective-and-preventive-actions-capa.

[117] Abhay Walvekar et al., "Deviation, Change, Control, and CAPA," in *Modern Aspects of Pharmaceutical Quality Assurance: Developing & Proposing Application Models, SOPs, Practical Audit Systems for Pharma Industry*, ed. Minal Ghante et al. (Springer Nature, 2024), https://doi.org/10.1007/978-981-99-9271-3_13.

eQMS Module	Regulatory Basis	Key Functional Requirements (FRS)	Data Integrity & Part 11 Controls
		document the investigation. **Action Tracking:** Clear distinction between Corrective Actions (CA) and Preventive Actions (PA) with assigned owners and due dates. **Trend Analysis:** Embedded Business Intelligence (BI) tools to identify recurring issues by product, process, or department.	authorized users can edit investigation reports or close actions, with segregation of duties (SoD) enforced.

4.2.1.4 Training Management System (TMS)[118] [119]

eQMS Module	Regulatory Basis	Key Functional Requirements (FRS)	Data Integrity & Part 11 Controls
4. Training Management System (TMS)	GMP, Personnel Qualification	**Curriculum Assignment:** Ability to assign training curricula based on job function, location, or equipment access. **Automated Retraining:** Automatically trigger retraining assignments when a linked SOP or work instruction is revised. **Competency Assessment:** Functionality to host and score required assessments/quizzes and record pass/fail results.	**Evidence of Completion:** Secure record of e-signature/digital sign-off to prove the user has read and understood the document. **Compliance Dashboard:** Real-time metrics showing the percentage of personnel compliant with their assigned training curriculum.

4.2.2 Additional Essential GxP Modules (Quality Assurance and Risk Mitigation)

These modules are crucial for proactive quality assurance, supply chain control, and post-market surveillance.

[118] "EudraLex - Volume 4 - Public Health - European Commission."

[119] Deeksha R Pai, *Personnel Training for Pharmaceutical Industry*, 2016.

4.2.2.5 Audit & Inspection Management [120] [121]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
5. Audit & Inspection Management	Audit Readiness	**Scheduling & Planning:** Tools to schedule internal, external, and supplier audits with automated notification. **Inspection Readiness Room:** Ability to quickly assemble and securely present required documents during a regulatory inspection (e.g., electronic "War Room"). **Finding Tracking:** Direct linkage of audit findings to the CAPA module.	Must support various audit types and allow secure, temporary access for external parties/auditors while tracking all evidence retrieval actions.

4.2.2.6 Supplier Quality Management (SQM) [122] [123]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
6. Supplier Quality Management (SQM)	Supply Chain Integrity	**Vendor Qualification Workflow:** Structured workflow for initial qualification, audit scheduling, and re-qualification based on risk/performance. **Approved Supplier List (ASL):** Dynamic list automatically updated based on qualification status and quality events. **SCAR Tracking:**	Requires integration potential with ERP/Procurement systems to ensure only approved suppliers are used for critical materials (master data control).

[120] Aisha Al Azawei et al., "The Management of Good Manufacturing Practice (GMP) Inspections: A Scoping Review of the Evidence," *Frontiers in Medicine* 12 (n.d.): 1687864, https://doi.org/10.3389/fmed.2025.1687864.

[121] Sowmya Vedanabhatla and N Vishal Gupta, *A REVIEW ON AUDITS AND COMPLIANCE MANAGEMENT*, 6 (2013).

[122] Hamid Salimian et al., "Supplier Quality Management and Performance: The Effect of Supply Chain Oriented Culture," *Production Planning & Control* 32, no. 11 (2021): 942–58, https://doi.org/10.1080/09537287.2020.1777478.

[123] Ali Bastas and Kapila Liyanage, "Sustainable Supply Chain Quality Management: A Systematic Review," *Journal of Cleaner Production* 181 (April 2018): 726–44, https://doi.org/10.1016/j.jclepro.2018.01.110.

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
		Tracking of Supplier Corrective Action Requests (SCARs) issued to vendors.	

4.2.2.7 Risk Management (QRM) [124]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
7. Risk Management (QRM)	ICH Q9, Proactive Quality	**Standardized Methodology:** Integrated tools for FMEA (Failure Mode and Effects Analysis) or other QRM methodologies. **Risk Scoring:** Calculation of Risk Priority Number (RPN): RPN = S x O x D. **Risk Mitigation Tracking:** Automated assignment and tracking of actions required to reduce identified risks, linking back to Change Control or CAPA.	Centralized repository for all quality-related risk assessments across the product lifecycle (ICH Q9 principle).

4.2.2.8 Complaint Management [125] [126]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
8. Complaint Management	Post-Market Surveillance	**Intake & Triage:** Structured workflow for documenting, classifying, and assessing complaints (e.g., regulatory reportability). **Medical Review:** Workflow steps requiring mandatory medical/safety review before closure. **Reporting:** Automatic generation of reports for regulatory agencies (e.g., MedWatch, MDRs) based on defined	Critical for Post-Market compliance; requires strict timelines and the ability to link to the Deviation/CAPA system for investigation.

[124] *ICH Guideline Q9 on Quality Risk Management*, n.d.

[125] Jadhav Santosh et al., *Systematic Approach for Complaint Handling in Pharmaceutical Industries- An Updated Review*, 3, no. 3 (n.d.).

[126] Glaucia Karime Braga, "Complaint Handling in Pharmaceutical Companies," *The Quality Assurance Journal* 11, no. 1 (2007): 16–21, https://doi.org/10.1002/qaj.398.

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
		criteria and strict timelines.	

4.2.2.9 OOS / OOT (QC Events)[127]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
9. OOS / OOT (QC Events)	Process Stability & Batch Disposition Control	**Phased Investigation:** Automated enforcement of the Phase 1 (Lab) and Phase 2 (Full) investigation structure per FDA/EMA guidance. **OOT Alerting:** Integrated statistical process control (SPC) tools to detect trends before OOS occurs. **Batch Decision:** Secure final disposition sign-off required for lot release or rejection.	Workflow must enforce a mandatory sequential workflow from initial alert to final QA disposition and link confirmed OOS/OOT to the CAPA module for permanent correction.

4.2.2.10 Knowledge Management (KM)[128] [129] [130]

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
10. Knowledge Management (KM)	**ICH Q10 (Knowledge Management)**, TQM/PDCA Principle	**Mandatory Capture:** System shall enforce a structured "Lessons Learned" entry upon closure of Major/Critical Quality Events. **Repository:** Dedicated centralized area for structured, non-document knowledge assets (e.g.,	**Learning Loop:** Enforces the capture of tacit knowledge and conversion to explicit knowledge, ensuring that mistakes systemically inform future process design and

[127] *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production*, n.d.

[128] "ICH Q10 Pharmaceutical Quality System - Scientific Guideline | European Medicines Agency (EMA)."

[129] Yu-Chung Hung et al., "Critical Factors in Adopting a Knowledge Management System for the Pharmaceutical Industry," *Industrial Management & Data Systems* 105, no. 2 (2005): 164–83, https://doi.org/10.1108/02635570510583307.

[130] Ganesh D. Bhatt, "Knowledge Management in Organizations: Examining the Interaction between Technologies, Techniques, and People," *Journal of Knowledge Management* 5, no. 1 (2001): 68–75, https://doi.org/10.1108/13673270110384419.

eQMS Module	Strategic Importance	Key Functional Requirements (FRS)	Implementation Detail
		process failure summaries). **Contextual Search:** Integrated search capability to find historical "Lessons Learned" relevant to a deviation being logged.	prevent recurrence.

4.3 Detailed Workflow Blueprints

The following blueprints translate the high-level Functional Requirements (FRS) of the eQMS modules into mandatory, step-by-step processes. These workflows illustrate how the digital system enforces **Data Integrity (DI)** and **GxP control** at every stage, providing the quantitative justification for efficiency gains.

Depending on the organization needs several workflows[131] can be created for each of the modules of an eQMS using native system configuration capabilities[132]. Each workflow must be validated prior release for usage. After go-live new workflows or changes to existing workflows must be conducted in a compliant manner namely under change control process of the organization addressing all implementation and validation activities.

4.3.1 DMS Workflow: SOP Creation & Approval Cycle [133]

This workflow ensures full lifecycle control of regulated documents (e.g., SOPs, Work Instructions), compliant with 21 CFR Part 11 electronic signature requirements. This automated sequence drastically reduces the cycle time required in manual or hybrid systems[134]. Note that an effective Document Management system must contain most ,if not all, documents of the organizations GMP Documents Quality pyramid and their relationships. This will not only add value by providing a readily available document correlation matrix but also play a pivotal role in version changes of a document where impact to all related or referenced documents can be easily found and assessed for necessary changes.

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131 Horace Gumba et al., “Implementation of an Electronic Quality Management System Using Q-Pulse: The KEMRI-Wellcome Trust Research Laboratories Experience,” *Annals of Clinical and Laboratory Research*, 2019.

132 Tahir Ahmad and Amy Van Looy, “Business Process Management and Digital Innovations: A Systematic Literature Review,” *Sustainability* 12, no. 17 (2020): 6827, https://doi.org/10.3390/su12176827.

133 Preeti Kulkarni and Charmy Kothari, “Documentation and Data Integrity in Pharmaceutical Industry,” in *Modern Aspects of Pharmaceutical Quality Assurance: Developing & Proposing Application Models, SOPs, Practical Audit Systems for Pharma Industry*, ed. Minal Ghante et al. (Springer Nature, 2024), https://doi.org/10.1007/978-981-99-9271-3_11.

134 Hang Thu Pho and Torben Tambo, “Integrated Management Systems and Workflow-Based Electronic Document Management: An Empirical Study,” *Journal of Industrial Engineering and Management* (Barcelona, Spain) 7, no. 1 (2014): 194–217, https://doi.org/10.3926/jiem.846.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Initiate Draft	Author creates a new document or a minor revision (e.g., V01.01) within a standardized template.	Document Author	**Control:** Auto-assigned unique **Document ID**. File is automatically watermarked "**DRAFT**" and is only editable by the Author and System Admin.
2. Review Cycle	Departmental Subject Matter Experts (SMEs) and Supervisors review content for technical accuracy and feasibility.	SMEs/Supervisors	**Gate:** All assigned reviewers must complete the review and provide an **e-signature (Part 11 compliant)**. Overdue tasks trigger automatic system escalation to management.
3. Quality Assurance (QA) Review	QA verifies compliance with regulatory requirements (GxP), corporate standards, and ensures correct linkages to other quality documents.	QA Specialist	**Mandatory Gate:** QA must **approve**; if rejected, the workflow returns to Step 1. The QA approval **locks the content** before final release.
4. Final Approval/Release	Document Owner/Site Head provides final authorization, committing the organization to the document.	Document Owner	**21 CFR Part 11 e-Signature** required. Triggers the document to be assigned the next **major version number** (e.g., V02.00) and sets the mandatory *Effective Date*.
5. Training Assignment	System automatically assigns the new effective version for training to all impacted personnel (linked via Job Role Codes).	Training Coordinator/System	**System Check:** Verifies the document is linked to appropriate **Job Codes** for targeted training. Completion is logged in the Training Management System (TMS).
6. Release	Document is moved to the "**Effective**" status, making it the sole accessible version for users.	System/QA	**Audit Trail:** Records the exact date/time of status change. All previous versions are automatically moved to "**Obsolete**" and secured in the archive, accessible only by authorized personnel.
7. Controlled Printing	System allows for document controlled printing, who, when and for what purpose requested the print. Also controlled printing allows for	System	**21 CFR Part 11 e-Signature** required for the print job and its status update.**Audit Trail:** Records the exact date/time of the print job and adds a watermark and a unique identifier to

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
	document distribution tracking after the print.		the printout.

4.3.2 Change Control Workflow: Major Change Implementation [135]

This workflow enforces a risk-based approach to all changes (e.g., equipment, process, documentation), ensuring validation and regulatory impacts are addressed and approved before execution. This digital process prevents unauthorized or unassessed changes, a key compliance failure point in paper systems.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Request Initiation	User submits the change request, detailing modification, rationale, and preliminary scope.	Requestor	**System Control:** Auto-assigns a sequential **Change Control ID** and date/time stamp.
2. Initial Risk Assessment & Classification	QA evaluates the potential impact (product quality, patient safety) and assigns a classification (e.g., Major, Minor).	QA Specialist	**Workflow Branching:** Major changes are auto-routed to the **Quality Review Board (QRB)**. The system enforces a mandatory link to a risk assessment record (QRM module).
3. Detailed Assessment	Relevant departments (Validation, Regulatory, Engineering) assess required actions (e.g., re-validation protocols, regulatory filing requirements, document updates).	Cross-functional Team	**Mandatory Gate:** A detailed **Impact Assessment form** (signed by all impacted departments) must be completed, locking the planned execution steps.
4. Approval of Plan	QRB/Site Management approves the comprehensive implementation and testing plan.	QRB/Change Owner	**Go/No-Go Decision:** Final **e-signature** locks the plan, authorizing resource commitment and formalizing the validation strategy.

[135] Walvekar et al., “Deviation, Change, Control, and CAPA.”

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
5. Implementation & Verification	Execution of the change (e.g., equipment installation, document updates, OQ/PQ testing).	Implementation Team	**System Check:** The system verifies all linked actions (CAPAs, work orders, validation protocols) are **closed and verified** before proceeding to the final closure step.
6. Closure & Effectiveness Check	QA verifies documentation (e.g., final validation report is attached) and schedules a **post-implementation effectiveness review** (e.g., 90 days out) to confirm the change did not introduce new risks.	QA Specialist	**Mandatory Gate:** Final closure requires sign-off on the **Effectiveness Check completion date**. The system archives the complete Change Control record.

4.3.3 Deviation Management Workflow: Intake and Investigation [136]

This workflow focuses on the immediate logging, containment, and root cause analysis (RCA) of the non-conformance event.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Deviation Intake & Containment	Log the non-conformance, its classification (Critical/Major/Minor), and document immediate containment actions.	Initiator	**System Control:** Auto-links the event to the affected batch/product. System auto-assigns a unique **Deviation ID** and records the time of receipt (start of investigation clock).
2. Investigation Ownership	QA assigns a formal investigator, required cross-functional team members, and sets mandatory due dates for the investigation.	QA Specialist	**System Check:** System sends **automated notifications and escalations** for overdue investigation tasks, enforcing timeliness.
3. Root Cause Analysis (RCA)	Investigation team uses integrated tools (e.g., 5 Whys, Fishbone	Investigation Team	**Mandatory Gate (Phase Completion):** RCA section must be

[136] Walvekar et al., “Deviation, Change, Control, and CAPA.”

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
	Diagram) to determine the true root cause, documenting all evidence.		**signed-off by the Investigation Owner and QA**. If a systemic CA/PA is required, the system *must* trigger and link to the dedicated CAPA workflow (4.3.4).
4. Deviation Closure	QA reviews the investigation conclusion and approves the deviation report closure, provided all immediate actions are complete and a linked CAPA has been initiated (if necessary).	QA Reviewer	**Control:** Requires a **Part 11 e-signature** for approval, locking the deviation record as submitted and audited.

4.3.4 CAPA Implementation Workflow: Action, Verification, and Closure [137]

This new, separate workflow focuses exclusively on the mandated **Corrective Action (CA) and Preventive Action (PA)** plan execution and the crucial closed-loop verification process.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. CAPA Action Plan Development	Develop Corrective (CA) and Preventive (PA) Actions based on the RCA findings, assigning owners and due dates.	CAPA Owner	**Workflow Linkage:** Automatic creation and tracking of all required actions (including re-training, equipment maintenance) as sub-tasks linked back to the Deviation record.
2. CAPA Action Implementation	Execution and documentation of the planned CA/PA actions by the assigned owners.	Action Owners	**Control:** System requires **evidence attachment** (e.g., training records, maintenance report) and formal **e-signature** to confirm action completion.
3. QA Review & Approval	QA reviews the action completion evidence and the overall plan for adequacy, completeness, and prevention of recurrence.	QA Reviewer	**Segregation of Duties (SoD):** Enforced check that the QA Reviewer cannot be the original action owner. Requires a **Part 11**

[137] Hung et al., “Critical Factors in Adopting a Knowledge Management System for the Pharmaceutical Industry.”

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
			e-signature.
Step 4. Knowledge Capture & Transfer	CAPA Owner summarizes the "Lesson Learned" (i.e., the specific insight or systemic correction) based on the final RCA and action plan, submitting the data to the KM module.	CAPA Owner	**Submission of the "Lessons Learned" structured summary** and creation of a linked **KM record (Module 10)** is required before proceeding to the Effectiveness Verification (EV)
5. CAPA Effectiveness Verification (EV)	System triggers verification after action closure to confirm the action **solved the problem and prevented recurrence**. This verification is scheduled for a future date (e.g., 6 months).	Verification Owner	**Mandatory Gate (Closed-Loop Principle):** Final closure of the CAPA is dependent on **verified effectiveness** and is locked by a final QA e-signature.

4.3.5 OOS / OOT (QC Events): Investigation and Resolution [138]

This specialized workflow strictly enforces compliance with regulatory guidance for lab results (Out-of-Specification/Out-of-Trend), protecting batch disposition integrity. The system's role is to mandate the sequential, phased investigation required before a final batch decision can be made.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Event Detection & Initial Alert	Analyst notes OOS/OOT result, ceases further testing, and logs the event in the eQMS module.	QC Analyst	**Auto-Alert:** System locks the affected test record and triggers the OOS/OOT workflow. **Data Linkage:** Mandatory link to original raw analytical data (e.g., from LIMS/instruments).
2. Phase 1: Lab Investigation	QC Supervisor checks calculations, equipment calibration status, sample preparation, and test procedure adherence to determine if an **Assignable Lab Error** occurred.	QC Supervisor	**Mandatory Gate:** Phase 1 conclusion (Assignable Lab Error or Non-Lab Error) must be documented and **signed-off (e-signature)** before proceeding.

[138] Walvekar et al., “Deviation, Change, Control, and CAPA.”

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
3. QA Review of Phase 1 Conclusion	QA reviews the Phase 1 documentation to validate if the conclusion is justified and compliant.	QA Specialist	**Control:** If the OOS is confirmed as a **Non-Lab Error**, the system automatically routes the investigation to Phase 2 (Broader/Manufacturing Investigation).
4. Phase 2: Full Investigation	Broader investigation into manufacturing process records, equipment deviation history, and material quality to find the **Root Cause** of the OOS result.	Inter-Departmental Team	**Workflow Linkage:** Mandatory linkage to a formal **CAPA/Deviation** module entry for thorough root cause determination and corrective action tracking.
5. Final Disposition & Closure	QA determines the final disposition of the batch (e.g., release, reject, or rework) and approves the full investigation report.	QA Manager	**Mandatory Gate:** Final disposition requires a **Part 11 e-signature**. The OOS record must be immutable and complete for regulatory submission.
6. OOT Alerting & Prevention	(System Function)	System	**Control:** Integrated **Statistical Process Control (SPC)** tools continuously monitor test data (e.g., purity, potency) to alert QA before results hit the OOS limit (OOT), enabling **predictive intervention**.

4.3.6 Training Management System (TMS): New Hire Training Curriculum [139]

This workflow links personnel records directly to required training curricula and the Document Management System (DMS)[140], ensuring continuous qualification compliance and mitigating the risk of untrained personnel performing GxP tasks.

[139] Yaser Dahman et al., "Overview of Good Manufacturing Practices (GMP)," 2025, https://doi.org/10.1016/B978-0-443-23848-2.00010-3.

[140] "Standard Operating Procedures (SOPs) and Auditing in Bioprocess Industries," in *Biotechnology Engineering* (Elsevier, 2025), https://doi.org/10.1016/B978-0-443-31476-6.00004-X; Pai, *Personnel Training for Pharmaceutical Industry*.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. User Creation & Assignment	HR/System Admin creates the new employee profile and assigns the required **Job Role Code** based on their function.	HR/System Admin	**System Control:** System automatically assigns the relevant Training **Curriculum** (set of SOPs and WIs) linked to that code.
2. Initial Training Completion	Employee completes assigned tasks (reading SOPs, passing required quizzes, viewing training media).	Employee	**Control:** Access to critical **GxP systems/equipment is restricted** until initial mandatory training is complete and recorded in the TMS.
3. Competency Assessment	Employee completes the required assessment/quiz linked to the document.	Employee	**Workflow Trigger:** If the employee fails, a mandatory **re-training cycle** is triggered and documented before a second attempt is allowed, ensuring competency.
4. Qualification Sign-off	Supervisor confirms the employee has demonstrated the ability to perform the job functions.	Supervisor	**Evidence of Completion:** Supervisor's **e-signature** locks the initial training record, marking the employee as "Qualified" for that curriculum.
5. Recertification Cycle	System monitors the revision status and effective date of all documents linked to the curriculum.	System	**Workflow Trigger:** If a trained SOP is revised (DMS Step 6), the system automatically creates a **re-training task** for the new version, ensuring ongoing compliance without manual intervention.
6. Compliance Dashboard	(System Function)	System/QA	**Control:** Real-time metrics display the percentage of personnel compliant with their assigned training curriculum, providing immediate feedback for audit readiness.

4.3.7 Audit Management Workflow: Internal Audit Cycle[141] [142] [143]

This workflow ensures systematic, traceable execution of internal and external audits, focusing on evidence collection, finding resolution, and improving overall audit readiness. The system's control over finding linkage is critical for preventing issues from falling through the cracks.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Planning & Scheduling	QA schedules the audit (Internal, Supplier, Regulatory) and defines the scope, criteria, and audit team.	QA Manager	**Control:** System tracks and flags mandatory regulatory audit frequency (e.g., annual) and enforces the creation of an Audit Plan record.
2. Checklist & Preparation	Lead Auditor finalizes the audit checklist and requests necessary pre-audit GxP documents and records from the audited area.	Lead Auditor	**Workflow Linkage:** System pulls relevant documents directly from the **DMS module**, ensuring only the effective versions are reviewed.
3. Execution & Finding Generation	The audit is conducted; findings and observations are formally documented and categorized (Critical/Major/Minor).	Audit Team	**Data Integrity:** Findings are non-editable once officially submitted by the Lead Auditor and are timestamped and attributed.
4. Report Finalization & Review	Draft audit report is generated. The Audited Area Manager reviews the findings for acknowledgment and feasibility of response.	Lead Auditor / QA	**Gate:** Audited Area Manager must formally **acknowledge the findings via e-signature** before the report is finalized and officially issued.
5. CAPA Linkage & Assignment	The system automatically creates formal **CAPA records** for all critical	QA Specialist	**Mandatory Control:** Audit report cannot be formally closed until

[141] Sindhuja Kannan et al., *Auditing as A Management Tool in Pharmaceutical Companies*, n.d.

[142] Mohini Tawade and Sudhir Pandya, *Optimizing Pharmaceutical Quality Audits: Enhancing Compliance and Performance through Best Practices*, 12, no. 03 (2023).

[143] "Article-The-Pharma-Innovation-Journal-2019-08-02-00709-713-Lebedynets-V.O.-Karamavrova-T.V..Pdf," n.d., accessed December 4, 2025, https://quality.nuph.edu.ua/wp-content/uploads/2019/06/Article-The-Pharma-Innovation-Journal-2019-08-02-00709-713-Lebedynets-V.O.-Karamavrova-T.V..pdf.

	and major findings, ensuring they are tracked as part of the closed-loop system.		**all resulting CAPAs are formally initiated** and assigned owners in the CAPA module.
6. Closure & Follow-up	QA verifies that all linked CAPAs are tracked to closure and that effectiveness checks (if required) are scheduled.	QA Manager	**Final Gate:** Audit is marked "**Closed**" only after CAPA linkage is confirmed, ensuring all issues are tracked to verified resolution.

4.3.8 Customer Audit Workflow: Hosting and Response[144] [145]

This workflow focuses on managing audits from external partners (Customers/Partners), ensuring rapid evidence retrieval to maintain commercial trust, and managing the approval of corrective actions by the external party.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Audit Request & Scheduling	Customer submits audit agenda. QA logs the event and blocks resources in the system calendar.	QA Host	**System Check:** System prevents scheduling conflicts with other major quality events (e.g., Regulatory Inspections or Plant Shutdowns).
2.Scope Definition & Access Setup	Define the specific systems, products, and areas the customer is authorized to view (e.g., specific batch records).	QA Manager	**Access Control:** System generates a temporary "Auditor View" account restricted strictly to the defined scope (e.g., only Product X records), hiding all other proprietary data.
3.Audit Execution (Front/Back Room)	Host the audit. "Runners" retrieve requested documents digitally from the DMS for review.	Audit Team	**Audit Trail:** The system logs every document opened, viewed, or printed during the audit session for security and traceability.
4.Receive & Log Observations	Customer sends final report. Findings are logged and risk-assessed.	QA Host	**Workflow Linkage:** Findings must be linked to the specific Product/Batch record to tag potential "at-risk" inventory in the ERP/Inventory system
5.Response & Plan	Draft the CAPA plan. Unlike	QA / Customer	**External Gate:** The workflow halts until

[144] Kannan et al., *Auditing as A Management Tool in Pharmaceutical Companies*.

[145] Tawade and Pandya, *Optimizing Pharmaceutical Quality Audits: Enhancing Compliance and Performance through Best Practices*.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
Approval	internal audits, this plan must be sent to and approved by the Customer.		an "External Approval" flag (email attachment or portal click) is recorded from the customer.
6.Commitment Tracking	Track specific promises made to the customer (e.g., "We will update the SOP by Q3").	System	**Alerting:** System sends "Commitment Due" alerts 30 days prior to the deadline to prevent commercial breach of contract.

4.3.9 Regulatory Authority Inspection Workflow (e.g., FDA/EMA)[146] [147] [148]

This high-stakes workflow activates the "Digital War Room," focusing on immediate retrieval, data integrity verification, and strict management of the formal response (e.g., FDA Form 483).

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1.Arrival & "War Room" Activation	Inspector arrives. System enters "Inspection Mode."	QA Head	**System Mode:** Triggers high-priority alerts to all Process Owners. Activates the "Inspection Dashboard" for real-time retrieval metrics.
2. Request Management	Inspector requests records (e.g., "Show me all complaints for Lot XYZ"). Request is logged in the system.	Scribe / Back Room	**KPI Tracking:** System tracks "Time to Retrieval" (Goal: <5 mins). Late retrieval triggers escalation to the Back Room Lead.
3. Staging & Review	Records are retrieved and reviewed by SMEs before being released to the inspector to ensure completeness.	SME / QA	**Digital Gate:** Documents cannot be projected/shared in the Front Room until the Back Room QA clicks "Release to Inspector."

[146] Al Azawei et al., “The Management of Good Manufacturing Practice (GMP) Inspections.”

[147] Tawade and Pandya, *Optimizing Pharmaceutical Quality Audits: Enhancing Compliance and Performance through Best Practices*.

[148] Kannan et al., *Auditing as A Management Tool in Pharmaceutical Companies*; Tawade and Pandya, *Optimizing Pharmaceutical Quality Audits: Enhancing Compliance and Performance through Best Practices*.

4. Daily Wrap-Up & Mitigation	Log daily observations. Initiate immediate containment actions if critical issues are found.	QA Management	**Risk Linkage:** Immediate linkage to the **QRM Module** to assess the impact of observations on license status or batch release.
5. Formal Response (483/EIR)	Receipt of formal findings. Drafting the response within mandatory statutory timelines (e.g., 15 days for FDA).	Regulatory Affairs / QA	**Regulatory Timer:** System acts as a statutory clock, sending daily countdown alerts to the Executive Team until the response is submitted
6.Commitment Verification	Execution of commitments made to the agency.	QA / Compliance	**Mandatory Lock:** All Regulatory Commitments are locked records; they cannot be modified or rescheduled without Head of Quality e-signature.

4.3.10 Supplier Quality Management (SQM) Workflow: Qualification to SCAR Management [149]

This workflow manages the entire supplier lifecycle, ensuring that only qualified vendors supply critical materials and that non-conformances are formally addressed via **SCARs (Supplier Corrective Action Requests)**. The digital system enforces risk-based decisions and maintains the dynamic **Approved Supplier List (ASL)**.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Initial Request & Risk Assessment	Procurement/User requests qualification for a new supplier. QA conducts an initial risk assessment (criticality of material/service).	Requester / QA	**Workflow Branching:** High-risk suppliers (e.g., critical raw material providers) automatically require an **on-site audit** (Step 3).
2. Qualification Package Review	Supplier submits required GxP documentation (certifications, quality manual, material specifications, etc.).	QA Specialist	**Mandatory Gate:** All essential qualification documents must be present, reviewed, and **signed off by QA** before the process can advance.
3. Supplier Audit	If required by the risk level, an audit is scheduled, conducted, and documented.	Lead Auditor	**Workflow Linkage:** Findings from the audit are automatically linked to the

[149] Salimian et al., “Supplier Quality Management and Performance.”

			Audit Management module (4.3.6) and subsequently to the CAPA system for tracking.
4. Final Approval & Status Assignment	QA determines the final qualification status (e.g., Approved, Conditional, Disapproved).	QA Manager	**Control:** The system automatically updates the **Approved Supplier List (ASL)**. Only suppliers on the ASL can be used by Procurement/ERP systems.
5. Quality Event (Non-Conformance)	A quality event (e.g., incoming material non-conformance) is logged against the supplier's performance record.	QC/Receiving	**Workflow Trigger:** Non-conformance automatically triggers the **SCAR sub-workflow** (Step 6) if the issue requires supplier action.
6. SCAR Assignment & Tracking	A formal SCAR is electronically issued to the supplier with mandatory response due dates and the request for their root cause investigation.	QA Specialist	**Control:** The supplier's ASL status may be downgraded (e.g., to "On Hold") if the SCAR is not addressed by the deadline, enforcing accountability.
7. Re-qualification Trigger	System monitors the supplier's qualification expiration date and performance history (SCAR volume).	System	**Workflow Trigger:** Automatic re-qualification workflow initiates 90 days before expiration, ensuring continuous compliance and preventing unintended use of expired vendors.

4.3.11 Risk Management[150] (QRM) Workflow: FMEA[151] and Risk Mitigation

This workflow ensures that quality risks are systematically identified, analyzed, controlled, and reviewed. It utilizes standardized methodologies like FMEA (Failure Mode and Effects Analysis) and enforces action tracking to reduce the Risk Priority Number (RPN), thereby promoting proactive quality assurance (ICH Q9).

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Risk Identification & Initiation	Define the scope (e.g., manufacturing process, new software feature) and identify potential failure modes and their causes.	Process Owner / QRM Lead	**Control:** System enforces use of a standardized GxP template (e.g., FMEA table) to ensure consistency.
2. Risk Analysis & Scoring	Assess the risk based on three factors: **Severity (S)**, **Occurrence (O)**, and **Detectability (D)**, using a defined numerical scale (e.g., 1–5).	QRM Team	**Control:** System automatically calculates the **Risk Priority Number (RPN)**: RPN = S*O*D.
3. Risk Evaluation & Prioritization	Compare the calculated RPN against a predefined **Acceptability Threshold**.	QA Reviewer	**Workflow Branching:** Risks exceeding the threshold (High/Critical RPN) automatically route to Step 4 (Mitigation).
4. Risk Control & Mitigation Plan	Develop actions required to reduce the risk score (typically by reducing 'Severity' or 'Occurrence').	Mitigation Owner	**Workflow Linkage:** Automatic creation of a linked **CAPA or Change Control** record for each mitigation action, ensuring formal tracking and closure.
5. Residual Risk Assessment	Re-score the risk after mitigation actions are implemented, calculating the new, lower **Residual RPN**.	QRM Team	**Mandatory Gate:** The residual RPN must be **below the acceptability threshold** for the risk assessment to be approved.
6. Risk Review &	QA approves the final QRM	QA Manager /	**Final Control:** The QRM record is

[150] Tim Niesen et al., "Towards an Integrative Big Data Analysis Framework for Data-Driven Risk Management in Industry 4.0," *2016 49th Hawaii International Conference on System Sciences (HICSS)*, January 2016, 5065–74, https://doi.org/10.1109/HICSS.2016.627.

[151] Zhongyi Wu et al., "Literature Review and Prospect of the Development and Application of FMEA in Manufacturing Industry," *The International Journal of Advanced Manufacturing Technology* 112, no. 5 (2021): 1409–36, https://doi.org/10.1007/s00170-020-06425-0.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
Monitoring	record. System schedules mandatory **periodic review** (e.g., annually or upon any major change).	System	locked. The system tracks the status of all linked mitigation actions until closure and effectiveness checks are complete.

4.3.12 Complaint Management Workflow: Intake, Investigation, and Reporting[152]

This workflow ensures that all product complaints are systematically logged, risk-assessed, investigated, and reviewed against mandatory regulatory reporting timelines (e.g., 24-hour, 5-day, 30-day requirements). Digital control[153] is vital for mitigating the high risk of non-compliance associated with time-sensitive reporting.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
1. Complaint Intake & Logging	Customer service or authorized user logs the complaint, capturing product ID, lot number, and detailed description.	Initiator	**Control:** System auto-assigns a unique **Complaint ID** and records the precise **date/time of receipt** (the start of the regulatory clock).
2. Risk & Triage Assessment	Review the complaint for potential severity, mandatory regulatory reporting (e.g., adverse events), and initial product impact.	Triage Specialist	**Workflow Branching:** High-severity or potentially reportable complaints automatically **fast-track** to Medical/Safety review.
3. Investigation	Detailed investigation to determine the root cause, including sample retrieval/testing and review of corresponding batch records.	Investigator	**Workflow Linkage:** System creates a linked **Deviation/CAPA record** if the complaint is confirmed to be product-related, ensuring systemic correction.
4. Medical/Safety Review	Review by a qualified professional to determine if the event meets mandatory regulatory reporting criteria	Safety Officer	**Mandatory Gate:** A formal determination of **reportability** must be documented, signed, and time-stamped, locking the regulatory

[152] Braga, “Complaint Handling in Pharmaceutical Companies”; Santosh et al., *Systematic Approach for Complaint Handling in Pharmaceutical Industries- An Updated Review*.

[153] Santosh et al., *Systematic Approach for Complaint Handling in Pharmaceutical Industries- An Updated Review*.

Step	Action/Activity	Responsible Role	Mandatory Control / Gate
	(e.g., MDRs, MedWatch).		reporting decision.
5. Regulatory Reporting & Filing	System generates the required electronic report file (if needed) and records the submission date and time.	Regulatory Affairs	**Control:** System tracks and sends **deadline alerts** when submission deadlines (e.g., 30 calendar days) are approaching, mitigating non-compliance risk.
6. Closure & Follow-up	QA approves the investigation and closure, ensuring all linked CAPAs are initiated and the regulatory filing is complete.	QA Manager	**Final Gate:** Final closure requires **e-signature** and must confirm the investigation and all required regulatory actions were completed and archived.

4.4 Non-Functional Requirements (URS Section)

Addressing the **Non-Functional Requirements (NFRs)** is crucial. These requirements define the system's performance, security[154] [155], and scalability[156]—aspects that enable the promised ROI and are key focus areas for GAMP 5 validation[157] and vendor management[158].

NFR Category	Strategic Requirement	Rationale / GxP Criticality
Performance	The system must load critical dashboards (e.g., CAPA aging report) within **3 seconds** and support **500 concurrent users** across all GxP sites during peak business hours.	Failure to meet performance requirements leads to poor user experience (UX), driving users to non-compliant workarounds.

[154] Ameni Ben Fadhel et al., "A Comprehensive Modeling Framework for Role-Based Access Control Policies," *Journal of Systems and Software* 107 (September 2015): 110–26, https://doi.org/10.1016/j.jss.2015.05.015.

[155] Das et al., "Considerations for Big Data Management in Pharmaceutical Manufacturing."

[156] Sommer, "Cloud Computing in Emerging Biotech and Pharmaceutical Companies."

[157] Daniel Friedli et al., "Validation of Computer Systems: Practical Testing of a Standard LIMS," *Pharmaceutica Acta Helvetiae*, Quality Assurance in Computer Validation Systems, vol. 72, no. 6 (1998): 343–48, https://doi.org/10.1016/S0031-6865(97)00032-0.

[158] Bastas and Liyanage, "Sustainable Supply Chain Quality Management."

NFR Category	Strategic Requirement	Rationale / GxP Criticality
Security & Access Control	Mandatory **Multi-Factor Authentication (MFA)** for all GxP functions. Strict **Role-Based Access Control (RBAC)** must be configurable to match organizational structure and enforce **Segregation of Duties (SoD)** (e.g., the person who writes an SOP cannot be the final QA approver).**Granular Data-Level Security:** The system must restrict visibility of specific records based on the user's **Site** (e.g., Site A vs. Site B) and **Product Family** (e.g., Confidential Oncology Project), ensuring users only access data relevant to their function. End-User Administrator perform User Management.	**GxP/Part 11 Mandate:** Protects electronic signatures and data integrity.
Scalability (SaaS Focus)	The vendor must demonstrate system architecture proven to scale for **Z% growth** in data volume and user count over a 5-year period without performance degradation.	Ensures the investment supports scalable business growth and avoids the need for costly replatforming.
IT Risk & Business Continuity (BCP)	Guaranteed uptime per SLA (e.g., 99.9%). Mandatory adherence to a formal **Disaster Recovery Plan (DRP)**. **Data Redundancy:** Vendor must demonstrate geo-redundant backups (data stored in two physically user-separate locations) to mitigate risks of natural disasters or localized data center failures. Set Recovery Point Objective (**RPO**) and Recovery Time Objective (**RTO**) (e.g. 4 hours RPO, 8 hours RTO)	Directly mitigates **Supply Chain Risk**. If the eQMS is down, batch release stops. Geo-redundancy ensures data survives even catastrophic regional events.
Integration	Must have published, validated **APIs/web services** to integrate seamlessly with other critical enterprise systems (e.g., LIMS, ERP, MES) for data exchange (e.g., batch data to Deviation/OOS).Also interfaces with BI Tools.	Ensures end-to-end data flow and eliminates manual data entry, which is a major Data Integrity risk.
User Experience (UX)	The eQMS design must prioritize an intuitive user interface to minimize complexity and training time.	**OCM Focus:** Promotes user adoption and maintains high data quality; difficult systems lead to non-compliant workarounds.
Multiple environments	The system uses a multi-tenant platform infrastructure and should have test, quality, production environments	Having test, quality and production environments serves for compliant change control procedures. Unofficial

NFR Category	Strategic Requirement	Rationale / GxP Criticality
		explorative testing is performed on test environment, quality environment reserved for official testing of changes initiated via change control and validation purposes and change is promoted to production environment after successful testing.
Private cloud (optional)	Software vendor is restricted from performing unauthorized changes and upgrading versions without the customer notification and consent. In case of version changes those are provided in a list alongside an impact assessment of the changes. Validation of changes and new versions must follow GAMP-5 validation principles.	**CSV/CSA focus**: system changes and upgrades are performed in a compliant manner to keep the software validation status compliant.

Advanced Reporting and Quality Metrics

The eQMS must move beyond mere documentation to become a strategic decision-making tool[159]:

Real-time Quality Dashboards:[160] [161]Capability to generate and display key quality metrics (KPIs) in real-time (e.g., CAPA aging, deviation recurrence rates, audit findings by site) for management review.

Trend Analysis and SPC: Embedded **Business Intelligence (BI)** tools capable of performing trend analysis and providing statistical process control (SPC) charts[162] for proactive quality monitoring (OOT alerting).

[159] Avigdor Zonnenshain and Ron S. Kenett, "Quality 4.0—the Challenging Future of Quality Engineering," *Quality Engineering* 32, no. 4 (2020): 614–26, https://doi.org/10.1080/08982112.2019.1706744.

[160] Niesen et al., "Towards an Integrative Big Data Analysis Framework for Data-Driven Risk Management in Industry 4.0."

[161] Ullagaddi, "Digital Transformation Strategies to Strengthen Quality and Data Integrity in Pharma."

[162] Sung Hyun Park et al., "Building a New Culture for Quality Management in the Era of the Fourth Industrial Revolution," *Total Quality Management & Business Excellence* 28, nos. 9–10 (2017): 934–45, https://doi.org/10.1080/14783363.2017.1310703.

Data Export[163]**:** Efficient capability to export and manipulate validated GxP data for regulatory submissions and internal management review.

4.5 Mapping of Digitalization Gaps and Value Delivery

This section serves as a quantitative bridge between the problem statement (1.2) and the financial analysis (Chapter 6). It uses the detailed workflows developed in 4.3 to highlight the tangible operational improvements enabled by the eQMS.

The analysis quantifies the estimated average reduction in cycle time and costs[164], demonstrating how the digital process directly solves the inefficiencies[165] of the paper-based/hybrid legacy system.[166]These operational efficiency gains—specifically the reduction in cycle times and manual administrative linkages—serve as the input parameters for the 'Savings Factor' variable in the simulation model presented in Chapter 6

Note: Cycle time reductions represent calendar duration (including waiting time). Financial ROI (Chapter 6) is calculated based on 'Man-Hour Effort' savings (active working time), which is a subset of the total cycle time

Quality Process (Workflow)	**Legacy/Paper-Based Constraint**	**eQMS Digital Assurance Result**	**Estimated Cycle Time Reduction**
Change Control Closure	Manual routing, paper signatures, non-centralized approval forms.	Automated sequential routing/escalation, electronic signature enforcement, centralized tracking.	**Reduction:** 45 days (Avg. 90 to 45 days)
Document Approval Cycle (SOP)	Physical movement, dependence on in-office presence for wet ink signatures.	Parallel review workflows, mobile access for e-signature, automated training triggers.	**Reduction:** 10 days (Avg. 14 to 4 days)
CAPA Final Closure	Delay awaiting	System-mandated effectiveness	**Reduction:** 60 days (Avg.

163 Davis et al., “Cloud Solutions for GxP Laboratories.”

164 Tawade and Pandya, *Optimizing Pharmaceutical Quality Audits: Enhancing Compliance and Performance through Best Practices*.

165 Ullagaddi, “Leveraging Digital Transformation for Enhanced Risk Mitigation and Compliance in Pharma Manufacturing.”

166 Glenn Hole et al., “Digitalization in Pharmaceutical Industry: What to Focus on under the Digital Implementation Process?,” *International Journal of Pharmaceutics: X* 3 (December 2021): 100095, https://doi.org/10.1016/j.ijpx.2021.100095.

Quality Process (Workflow)	Legacy/Paper-Based Constraint	eQMS Digital Assurance Result	Estimated Cycle Time Reduction
	paper-based effectiveness check verification and physical archiving.	verification step, digital record linking, automated audit trail.	120 to 60 days)
Audit Preparation Time	Physically compiling and retrieving records from decentralized archives (the "War Room" scramble).	Instant, centralized retrieval of all validated GxP records (DMS, CAPA, Training) using a secure electronic inspection room.	**Reduction:** 80% of QA/IT labor hours.
Training Reconciliation	Manual tracking of completion, cross-referencing personnel files with document versions.	Automatic assignment upon document release, real-time compliance dashboards, e-signature proof of reading.	**Reduction:** 95% of administrative effort, 0% risk of using untrained personnel.

This value mapping confirms that the transition to an eQMS delivers not only compliance but also measurable operational efficiency[167], directly informing the financial justification in Chapter 6.

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[167] Gomaa, *Quality Management Excellence in the Era of Industry 4.0 (Quality 4.0): A Comprehensive Review, Gap Analysis, and Strategic Framework*.

Chapter 5 Implementation, Validation, and Strategic Impact

5.1 GAMP 5 Validation and Implementation Strategy (Cloud SaaS)

This chapter addresses the specific methodological strategy required to implement the eQMS blueprint (Chapter 4) while maintaining strict adherence to GxP requirements. The core challenge is leveraging the efficiency of the SaaS model without compromising the pharmaceutical company's ultimate accountability for patient safety and data integrity. [168]

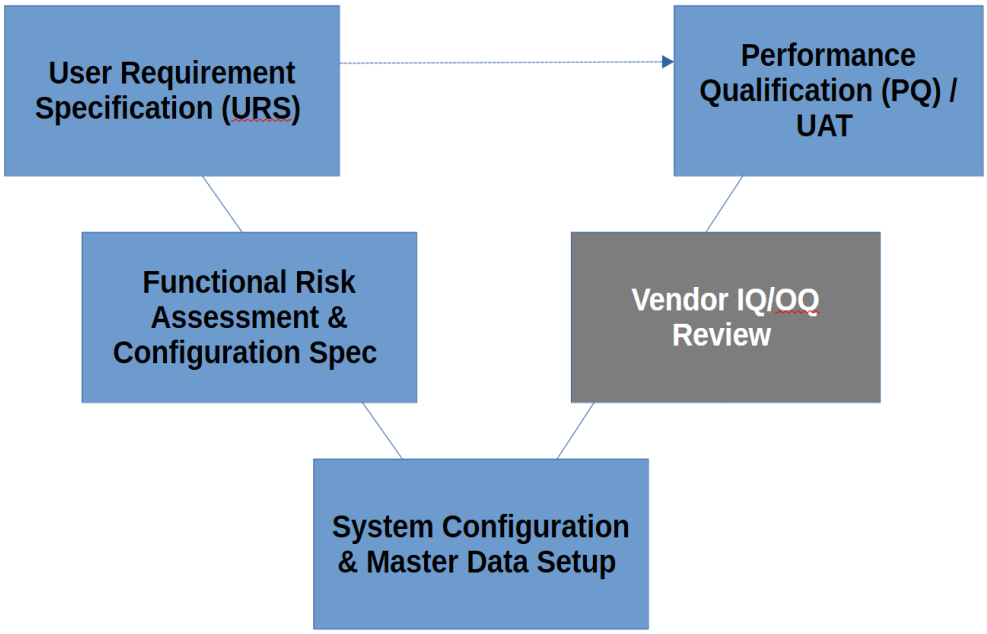

Figure 2: The GAMP 5 V-Model adapted for SaaS eQMS Configuration. *Source: Author's elaboration, based on ISPE GAMP 5 (2nd Edition).*

[168] Francisca Pedro et al., "Impact of GAMP 5, Data Integrity and QbD on Quality Assurance in the Pharmaceutical Industry: How Obvious Is It?," *Drug Discovery Today* 28, no. 11 (2023): 103759, https://doi.org/10.1016/j.drudis.2023.103759.

5.1.1 GAMP 5 Risk-Based Validation Approach for SaaS[169]

For a Cloud (SaaS) eQMS, the validation strategy must be explicitly risk-based, differentiating between the system's inherent functions (provided by the vendor) and the company's unique configuration (owned by the user).

1. **System Categorization:** A COTS eQMS, which is configured to match specific GxP workflows (e.g., the Change Control steps detailed in 4.3.2), is typically classified as **GAMP Category 4 (Configurable Software)**. This classification mandates that the validation effort focuses primarily on the **configuration and the unique workflows**.
2. **Mandate for Prospective Validation:** Unlike legacy on-premise remediation projects which often utilize retrospective validation, the deployment of a new Cloud SaaS eQMS requires a strictly **Prospective Validation** strategy. Because the SaaS environment is dynamic, the system must be fully qualified (IQ/OQ/PQ) prior to Go-Live. Retrospective validation is restricted solely to the *Data Migration* phase (verifying that historical data from the legacy system was transferred correctly), ensuring a clear "cut-over" to the new, proactively validated state.
3. **Customization and Validation Risk Mitigation**:Any necessary configuration must be closely managed, as every layer of customization moves the system closer to a high-risk **GAMP Category 5 (Custom/Hybrid)** classification. From a TCO perspective, **customization exponentially increases the complexity, time, and cost of validation** for initial deployment and ongoing maintenance. The validation strategy must therefore include a robust **Change Request Review Board** focused on challenging business users to adapt their processes to OOTB functionality before approving any custom development, thus safeguarding the system's long-term upgradability and cost efficiency.
4. **Leveraging Supplier Documentation (IQ/OQ):** A critical efficiency gain in the SaaS model is the ability to rely on the vendor's evidence. The pharmaceutical company does not need to re-validate the underlying software code or the cloud infrastructure. Instead, the strategy involves:

   Vendor Audit:[170] Conducting a thorough initial and periodic audit of the vendor's QMS and their compliance evidence (e.g., SOC 2 reports).

   Assessment of Vendor's IQ/OQ: Reviewing and formally accepting the vendor's Installation Qualification (IQ) and Operational Qualification (OQ) reports, which prove the software application and cloud infrastructure are installed and function correctly.

[169] Ullagaddi, “Cloud Validation in Pharma: Compliance and Strategic Value.”

[170] Sommer, “Cloud Computing in Emerging Biotech and Pharmaceutical Companies.”

5. **Shared Responsibility Model[171]:** The core of the Cloud validation strategy is the clear delineation of responsibilities[172], formally documented in the Quality Agreement (QA) and Validation Plan (VP).

Responsibility Area	User (Pharmaceutical Company)	Supplier (SaaS Vendor)
Platform/Infrastructure	Ongoing review and audit of security.	Maintenance, patching, security, and continuous qualification of the Cloud platform (IaaS/PaaS).
Software Code Functionality	**Performance Qualification (PQ)** of business processes.	Development, validation (IQ/OQ), and release of software updates and new features.
Data Integrity & Configuration	Defining the **URS**, configuring workflows, managing user access, and ensuring **data quality**.	Providing the validated tools (e.g., audit trail, e-signature functionality).

This model ensures the company focuses resources on testing the **unique high-risk areas** (their specific GxP workflows), while accepting the vendor's assurances on the low-risk, non-configurable core functions.

5.1.2 Validation Deliverables and Activities

The validation process follows the V-Model, focusing on generating the following key deliverables, scaled according to the risk-based approach:

1. **Validation Plan (VP):** The initial, overarching document defining the project scope, validation strategy (including GAMP 5 classification and the Shared Responsibility Model), roles, responsibilities, and acceptance criteria.
2. **Installation Qualification (IQ):** Focuses on verifying the successful installation of the software in the user's specific environment. For Cloud SaaS, this primarily involves verifying the proper **configuration of the cloud instance, security settings, user roles, and access controls[173]** against the requirements in the URS.
3. **Operational Qualification (OQ):** Tests the core functional requirements (FRS) defined in Chapter 4. This phase ensures the system's functions (e.g., e-signature integrity, automatic routing, audit trail generation) work correctly and as expected by the vendor's specifications.

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[171] Reyes and Mendoza, *Exploring the Impact of Shared Responsibility Models on Cloud Security Posture and Vulnerability Management*.

[172] Hamed Tabrizchi and Marjan Kuchaki Rafsanjani, "A Survey on Security Challenges in Cloud Computing: Issues, Threats, and Solutions," *The Journal of Supercomputing* 76, no. 12 (2020): 9493–532, https://doi.org/10.1007/s11227-020-03213-1.

[173] Tabrizchi and Kuchaki Rafsanjani, "A Survey on Security Challenges in Cloud Computing."

4. **Performance Qualification (PQ):** This is the most crucial phase owned by the user. It tests the system in a real-world, **end-to-end business process scenario**. For instance, a PQ test case would run through the entire CAPA workflow (4.3.3) from initiation to effectiveness check closure, ensuring the configuration supports the company's unique GxP requirements.

5.1.3 Strategic Implementation and Change Management

The validation process must be tightly integrated with the overall implementation roadmap and the OCM strategy[174] (2.6).

Implementation Phases: The project must proceed through controlled phases: Selection, Configuration/Design, Data Migration (moving legacy records), Validation (IQ/OQ/PQ), Go-Live, and Post-Implementation Review.

OCM Role: The OCM strategy is critical during the validation phase. Users, trained and supported by the OCM plan, must be fully involved in writing and executing the PQ test scripts. This involvement builds **system ownership** and validates the system's fitness for use, directly addressing potential user resistance before go-live.

5.2 Measuring Operational Impact (Quantitative Analysis)

The successful strategic deployment of a Cloud eQMS must be validated not only through GxP compliance but also through measurable operational improvements. This section defines the quantitative metrics used to assess the "before and after" impact of the digitalization project, directly addressing Research Question Q1.

The analysis is structured around three categories of metrics that demonstrate value realization beyond compliance: Quality, Efficiency/Cost, and Compliance Readiness.

[174] Kasei Miura et al., “A Proposal of Architecture Framework and Performance Indicator Derivation Model for Digitalization of Quality Management System,” in *Innovation in Medicine and Healthcare*, ed. Yen-Wei Chen et al. (Springer, 2021), https://doi.org/10.1007/978-981-16-3013-2_11.

5.2.1 Key Performance Indicators (KPIs)[175] [176] [177] and Key Risk Indicators (KRIs)

KPI Category	Metric	Definition and Goal	Link to eQMS Module
Quality Metrics	**Right First Time (RFT) Rate**	Percentage of batches, deviations, or documents passing their first review/submission cycle without requiring rework. **Goal:** Increase RFT by improving documentation accuracy and process control.	CAPA, Deviation, DMS
	Deviation Recurrence Rate	Frequency of similar deviation types occurring within a specified period (e.g., recurrence by process, equipment, or site). **Goal:** Decrease recurrence by enforcing robust Root Cause Analysis (RCA) and permanent CAPA effectiveness checks.	CAPA, QRM
	CAPA Backlog Size	Number of open CAPAs exceeding their established due dates. **Goal:** Reduce backlog to near zero by enforcing digital escalation and tracking timeliness.	CAPA
Efficiency/Cost Metrics	**Average Cycle Time Reduction**	Time saved in days/hours for high-volume processes (e.g., Document Approval, Change Implementation, Batch Release). **Goal:** Calculate the financial value of time saved (used in ROI model).	DMS, Change Control, OOS
	Training Completion Rate	Percentage of required GxP training completed on time per user/role. **Goal:** Increase completion rate to maintain continuous personnel qualification compliance.	TMS
	Administrative Overhead Cost	FTE-hours spent on non-value-added activities (e.g., filing, searching for records, manual signature gathering). **Goal:** Re-deploy	DMS, Audit Management

[175] Urszula Balon et al., "KEY PERFORMANCE INDICATORS (KPIs) IN THE QUALITY MANAGEMENT SYSTEM."

[176] "FDA Quality Metrics | ISPE | International Society for Pharmaceutical Engineering," accessed November 16, 2025, https://ispe.org/initiatives/quality-metrics/fda-quality-metrics.

[177] ISPE, *ISPE Quality Metrics Initiative - Quality Metrics Pilot Program - Wave 2*, June 2016, https://ispe.org/sites/default/files/regulatory/2023/QMWAVE2DL.pdf.

KPI Category	Metric	Definition and Goal	Link to eQMS Module
		administrative resources to value-added quality roles.	
Compliance Readiness	**Inspection Readiness Time**	Time required to compile all requested GxP records (e.g., the last 10 CAPAs, related change controls, and training records) during an audit. **Goal:** Reduce time from days to minutes using the electronic "War Room."	Audit Management, DMS
	Data Integrity Index (DI)	A computed score reflecting the rate of audit trail failures, data omissions, or manual data entry errors. **Goal:** Near-perfect DI index enforced by automated system controls.	All Modules (Audit Trail)

Strategic Key Risk[178] Indicators (KRIs) for eQMS

KRI Category	Metric	Risk Signal (What it predicts)
Compliance Risk	**% of Open CAPAs > 60 Days**	**High Compliance Risk:** A growing backlog indicates a systemic inability to resource quality issues, often a precursor to regulatory observations ("Failure to follow procedures").
Data Integrity Risk	**Failed Login Attempts & Privileged User Activity**	**Cybersecurity Event:** A spike in failed logins or unusual activity by "Admin" accounts may signal a brute-force cyber attack or an internal threat actor.
Operational Risk	**System Availability < 99.9%**	**Business Discontinuity:** Frequent downtime disrupts batch release and supply chain reliability.
Culture Risk	**Ratio of "Human Error" Root**	**Weak Investigation Culture:** If >40% of deviations are blamed on "Human Error," it signals that true root causes (process/system) are not being identified, leading to recurrence.

[178] Davis et al., “Cloud Solutions for GxP Laboratories.”

KRI Category	Metric	Risk Signal (What it predicts)
	Causes	

5.2.2 Quantifying Value for ROI Analysis

The quantitative analysis in this phase collects the "before" metrics (using secondary data and industry benchmarks) to establish a baseline.[179] The "after" metrics will be projected based on the validated efficiency gains enabled by the digital workflows (Chapter 4). This projected improvement forms the basis for the financial quantification in Chapter 6[180].

Example: Efficiency Gain	Baseline (Paper)	Target (eQMS)	Financial Impact (Per Event)
Document Approval Cycle	14 days (Avg.)	4 days (Avg.)	10 days of labor saved
Change Control Closure	90 days (Avg.)	45 days (Avg.)	45 days of delay avoided
Deviation Investigation Cost	High (due to time extensions/fines)	Low (due to timely RCA/closure)	Reduced risk of warning letters (Cost Avoidance)

By systematically tracking and projecting these KPIs, the research transitions from discussing theoretical capability to demonstrating verifiable, bottom-line strategic value.

5.3 Managing Organizational Change and Adoption

The successful implementation of the eQMS hinges on overcoming the cultural and behavioral inertia inherent in abandoning established paper-based GxP control methods. This section details the necessary **Organizational Change Management (OCM)** strategy, drawing on the theoretical models introduced in Section 2.6 to ensure high user adoption and data quality.

5.3.1 OCM Strategy: Addressing Cultural Resistance[181]

The OCM plan must directly mitigate the **fear of transparency** associated with digital, audited workflows. Key strategies include:

[179] Pho and Tambo, “Integrated Management Systems and Workflow-Based Electronic Document Management.”

[180] Ida Foley et al., “Implementation of a Lean 4.0 Project to Reduce Non-Value Add Waste in a Medical Device Company,” *Machines* 10, no. 12 (2022): 1119, https://doi.org/10.3390/machines10121119.

[181] Ali and Johl, “Soft and Hard TQM Practices.”

Executive Sponsorship and Communication: Secure visible sponsorship from the highest level of Quality and Operations management. Communication must consistently frame the eQMS as an **investment in sustainable compliance and patient safety** (mitigating regulatory risk), not as a punitive system for tracking errors. This establishes the "Sense of Urgency" (Kotter's Model).

Stakeholder Management Plan[182]: A formal plan is required to identify resistance and manage engagement across critical groups:

Operators/Technicians: Focus training on making their daily tasks easier and faster, highlighting the elimination of repetitive paperwork[183].

QA/Compliance Staff: Re-position their roles from manual document control to **strategic data analysis** and systemic improvement (TQM alignment) [184].

IT Department: Must transition from managing on-premise hardware to acting as **IT Business Partners (ITBP)**. This requires upskilling in GxP regulations and Business Analysis[185] to help Quality stakeholders translate complex regulatory requirements into standard software configurations, effectively bridging the "Knowledge Gap" between Quality and Tech.

The ADKAR Approach to Implementation:[186] The plan should track progress against the ADKAR model to ensure users are not just trained, but motivated:

Awareness & Desire: Conduct roadshows and workshops demonstrating the **Cost of Poor Quality (COPQ)[187]** of the paper system to create a personal *desire* for change.

Reinforcement: Use early system metrics (e.g., faster document approval) to celebrate "short-term wins" and reinforce the new compliant behavior.

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182 Antony et al., “Quality 4.0 Conceptualisation and Theoretical Understanding.”

183 Ali and Johl, “Soft and Hard TQM Practices.”

184 Kashif Ali and Satirenjit Kaur Johl, “Impact of Total Quality Management on SMEs Sustainable Performance in the Context of Industry 4.0,” in *Proceedings of International Conference on Emerging Technologies and Intelligent Systems*, ed. Mostafa Al-Emran et al. (Springer International Publishing, 2022), https://doi.org/10.1007/978-3-030-82616-1_50.

185 Sheth et al., “A Systematic Approach for Identifying and Reducing Gaps between the Pharma and Software Industry and Transforming Quality through Digitalization in the Pharma Industry.”

186 Jeff Hiatt and Jeffrey Hiatt, *ADKAR: A Model for Change in Business, Government and Our Community* (2006), https://www.researchgate.net/publication/237035168_ADKAR_A_Model_for_Change_in_Business_Government_and_Our_Community.

187 Freiesleben, “The Opportunity Costs of Poor Quality.”

5.3.2 Training Strategy and System Qualification

Training serves two purposes: providing the *knowledge* and *ability* (ADKAR) to operate the system, and serving as the final step in the system's qualification (Personnel Qualification).

Role-Based Training[188]: Training must be highly segmented based on the user's role and specific access rights, focusing only on the modules and workflows they will use (e.g., only **Change Control Owner** training for Engineering). This minimizes unnecessary information and reduces resistance.

Hands-on, Real-World Simulation: Training should use the actual validated eQMS environment and focus on running end-to-end business scenarios (e.g., "Log a Deviation and link it to a CAPA"). This mirrors the **Performance Qualification (PQ)** testing, reinforcing that the system is fit for use.

Proof of Competency: The Training Management System (TMS) must electronically track not just attendance, but successful completion of required quizzes and assessments, providing secure **e-signature evidence of personnel qualification** for GxP tasks.

Effective OCM ensures that the robust technical solution built and validated in Chapters 4 and 5 is actually used correctly, guaranteeing the integrity of the data and, ultimately, the realization of the projected ROI.

Chapter 6: Strategic Impact and Conclusion

6.1 Total Cost of Ownership (TCO) and Return on Investment (ROI) Analysis

This section moves beyond operational metrics to quantify the financial feasibility and strategic value of transitioning from a legacy paper/hybrid QMS to a Cloud-based eQMS. The analysis demonstrates that the investment is strategically necessary for sustainable compliance and financially justified by its high Return on Investment (ROI).[189]

[188] Ben Fadhel et al., “A Comprehensive Modeling Framework for Role-Based Access Control Policies.”

[189] André Gil Curado and António Abreu, “Application of Lean Methodologies in the Reduction of Setup Times in the Pharmaceutical Industry,” *Millenium - Journal of Education, Technologies, and Health*, no. 8 (January 2019): 37–52, https://doi.org/10.29352/mill0208.04.00220.

6.1.1 Components of Total Cost of Ownership (TCO)

The TCO analysis identifies all direct and indirect costs over a defined period (e.g., 5 years) for the new eQMS solution, benchmarked against the frequently underestimated TCO of maintaining the current legacy/paper system[190] [191] .

Image 6.1 Total Cost of Ownership, Author: Joebite
Source:"https://www.dreamstime.com/total-cost-ownership-tco-iceberg-model-concept-price-profit-analysis-purchase-percent-above-water-surface-image249789499"

TCO Component	Legacy System Cost Contribution	Cloud eQMS Cost Contribution (SaaS)
A. Acquisition & Licensing	Low: Maintenance on aging on-premise software licenses.	**High (OpEx):** Annual or monthly recurring subscription fees (based on user count/modules).

[190] Haneen Alosert et al., "Data Integrity within the Biopharmaceutical Sector in the Era of Industry 4.0," *Biotechnology Journal* 17, no. 6 (2022): 2100609, https://doi.org/10.1002/biot.202100609.

[191] Baldwin and Cromity, "SaaS and Cloud Computing, the Rise of Compartmentalizing Users Online Via Subscription."

TCO Component	Legacy System Cost Contribution	Cloud eQMS Cost Contribution (SaaS)
B. Implementation & Validation (One-Time CapEx)	Low: Ad-hoc system modifications; High: Internal labor for manual validation (CSV) efforts.	**High:** External Consulting Fees for GxP/CSV experts; Internal Labor (QA/IT) for URS/PQ testing; **Data Migration** costs.
C. Operational & Maintenance	High: Internal IT hardware/server maintenance, server replacement (CapEx), backup/DR management.	**Low (OpEx):** Reduced internal IT staff for infrastructure; Cost of managing vendor release cycles and re-validation (reduced effort due to CSA/Shared Responsibility).However, requires operational effort for managing complex user access matrices (Site/Product visibility) to ensure data privacy.
D. Cost of Poor Quality (COPQ)	**Very High (Hidden Cost):** Batch failures, prolonged investigations, scrap, fines, and high administrative overhead (clerical labor).	**Low:** Expected decrease due to proactive quality control, trend analysis, and workflow enforcement.

The comparative TCO model proves that while the initial implementation cost of the eQMS is substantial, the long-term operational costs and the reduction in hidden COPQ[192] costs make the digital system financially superior over the 5-year life cycle[193].

[192] "What Is Cost of Quality (COQ)? | ASQ," accessed November 16, 2025, https://asq.org/quality-resources/cost-of-quality?srsltid=AfmBOop28GAIzgqHdRnBYOCznM-Cq6e3dgdCIdDzSkEgpNAuzWY091U1.

[193] Jiju Antony et al., "Quality 4.0 and Its Impact on Organizational Performance: An Integrative Viewpoint," *The TQM Journal* 34, no. 6 (2021): 2069–84, https://doi.org/10.1108/TQM-08-2021-0242.

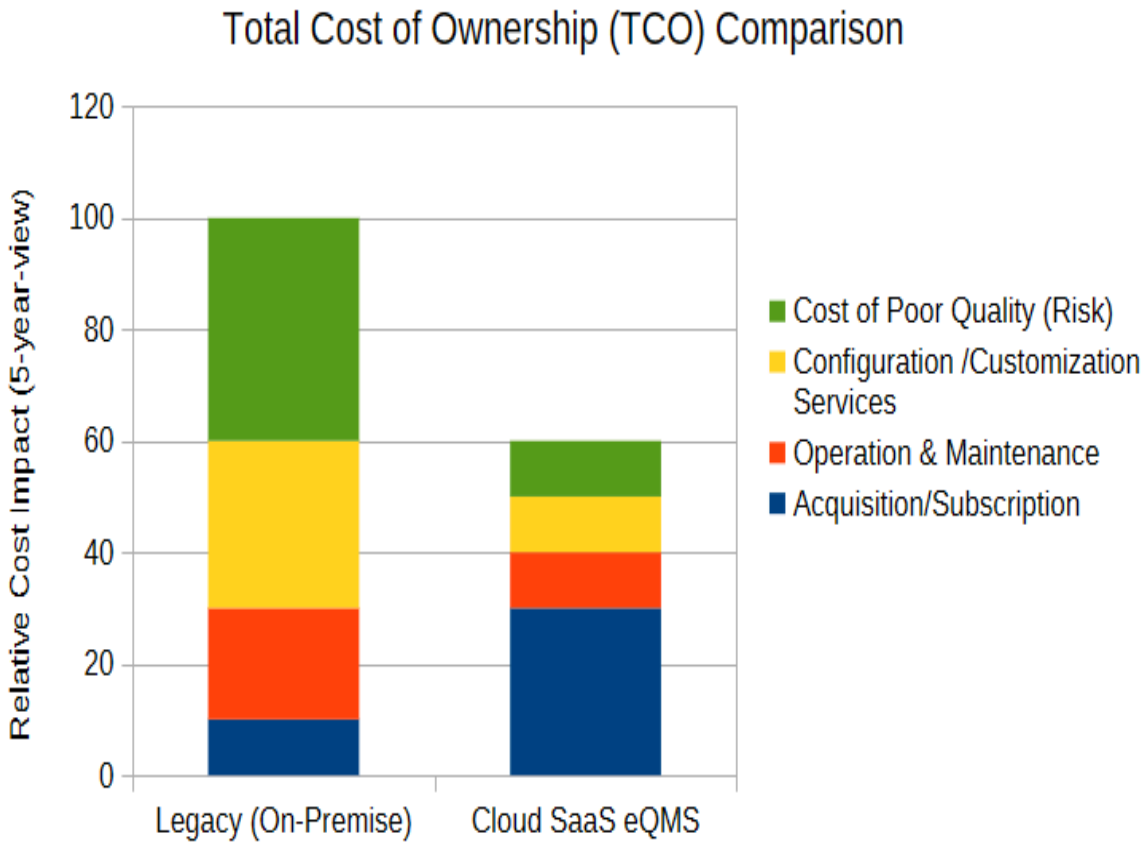

Figure 3: Comparative Total Cost of Ownership (TCO) Analysis. *Source: Author's elaboration based on TCO frameworks by Zachariassen & Arlbjørn (2011) and Schniederjans & Hales (2016)*

6.1.2 Financial Quantification of Return on Investment (ROI)

The ROI quantification is structured around three primary value drivers that convert the operational improvements (from 4.4 and 5.2) into quantifiable financial returns.

ROI = ((Total Financial Benefits - Total Costs) / Total Costs) * 100

6.1.2.1 Econometric Validation of Efficiency Gains

To validate the financial assumptions of the ROI model, a multivariate regression analysis was performed on the simulated dataset of N=1,000 observations (500 legacy, 500 digital). The model utilized a Man-Hour based cost structure (Cost = Hours * €50) to isolate the "Digital Dividend."

The Ordinary Least Squares (OLS) regression yielded a **System State coefficient (β1) of -391,22** ($p < 0.001$) and an **R-Squared** of **0.830**.

Strategic Interpretation:

Holding event complexity and department count constant, the transition from Legacy to Digital results in a statistically significant saving of **€ 391,22** per quality event in direct labor.

The Cost of Complexity: The model demonstrates that for every unit increase in Complexity Index (1-5), costs rise by **€619.42** , highlighting the need for digital systems to manage high-complexity events like CAPAs.

The Linkage Penalty: In the legacy state, the model confirmed that manual linkages (e.g., connecting a Deviation to a CAPA) add significant 'drag' to the process. The eQMS automates this linkage, effectively nullifying this penalty, as visualized in the cost variance analysis.

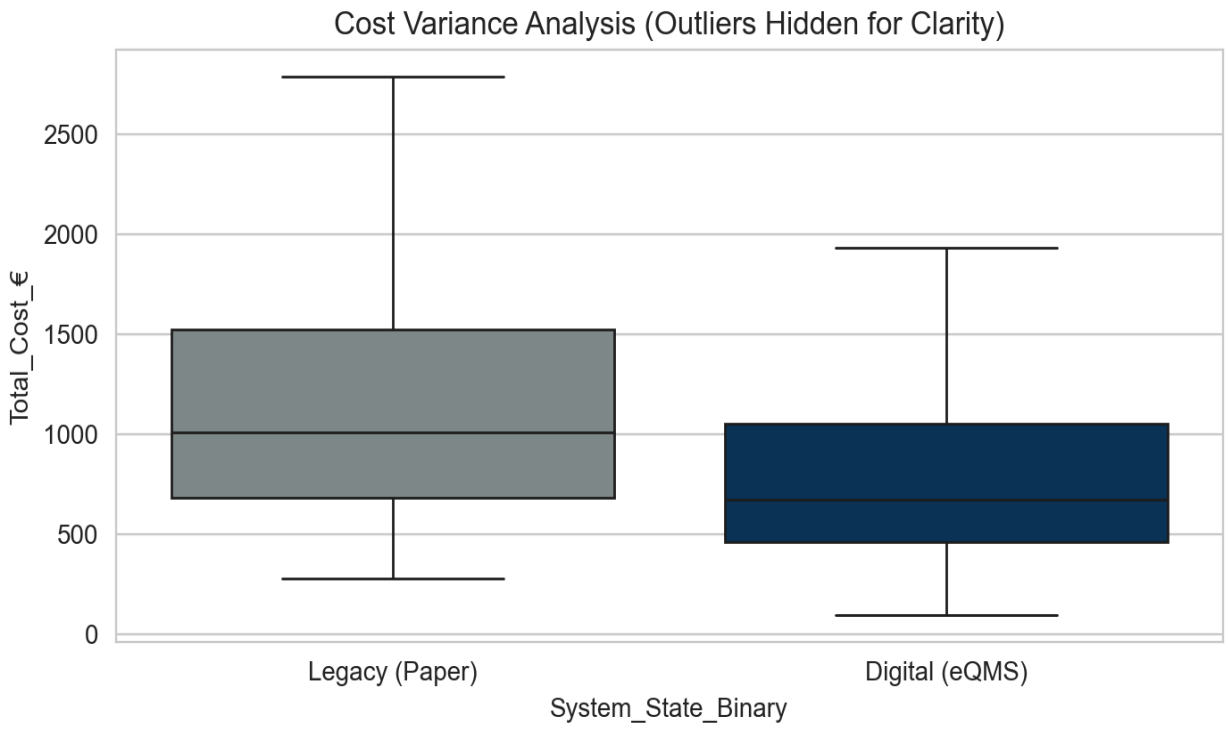

Figure 6.1: Cost Variance Analysis (Derived from Simulation Tool).

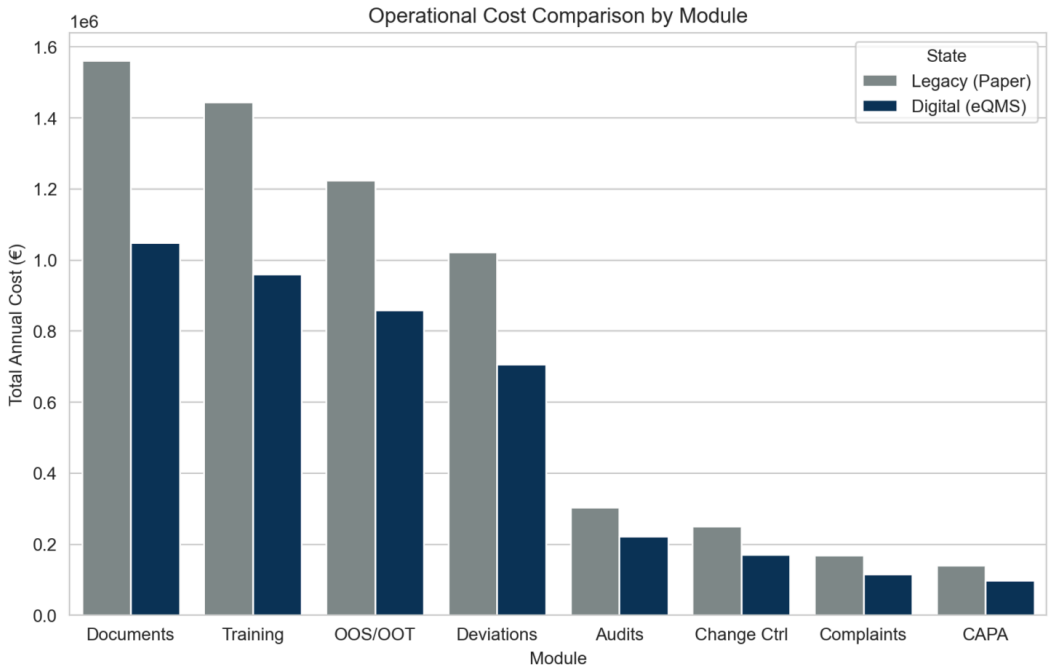

Figure 6.2: Module Cost Bar Chart (Derived from Simulation Tool).

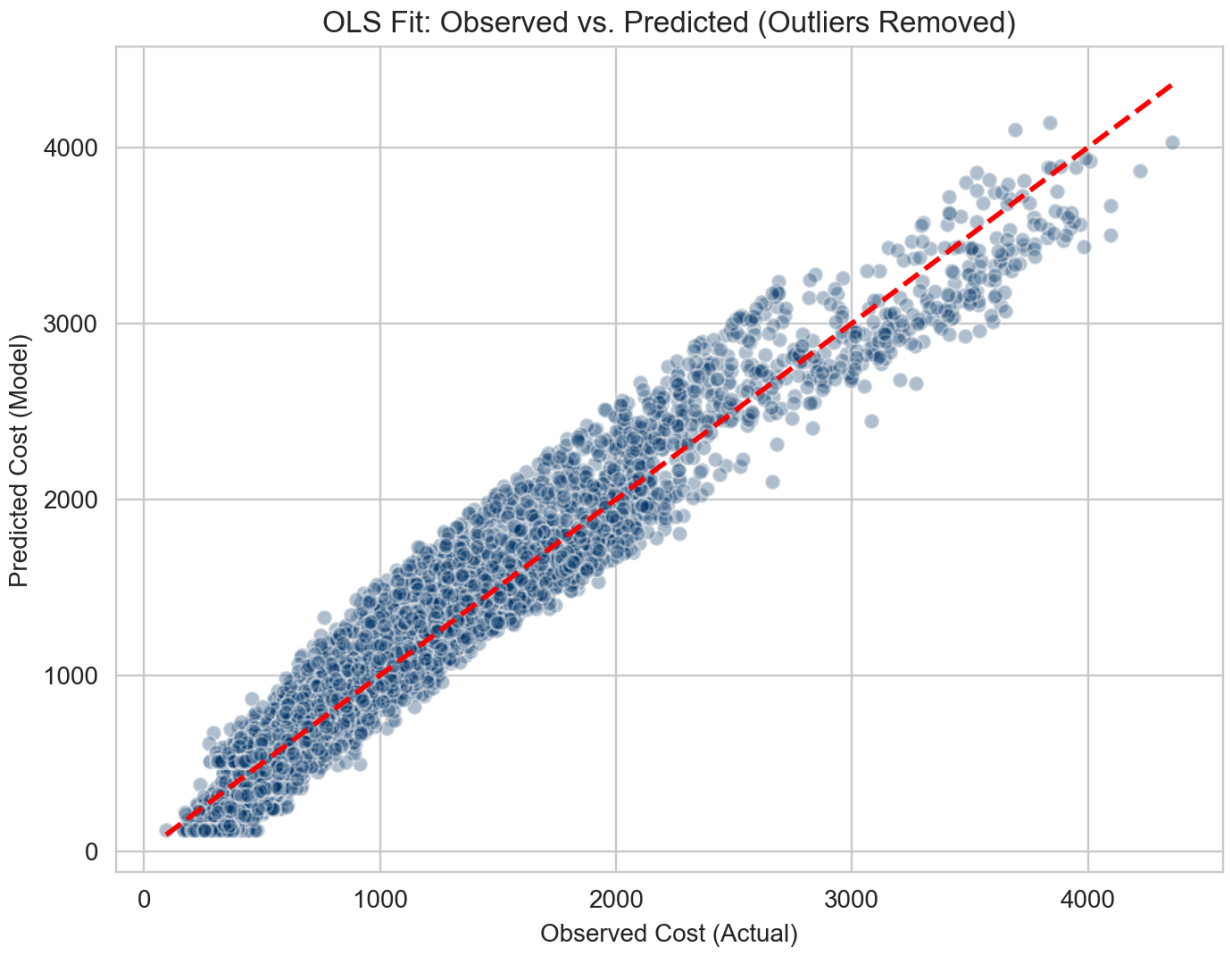

Figure 6.3: OLS Predicted vs. Observed (Derived from Simulation Tool).

6.1.2.2 Projected Annual ROI

Based on the coefficient β1 (-391,2173), we can project the annual savings for a **mid-sized organization** processing 1.000 quality events per year:

Annual **Hard Savings** = 1,000 events * € **391.2173** = **€ 391,820**

This quantifiable labor saving provides the "Hard Savings" required to offset the annual SaaS subscription costs, typically resulting in a positive ROI within Year 1. It is important to note that this figure utilizes the **"Weighted Probability"** model (Appendix C), which realistically accounts for the fact that low-cost events (like Training and SOP Revisions) occur much more frequently than high-cost CAPAs.
Also this figure **does not yet include** the savings from COPQ (e.g., avoided fines, scrapped batches).

A. Efficiency[194] Gains (**Hard Savings**):[195]

This category provides direct, measurable labor savings.

Reduced Cycle Times: Calculating the financial value of time saved across high-volume quality processes. For example, the estimated 45-day reduction in Change Control closure time (4.4) translates into earlier completion of projects and faster release of new or modified products.

Cycle Time Savings = Time Saved per Event * Labor Rate * Annual Event Volume

Reduced Clerical Overhead: Value of Full-Time Equivalents (FTEs) that can be re-deployed from managing paper archives, manual approvals, and training reconciliation (estimated at 80-95% reduction in these tasks).

Reduced Archiving Costs: Elimination of physical storage and retrieval fees for paper records.

B. Quality Improvements (Value Creation)[196]:

This category links the system's analytical capabilities to increased revenue and throughput.

Faster Batch Release: The value of revenue realized earlier due to reduced QC Event (OOS/OOT) investigation times (4.3.4) and quicker final quality sign-off.

Reduced Deviation/Failure Rate: Financial benefit from better trend analysis and proactive Risk Management (4.3.8) leading to fewer manufacturing errors or batch failures (i.e., less scrap/rework).

Knowledge Loss Mitigation & Reduced Onboarding Time. This quantifies the value of retained institutional knowledge, reducing the time new personnel take to achieve peak performance and mitigating the risk of preventable human error and associated batch failures (Cost of Poor Quality).

C. Regulatory Risk Mitigation (Cost Avoidance):

This is the most critical strategic financial value for the executive team.

Reduced Risk of Warning Letters/Fines:[197] Quantify the potential financial impact of a serious regulatory infraction (e.g., major FDA fine, product recall, consent decree). The implementation of a **Data Integrity (DI) compliant system** (enforced by Part 11 controls) reduces the probability of these high-impact events, calculated as an annual **Cost Avoidance** value.

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194 Ullagaddi, “Leveraging Digital Transformation for Enhanced Risk Mitigation and Compliance in Pharma Manufacturing.”

195 Foley et al., “Implementation of a Lean 4.0 Project to Reduce Non-Value Add Waste in a Medical Device Company.”

196 Jiju Antony et al., “Benefits, Challenges, Critical Success Factors and Motivations of Quality 4.0 – A Qualitative Global Study,” *Total Quality Management & Business Excellence* 34, nos. 7–8 (2023): 827–46, https://doi.org/10.1080/14783363.2022.2113737.

197 Alosert et al., “Data Integrity within the Biopharmaceutical Sector in the Era of Industry 4.0.”

Faster Audit Response: Value of time saved during regulatory inspections due to the immediate, secure access to GxP records (the "electronic war room" concept).

6.1.3 Sensitivity Analysis and Strategic Recommendation

1. **Sensitivity Analysis:** To demonstrate robustness, the ROI calculation should be tested against conservative variables (e.g., assuming cycle time savings are only 50% of the target or that external consulting costs are 20% higher). This analysis shows the executive team the range of possible returns and the project's resilience to unforeseen costs.
2. **Strategic Financial Justification:** The conclusion must position the eQMS as an **investment in sustainable, scalable compliance** rather than a mere cost center. The calculated ROI proves that the shift from a reactive, high-risk legacy system to a proactive, digital platform is the only fiscally responsible path forward for the organization.

6.2 Managerial and Strategic Recommendations

This section provides the essential, actionable guidance for executive leadership, summarizing the answers to the key research questions and detailing how the developed strategic framework addresses the original problem statement.

6.2.1 Synthesis of Research Findings

The research successfully validated the premise that the Cloud eQMS is a strategic imperative by providing the following key findings:

1. **Q1 (Operational Performance):** The analysis (Chapter 5.2) confirmed a direct, quantifiable correlation between the system's automated workflows and operational KPIs, projecting an average cycle time reduction of **40% to 60%** across critical processes (CAPA, Change Control, DMS). This proves the eQMS is a value driver[198], not just a compliance cost.
2. **Q2 (Compliance Strategy)[199]:** The GAMP 5 validation strategy for SaaS (5.1) is feasible and cost-effective, provided the organization meticulously defines the **Shared Responsibility Model** in the Quality Agreement. The key finding is that leveraging the vendor's IQ/OQ evidence and adopting a **Computer Software Assurance (CSA)** mindset (focusing PQ on high-risk configuration) is mandatory for achieving rapid time-to-value.
3. **Q3 (Strategic Management):** The OCM analysis (5.3) highlighted that success is contingent upon addressing the **cultural shift** from paper control to digital assurance. The most critical managerial action is transparent communication that frames the audit trail as a tool for **systemic improvement (TQM)**, not individual penalty.

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[198] Abhinav S Warrier, *Automation in Pharmaceutical Quality Assurance: A Comprehensive Review*, 2025.

[199] Ullagaddi, “Cloud Validation in Pharma: Compliance and Strategic Value.”

4. **Q4 (Financial Justification):** The comprehensive TCO/ROI analysis (6.1) proved the investment's financial viability, demonstrating that the projected savings from efficiency and the quantified value of **regulatory risk avoidance** (mitigating COPQ) yield a compelling positive return over the five-year lifecycle.The econometric model (Appendix C) confirmed a **direct labor saving of €391 per event**, providing the "Hard Savings" required to offset the SaaS subscription costs.

6.2.2 Managerial Recommendations

Based on these findings, the following strategic recommendations are provided for the executive team:

Management commitment and support:[200] management commitment and support are critical to the success of improvement efforts[201]

Prioritize Value-Driven Sourcing: When selecting an eQMS vendor, the decision must prioritize **GxP domain expertise** and the vendor's willingness to clearly define the **SaaS Shared Responsibility Model** over initial licensing cost. A specialized vendor offering continuous validation support provides the greatest long-term cost avoidance.

Utilize Algorithmic TCO Modeling: Management should move beyond static Excel estimations. It is recommended to utilize the **Configurable Decision Support Tool (Appendix C)** developed in this research. By inputting their specific local labor rates and event volumes into the script, leaders can generate a precise, location-specific business case rather than relying on generic industry averages.

Invest in OCM as Capital Expenditure (CapEx): The budget for Organizational Change Management (OCM) and role-based training should be treated as a **non-negotiable capital investment**, equal in criticality to validation testing. Lack of effective OCM is the highest risk to the project's ROI.

Adopt a Phased Implementation Strategy (Avoid "Big Bang"): The organization must avoid high-risk, multi-module "Big Bang" deployment. Implementation should follow a phased approach[202], starting with the foundational modules like the **Document Management System (DMS)** and the **Training Management System (TMS)**. Success in these modules builds user confidence, establishes the core compliance environment, and allows for effective Organizational Change Management (OCM) before tackling complex, transactional workflows like CAPA and Change Control. Established a "lessons learned" handover throughout the implementation phases which is especially important if business owners change between modules

Establish a Digital Quality Review Board: Create a cross-functional governance body (QA, IT, Operations, Finance) to oversee the eQMS implementation. This board must transition the focus of

[200] Ali and Johl, "Soft and Hard TQM Practices."

[201] Kauppinen et al., "Implementing Requirements Engineering Processes throughout Organizations."

[202] Vanita Bhoola, "Impact of Project Success Factors in Managing Software Projects in India: An Empirical Analysis," *Business Perspectives and Research* 3, no. 2 (2015): 109–25, https://doi.org/10.1177/2278533715578555.

Management Review from procedural compliance to **data-driven trend analysis** generated by the eQMS dashboards.

Formalize the Strategic Roadmap: Utilize the three-phase roadmap developed in this thesis (Readiness/URS --> Validation/Selection --> Deployment/OCM) as the formal project governance structure.

Invest in Knowledge Management Governance: Management must assign an accountable process owner (**Knowledge Champion**) responsible for curating, auditing, and promoting the use of the "Lessons Learned" repository. This is critical for ensuring the system is used as a **learning tool**, aligning with TQM principles, not just an archive.

6.2.3 Future Outlook: Pharma 4.0 Integration

The eQMS is the first step toward **Pharma 4.0**. Management must strategically plan for future integration of the eQMS with advanced technologies to maximize long-term ROI:

AI/ML Integration: Leveraging eQMS data (CAPA text, deviation frequency) with Artificial Intelligence and Machine Learning (AI/ML) tools to enable **predictive quality assurance** and automate root cause hypothesis generation.[203]

IoT and Digital Thread: Integrating the eQMS with IoT sensors and Manufacturing Execution Systems (MES) to create a **seamless digital thread** from raw material to final product, enforced by digital quality controls.

6.3 Conclusion: Strategic Contribution and Final Deliverable

This thesis established that the digitalization of Quality Management Systems (QMS) through a Cloud-based Electronic Quality Management System (eQMS) is not merely a technological upgrade but a **strategic, financially justifiable, and GxP-mandated necessity** for the modern pharmaceutical industry. The research successfully moved beyond the technical adoption discussion to provide a comprehensive, management-level roadmap.

[203] Melanie Bennett Brewer and KARI MILLER, “The Impact of Generative AI in Quality Management,” *IQVIA*, n.d., https://www.iqvia.com/-/media/iqvia/pdfs/library/white-papers/the-impact-of-generative-ai-in-quality-management.pdf.

6.3.1 Summary of Contribution

The primary contribution of this research is the development of a **data-driven Strategic Roadmap** supported by a validated artifact—the **eQMS URS Blueprint**[204] (Chapter 4). This deliverable successfully bridges the gap between high-level strategic planning and granular GxP compliance by:

1. **The Configurable ROI Artifact:** Development of a python-based, reproducible **Decision Support Tool** (Appendix C). This allows future researchers and practitioners to adjust inputs (e.g., currency, wage rates, process mix) to model their specific scenarios, elevating the research from a static case study to a dynamic utility.
2. **Enforcing Technical Integrity:** Translating broad mandates (21 CFR Part 11, Data Integrity, ICH Q10) into ten detailed, traceable, and closed-loop workflow blueprints (4.3).
3. **Integrating Management Strategy:** Incorporating **Organizational Change Management (OCM)** (2.6, 5.3) and a **GAMP 5 Shared Responsibility Model** (5.1) directly into the implementation roadmap, acknowledging that successful deployment is dependent on cultural adoption, not just validation.

6.3.2 Final Strategic Roadmap

The research culminates in a three-phase managerial guide for eQMS implementation, serving as the ultimate deliverable:

Phase	Strategic Focus	Core Deliverables
Phase 1: Readiness & Blueprinting	Strategic Alignment and Financial Justification	Final **URS Blueprint**, formal **TCO/ROI Justification**, creation of the cross-functional **Guiding Coalition**.
Phase 2: Selection & Validation	Compliance and Vendor Risk Mitigation	Selection of the ideal SaaS vendor, formal **Quality Agreement/SLA**, execution of **IQ/OQ/PQ** using the risk-based CSA methodology.
Phase 3: Deployment & OCM	Value Realization and Cultural Integration	Execution of **Role-Based Training**, successful **Go-Live**, and final **Effectiveness Verification** of key processes to lock in the measured ROI.

[204] Daniel Méndez Fernández et al., "Field Study on Requirements Engineering: Investigation of Artefacts, Project Parameters, and Execution Strategies," *Information and Software Technology* 54, no. 2 (2012): 162–78, https://doi.org/10.1016/j.infsof.2011.09.001.

6.4 Future Research[205]: The Evolving Digital Quality Landscape

The digitalization of the QMS is a foundational step, but the field of Quality 4.0 is continuously evolving. The following areas are suggested for further academic and managerial research:

1. **AI/ML Integration in eQMS for Predictive Quality:** Further study is required to develop frameworks and pilot programs for integrating Artificial Intelligence and Machine Learning algorithms directly into eQMS data streams. This research could focus on using historical deviation and CAPA text data to **automate root cause hypothesis generation** or establish **predictive maintenance schedules** before equipment failures lead to an Out-of-Specification (OOS) event.
2. **Blockchain for Supply Chain Quality and Traceability:** Research should explore the feasibility and GxP validation requirements for using distributed ledger technology (blockchain) to manage immutable quality data (e.g., Certificates of Analysis) across global supply chains. This could drastically simplify supplier qualification and enhance product traceability, further securing the supply chain integrity addressed in the SQM module.
3. **Quantifying the ROI of Computer Software Assurance (CSA):** While this thesis advocates for CSA, future research should gather large-scale empirical data to precisely quantify the reduction in validation hours and associated labor costs achieved by companies that have fully transitioned from traditional CSV to the modern CSA approach. This would provide an even more refined ROI calculation for future eQMS projects.

Appendices and References

Appendix A: Sample User Requirement Specification (URS) Blueprint

This appendix provides the detailed functional and non-functional requirements necessary to support the strategic objectives defined in this thesis. These requirements serve as the basis for vendor selection and the Operational Qualification (OQ) testing phase.

1. System Architecture, SaaS, and General Controls

These requirements define the technological foundation, ensuring scalability, availability, and compliance with Cloud validation strategies.

ID	Category	Requirement Description
SYS-001	**Deployment Model**	The solution must be available as a Cloud Software-as-a-Service (SaaS) platform to minimize internal infrastructure maintenance.

[205] Phuvamin Suriyaamporn et al., "The Future Trends of Artificial Intelligence and Innovative Technologies in the New Era of Pharmaceutical Sciences and Industry 4.0," *Drug Development and Industrial Pharmacy* 0, no. 0 (2025): 1–14, https://doi.org/10.1080/03639045.2025.2590707.

ID	Category	Requirement Description
SYS-002	**Multi-Site Capability**	The system must support deployment across multiple global sites, allowing for site-specific data segregation where necessary.
SYS-003	**Infrastructure Validation**	The SaaS vendor must provide evidence that the underlying hosting infrastructure (IaaS) is qualified and validated for GxP data storage.
SYS-004	**Environment Segregation**	The system architecture must utilize a multi-tenant infrastructure that provides distinct environments for Testing (Validation), Quality (Staging), and Production.
SYS-005	**Scalability**	The system must support a scalable user base, initially supporting up to 1,000 named users with the capacity for expansion.
SYS-006	**Availability (SLA)**	The system must guarantee high availability (e.g., 99.9% uptime) 24/7, excluding pre-scheduled maintenance windows defined in the Service Level Agreement (SLA).
SYS-007	**Upgrade Control**	System upgrades and patches must not be forced upon the production environment; the customer must have an "opt-in" period to perform impact assessments.
SYS-008	**Disaster Recovery**	The vendor must possess a formally verified Disaster Recovery (DR) plan with defined Recovery Point Objectives (RPO) and Recovery Time Objectives (RTO).
SYS-009	**Mobile Readiness**	The user interface must be responsive and accessible via mobile devices (tablets) to facilitate real-time data entry on the shop floor (Industry 4.0 enabler).
SYS-010	**Localization**	The user interface must support multi-language capabilities, specifically supporting English and Greek.
SYS-011	**Data Export**	The system must allow authorized users to export metadata and records in standard formats (Excel, CSV, PDF) for external analysis.

2. Security[206], Access Control[207], and Electronic Signatures

*These requirements ensure strict adherence to **FDA 21 CFR Part 11** and **EU Annex 11** regarding Data Integrity and Audit Trails.*

ID	Category	Requirement Description
SEC-001	**Unique Identity**	The system must assign and enforce a unique User ID for every individual; sharing of credentials must be technically prevented.
SEC-002	**Authentication**	Access must require secure authentication, supporting Single Sign-On (SSO) integration (e.g., Azure AD) and Multi-Factor Authentication (MFA).
SEC-003	**Role-Based Access**	The system must utilize granular Role-Based Access Control (RBAC) to restrict visibility and edit rights based on user function (e.g., Read-Only, Author, Approver).
SEC-004	**Audit Trail**	The system must generate a secure, computer-generated, time-stamped audit trail that records the date, time, user, and value change for all GxP actions.
SEC-005	**Audit Trail Integrity**	The audit trail functionality must be always active and cannot be disabled by any user, including administrators.
SEC-006	**Electronic Signature**	Electronic signatures must employ two distinct identification components (ID and Password) and must be linked permanently to the respective record.
SEC-007	**Session Management**	The system must enforce an automatic session timeout after a configurable period of inactivity to prevent unauthorized access.
SEC-008	**Site-Level Segregation**	The system must allow data partitioning so that users at a specific manufacturing site only have visibility of records (Deviations, CAPAs) relevant to their location, while Global Quality users can view data across all sites.
SEC-009	**Product-Level Security**	The system must provide the ability to restrict access to specific records based on "Product" or "Project" tags, ensuring sensitive intellectual property is accessible only to authorized project teams.

[206] Tabrizchi and Kuchaki Rafsanjani, “A Survey on Security Challenges in Cloud Computing.”

[207] Ben Fadhel et al., “A Comprehensive Modeling Framework for Role-Based Access Control Policies.”

3. Workflow and Process Automation[208]

These requirements define the "Digitalization" aspect, moving from static records to dynamic, automated processes.

ID	Category	Requirement Description
WFL-001	**Standard Workflows**	The system must provide pre-validated, "Out-of-the-Box" (OOTB) workflows for core processes (CAPA, Deviation, Change Control) based on industry best practices.
WFL-002	**Configurability**	Administrators must be able to configure workflow steps, rules, and mandatory fields without requiring custom coding or vendor intervention.
WFL-003	**Notifications**	The system must support automated email notifications and dashboard alerts triggered by workflow steps (e.g., "Pending Approval," "Due Date Approaching").
WFL-004	**Escalation**	The system must allow for the configuration of escalation rules that notify management when a critical task exceeds its due date.

4. Document Management System (DMS) Module

Focuses on the lifecycle of SOPs, policies, and specifications.

ID	Category	Requirement Description
DMS-001	**Lifecycle Management**	The system must manage the complete document lifecycle: Draft, Review, Approval, Effective, and Obsolete/Archived.
DMS-002	**Version Control**	The system must automatically manage version numbers (e.g., 1.0, 1.1) and retain a complete history of all previous versions.
DMS-003	**Collaborative Review**	The system must support parallel or sequential review cycles where Subject Matter Experts (SMEs) can annotate comments directly on the electronic file.
DMS-004	**Watermarking**	The system must dynamically apply watermarks (e.g., "DRAFT," "CONFIDENTIAL," "OBSOLETE") to documents based on their current status.
DMS-00	**Controlled Printing**	The system must track and log the printing of controlled documents, allowing

[208] "The Link between Business Process Management and Quality Management - ProQuest," accessed December 4, 2025, https://www.proquest.com/docview/2548600253?pq-origsite=gscholar&fromopenview=true&sourcetype=Scholarly%20Journals#.

ID	Category	Requirement Description
5		for the assignment of unique print IDs to prevent unauthorized duplication.
DMS-006	TMS Integration	Approval of a new SOP version must automatically trigger the creation of a training requirement in the Training Module (TMS).

5. Quality Events, CAPA, and Root Cause Analysis

Focuses on the "Check" and "Act" phases of PDCA.

ID	Category	Requirement Description
CAPA-001	Event Intake	The system must provide a standardized intake form for all Quality Events (Deviations, Non-Conformances) with mandatory classification fields.
CAPA-002	Root Cause Analysis	The system must provide integrated tools or dedicated sections to document Root Cause Analysis (e.g., 5 Whys, Fishbone).
CAPA-003	Action Tracking	The system must distinguish between Correction, Corrective Action (CA), and Preventive Action (PA), allowing individual assignment and tracking.
CAPA-004	Effectiveness Check	The system must enforce a mandatory Effectiveness Verification (EV) step scheduled after CAPA closure to validate that the issue has not recurred.
CAPA-005	Investigation Linkage	The system must allow the creation of "child" investigations linked to a "parent" deviation to support complex problem solving.

6. Change Control Module

Focuses on risk-based change management.

ID	Category	Requirement Description
CHG-001	Change Request	The system must allow users to initiate change requests affecting documents, equipment, or processes with a preliminary scope definition.
CHG-002	Impact Assessment	The workflow must require a cross-functional impact assessment (e.g., Regulatory, Quality, Engineering) before a change plan is approved.
CHG-003	Action Management	The system must track all implementation tasks (e.g., update SOP, calibrate equipment) and prevent Change Closure until all tasks are verified.

7. Training Management System (TMS) Module

Focuses on personnel qualification and competence.

ID	Category	Requirement Description
TMS-00	Curriculum	The system must allow the creation of role-based training curricula (groups

ID	Category	Requirement Description
1	Management	of courses/SOPs) assigned to specific Job Codes.
TMS-002	Assessment & Quizzes	The system must support the creation of graded quizzes/exams to verify comprehension of the training material.
TMS-003	Automated Retraining	The system must automatically trigger a retraining assignment for all affected users when a linked document (SOP) is revised in the DMS.
TMS-004	Compliance Reporting	Managers must have access to real-time dashboards showing the training compliance status (Qualified/Overdue) of their direct reports.

8. Supplier Quality Management (SQM) Module

Focuses on supply chain integrity.

ID	Category	Requirement Description
SQM-001	Supplier Database	The system must maintain a consolidated database of Suppliers, Manufacturers, and Brokers, linked to the materials they supply.
SQM-002	Qualification Workflow	The system must enforce a workflow for supplier onboarding, requiring audit completion and document collection before status is set to "Approved."
SQM-003	SCAR Management	The system must allow the generation and tracking of Supplier Corrective Action Requests (SCARs) linked directly to incoming material non-conformances.

9. Knowledge Management (KM) & Risk Management (QRM)

Strategic requirements for TQM and Organizational Learning (Thesis Focus).

ID	Category	Requirement Description
KM-001	Lessons Learned	The system must include a dedicated object or field for capturing "Lessons Learned" upon the closure of major quality events.
KM-002	Contextual Search	The system should provide intelligent search capabilities to suggest relevant historical deviations or knowledge assets during new record creation.
QRM-001	Risk Register	The system must provide a centralized Risk Register to aggregate risks identified across all modules (CAPA, Change, Audit).
QRM-002	Risk Scoring	The system must support configurable risk matrices (e.g., RPN = Severity × Occurrence × Detection) to objectively score quality risks.

10. Reporting and Interfacing

Ensures data visibility and ecosystem connectivity.

ID	Category	Requirement Description
INT-001	**ERP Integration**	The system must utilize validated APIs to exchange critical master data (e.g., Batches, Materials) with the Enterprise Resource Planning (ERP) system.
INT-002	**LIMS Integration**	The system must integrate with Laboratory Information Management Systems (LIMS) to automatically initiate OOS investigations based on lab results.
RPT-001	**Self-Service Reporting**	Users must be able to create, save, and share ad-hoc reports and queries without IT assistance (Point-and-click configuration).
RPT-002	**Dashboards**	The system must provide visual dashboards for real-time monitoring of KPIs (e.g., Open CAPAs, Training Compliance, Audit Findings).

Appendix B: Sample GAMP 5 System Classification and Risk Assessment Matrix

Appendix B: Sample GAMP 5 System Classification and Risk Assessment Matrix
This appendix formalizes the risk-based approach to the validation of the Cloud Software-as-a-Service (SaaS) Electronic Quality Management System (eQMS) as described in Chapter 5.1. The strategy leverages the ISPE GAMP 5 Guide to ensure validation effort is proportionate to the system's risk to GxP (Good Practices).

1. GAMP 5 System Classification (eQMS)

The classification determines the base validation strategy. An off-the-shelf (COTS) eQMS that is configured to match specific organizational workflows falls into the following category:

Parameter	Classification	Rationale
GAMP 5 Category	**Category 4: Configurable Software**	The core software code and infrastructure (Cloud) are provided by the vendor. The pharmaceutical company configures the application (workflows, user roles, forms) to meet its unique GxP requirements (URS).
Required Approach	Risk-Based Validation / CSA	Focus validation effort (PQ) on the unique configuration and high-risk workflows, while leveraging the vendor's documentation for the inherent low-risk functions (IQ/OQ).
System Impact	**Direct GxP Impact**	The system directly controls GxP records, audit trails, and the timing of critical quality events (e.g., CAPA closure, document release).

2. Risk Assessment Methodology

The validation risk is assessed based on the potential impact of a system failure (i.e., incorrect configuration or malfunction) on the three GxP pillars: **Patient Safety (P), Product Quality (Q),** and **Data Integrity (DI).**

A. Risk Scoring Matrix

Impact	Description	Risk Level
CRITICAL	Failure would directly compromise Product Quality or Patient Safety (e.g., system fails to enforce electronic signature on batch release documentation).	**High (H)**
MAJOR	Failure would lead to a regulatory compliance breach or significant loss of Data Integrity (e.g., audit trail fails to record a critical action).	**Medium (M)**
MINOR	Failure affects usability or efficiency but does not compromise GxP compliance or P/Q/DI (e.g., incorrect label on a dashboard report).	**Low (L)**

B. Application of Risk to Functional Requirements (Example)

Functional Requirement (FRS)	Risk Drivers (P/Q/DI)	Risk Score	Validation Strategy (CSA)
FR-4.3.2-A: The system shall automatically route a Major Change Control request to the Quality Review Board (QRB).	DI (Failure to enforce mandatory review).	**M**	Formal PQ Script (Testing the routing logic and approval structure).
FR-4.3.3-B: The system shall enforce Segregation of Duties (SoD) preventing the Deviation Investigator from approving the final CAPA closure.	P/Q/DI (Failure allows potential cover-up/conflict of interest).	**H**	**Critical PQ Script** (Testing the user role permissions and SoD checks).
FR-4.3.1-C: The system shall automatically record all revision history for an SOP in a secured, non-editable audit trail.	DI (Part 11 compliance).	**H**	Leverage Vendor OQ (Testing audit trail functionality), plus confirmatory PQ of audit trail visibility.

3. GAMP 5 V-Model: Validation Phase Mapping

The V-Model maps the requirements definition phases to the testing phases. The table below outlines the key activities and deliverables for each phase, highlighting the **Shared Responsibility** (Chapter 5.1).

Phase (V-Model Side)	Strategic Activity	Key Stakeholder	Deliverable/Output
Project Initiation	Secure Executive Sponsorship and Project Charter.	Project Sponsor, QA Director	Approved Budget (TCO), Project Charter, Resource Allocation.
Requirements (URS)	Define the **User Requirement Specification (URS)**, **Functional Specification (FRS)**, and **Data Migration Strategy.**	Business Users, QA Process Owners	Final URS Document, Functional Specification (FS), Data Migration Plan (DMP).
Design & Configuration	Configure the eQMS workflows (4.3) and establish security and user roles. **(Fit-to-Standard enforced).**	System Administrator, Vendor Consultant	Configuration Specification (CS), Traceability Matrix (TM).
Data Migration	Execution of the data transfer, including historical GxP records (e.g., closed CAPAs, effective SOPs) from the legacy system.	Data Migration Team, QA	Data Migration Execution Report.
Testing: IQ (Installation)	Verify the cloud instance is installed, secured, and configured as per vendor/URS standards (e.g., user groups, access controls).	**Vendor (Evidence provided),** IT Department (Acceptance)	Installation Qualification (IQ) Report.
Testing: OQ (Operational)	Verify that core functions (e.g., e-signature, audit trail, automated routing) work correctly as per the FRS.	**Vendor (Evidence provided),** QA Team (Acceptance)	Operational Qualification (OQ) Report.
Testing: PQ (Performance)	Execute high-risk, end-to-end business scenarios (e.g., a Major Change Control from start to finish) and **verify integrity of migrated GxP data. (Core CSA/User Responsibility).**	QA/OCM/End Users	Performance Qualification (PQ) Report, **Migration Verification Report (MVR).**
Final Release	Formal management sign-off, system release, and commencement of OCM activities (Training, Go-Live).	QA Manager, Project Sponsor	**Validation Summary Report (VSR),** Go-Live Approval, Trained Users.

Post Go-Live	Execute the mandatory CAPA Effectiveness Verification (EV) plan on critical processes.	QA Process Owners	System Review & Periodic Audit Report.

Appendix C: Econometric Model Specification & Man-Hour Cost Analysis

C.1 Tool Overview and Architecture

To overcome the limitations of static spreadsheet models, which often fail to account for the variability inherent in quality processes, a custom **Monte Carlo Simulation Engine** was developed for this thesis. The tool, built using **Python** and the **Streamlit** framework, allows for stochastic modeling of ROI based on variable input parameters.

The application operates on a "Digital Twin" logic: for every simulated Quality Event (e.g., a Deviation), the engine generates two scenarios—**Legacy (Paper-based)** and **Digital (SaaS eQMS)**—allowing for a matched-pair statistical analysis of cost efficiency.

C.2 Stochastic Model Logic

The core value of this tool lies in its transition from deterministic averages to probabilistic distributions. The simulation logic follows four key steps:

1. Event Generation

The model generates N independent quality events (default N=5,000). The frequency of each event type (e.g., CAPA vs. Training) is weighted based on the "Annual Volume" input by the user, ensuring the simulated sample mirrors the organization's actual operational profile.

2. Complexity as a Driver

Instead of assigning a fixed cost to every deviation, the model assigns a **Complexity Score** (1–5) to each event using a **Log-Normal Distribution**.

> *Rationale:* In quality management, process cycle times are rarely normally distributed; they are right-skewed. Most events are simple (low cost), but a "long tail" of highly complex investigations exists. The Log-Normal distribution accurately models this real-world risk.

3. Dynamic Resource Allocation

The engine calculates the effort (Man-Hours) for each event based on its complexity:

> **Departmental Involvement:** Modeled as a Poisson distribution scaled by complexity ($\lambda = 1 + 0.7 * Complexity$). A complex Critical Deviation naturally draws in more departments (e.g., QC, Engineering, RA) than a minor documentation error.

Linkage Penalties: In the "Legacy" state, the model applies penalty hours for manual cross-referencing (e.g., linking a Complaint to a CAPA). In the "Digital" state, this penalty is removed or reduced based on the "Savings Factor," simulating automated system linkages.

4. Cost Calculation and Regression

Total Cost is calculated as:

Total Cost = Man-Hours*Hourly Labor Rate

The tool then performs an Ordinary Least Squares (OLS) regression to determine the statistical significance of the savings. It automatically applies HC3 Robust Standard Errors (Heteroscedasticity-Consistent Covariance Matrix) if the White Test detects non-constant variance, ensuring the calculated ROI is statistically rigorous.

C.3 User Instructions and Configuration

The web application is designed with a "No-Code" interface, allowing Quality Managers to run complex simulations without programming knowledge.

Step 1: Define Financial Parameters (Sidebar)

Avg Labor Rate: Input the fully burdened hourly cost of quality personnel (e.g., €50/hr).

Savings Factor (%): Adjust the "Efficiency Realization" slider.

100%: Assumes the digital system works perfectly and eliminates all manual friction.

50% (Recommended): A conservative baseline assuming human latency remains.

Risk & COPQ: Input the estimated "Average Cost of Failure" (e.g., batch rejection cost) to model the risk avoidance benefit.

Step 2: Configure the Quality Pyramid (Main Dashboard)

The "QMS Configuration" table is pre-loaded with SME-validated baseline data but is fully editable.

Module: Select the QMS module (e.g., Deviations, Documents).

Annual Volume: Input the estimated number of events per year for your site.

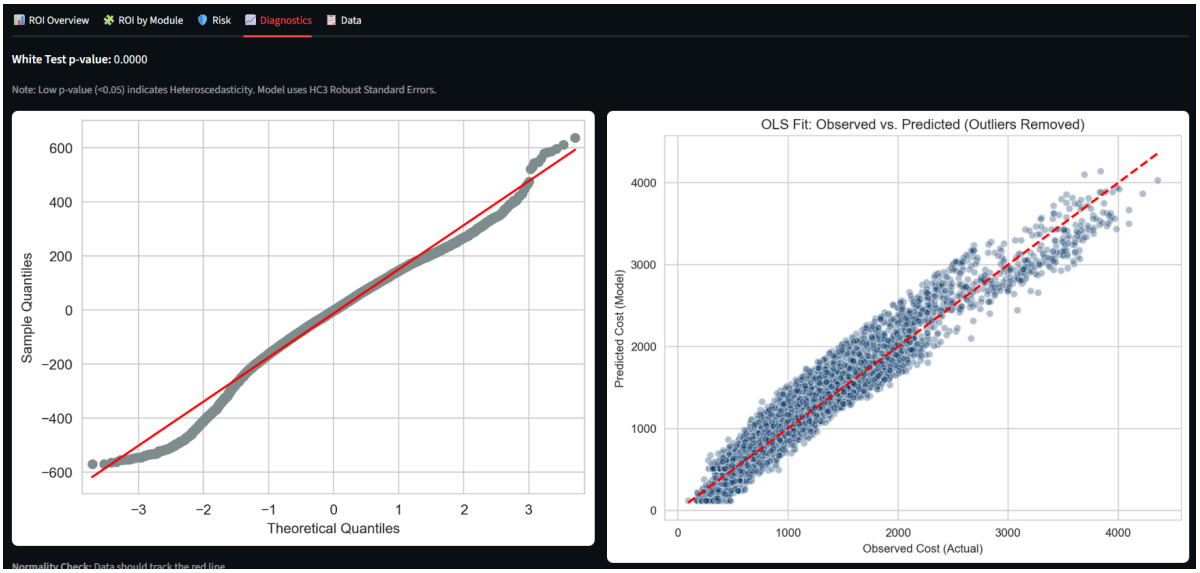
Note: Ensure volumes for "Work Instructions" and "Forms" reflect the high frequency of document issuance (Level 3 & 4 of the Quality Pyramid).

Complexity (1-5): Set the baseline difficulty. A higher score increases the simulated variability and departmental involvement.

Step 3: Execution and Analysis

Click the **"Run Simulation"** button. The engine will perform 5,000+ Monte Carlo iterations. Results are displayed in five tabs:

1. **ROI Overview:** High-level executive summary of Net Present Value (NPV) and ROI.
2. **ROI by Module: –** A comparative bar chart visualizing where the savings are generated (e.g., high-volume document tasks vs. high-cost CAPAs).
3. **Risk Analysis:** Quantifies the "Cost Avoidance" benefits (reduced regulatory risk).
4. **Diagnostics:–** Displays the "Observed vs. Predicted" costs to validate model fit. Alongside model



```
                            OLS Regression Results
==============================================================================
Dep. Variable:           Total_Cost_€   R-squared:                       0.830
Model:                          OLS   Adj. R-squared:                  0.830
Method:               Least Squares   F-statistic:                     1998.
Date:              Mon, 08 Dec 2025   Prob (F-statistic):               0.00
Time:                      01:44:57   Log-Likelihood:                -71246.
No. Observations:              9898   AIC:                         1.425e+05
Df Residuals:                  9890   BIC:                         1.426e+05
Df Model:                         7
Covariance Type:                HC3
==============================================================================
                     coef    std err          z      P>|z|      [0.025      0.975]
------------------------------------------------------------------------------
const           -224.6760     18.024    -12.465      0.000    -260.002    -189.350
System_State_Binary -391.2173      6.516    -60.044      0.000    -403.987    -378.447
Complexity       619.4222     15.536     39.870      0.000     588.972     649.872
Dept_Count       118.7639      2.671     44.468      0.000     113.529     123.999
Link_CAPA        197.4596      7.102     27.803      0.000     183.540     211.380
Link_CC          220.3368      4.771     46.183      0.000     210.986     229.688
Link_Doc         100.9434     11.269      8.957      0.000      78.856     123.031
Link_Comp        142.5824     12.464     11.440      0.000     118.154     167.011
==============================================================================
Omnibus:                    18401.032   Durbin-Watson:                   1.348
Prob(Omnibus):                  0.000   Jarque-Bera (JB):         45067253.533
Skew:                          13.832   Prob(JB):                         0.00
Kurtosis:                     332.410   Cond. No.                         10.3
==============================================================================

Notes:
[1] Standard Errors are heteroscedasticity robust (HC3)
```

5. Data: Allows the user to download the raw simulated dataset (.csv) for external audit or validation.

C.4 System Requirements

Language: Python 3.9+

Libraries: streamlit, pandas, numpy, statsmodels, matplotlib, seaborn

Deployment: Can be hosted locally or on any containerized Cloud platform (AWS, Azure, Heroku).

C.5 CODE

To ensure reproducibility and transparency, the Decision Support Tool developed for this research has been deployed as a live web application. The application allows the examination of the underlying Python code and the execution of the Monte Carlo simulation using custom parameters.

Live URL: https://eqms-roi-simulator-mba-tqm-thesis-unipi.streamlit.app

Python code is available below:

```
"""
Cloud eQMS ROI Simulator - Monte Carlo Engine (MBA TQM Thesis , University of Piraeus)
Author: Dimitrios Vergis
Thesis: Digital Transformation in Pharma: A Strategic Framework for Cloud eQMS Validation and ROI Analysis
Description:
    Enterprise simulation with configurable inputs to adopt to different business scenarios and regions based on complexity driven logic.
    Features HC3 robust regression, Module-based analytics, and visualization.
"""

import streamlit as st
import pandas as pd
import numpy as np
import matplotlib.pyplot as plt
import seaborn as sns
import statsmodels.api as sm
import statsmodels.stats.api as sms

# ==========================================================
# 0. CONFIGURATION & VISUAL THEME
# ==========================================================
UNIPI_PALETTE = ['#7f8c8d', '#003366']  # Legacy (Grey) vs Digital (Navy)
sns.set_palette(UNIPI_PALETTE)
sns.set_style("whitegrid")

# ==========================================================
# 1. BASELINE PROCESS METADATA (SME Validated)
# ==========================================================
```

```
# Updated with specific volumes for Work Instructions and Forms
PROCESS_METADATA = [
    # Module, Event Name, Annual Vol, Leg Hrs, Dig Hrs, Leg Days, Dig Days, Complexity

    # --- TRAINING ---
    ("Training", "Training Assignment (Read&Und)", 1500, 0.5, 0.1, 5.0, 1.0, 1.0),
    ("Training", "OJT Assessment / Qual", 200, 2.5, 1.0, 10.0, 3.0, 2.0),
    ("Training", "Ext. Training Verification", 100, 1.0, 0.3, 7.0, 2.0, 1.0),

    # --- DOCUMENTS ---
    ("Documents", "SOP Revision (Minor/Admin)", 50, 6.0, 3.0, 20.0, 10.0, 2.0),
    ("Documents", "SOP Creation / Major Rev", 30, 15.0, 8.0, 45.0, 20.0, 3.5),
    ("Documents", "SOP Periodic Review", 80, 8.0, 4.0, 30.0, 15.0, 2.5),
    ("Documents", "Work Instruction (New/Rev)", 500, 4.0, 2.0, 15.0, 5.0, 1.5),
    ("Documents", "Form/Logbook Issuance & Rev", 1000, 0.5, 0.1, 2.0, 0.5, 1.0),

    # --- DEVIATIONS ---
    ("Deviations", "Deviation (Minor / Event)", 500, 8.0, 5.0, 25.0, 15.0, 2.0),
    ("Deviations", "Deviation (Major / Non-Conf)", 50, 20.0, 12.0, 45.0, 25.0, 3.5),
    ("Deviations", "Deviation (Critical)", 10, 40.0, 25.0, 60.0, 30.0, 5.0),

    # --- OOS / OOT ---
    ("OOS/OOT", "OOT / Lab Error (Minor)", 500, 10.0, 6.0, 15.0, 5.0, 2.0),
    ("OOS/OOT", "OOS Confirmed (Major)", 100, 25.0, 15.0, 30.0, 15.0, 4.0),
    ("OOS/OOT", "OOS Critical / Field Alert", 10, 80.0, 50.0, 45.0, 20.0, 5.0),

    # --- CAPA ---
    ("CAPA", "CAPA Plan & Execution", 40, 15.0, 10.0, 60.0, 40.0, 3.5),
    ("CAPA", "Effectiveness Check (EC)", 30, 8.0, 4.0, 90.0, 45.0, 3.0),

    # --- CHANGE CONTROL ---
    ("Change Ctrl", "CC (Like-for-Like / Admin)", 50, 6.0, 3.0, 15.0, 5.0, 2.0),
    ("Change Ctrl", "CC (Minor / Process Adj)", 30, 12.0, 6.0, 30.0, 15.0, 3.0),
    ("Change Ctrl", "CC (Major / Equipment)", 15, 30.0, 18.0, 90.0, 45.0, 4.5),
    ("Change Ctrl", "CC (Emergency / Temporary)", 25, 20.0, 12.0, 5.0, 2.0, 4.5),

    # --- COMPLAINTS ---
    ("Complaints", "Complaint (Non-Medical)", 60, 12.0, 7.0, 30.0, 15.0, 3.0),
```

```
    ("Complaints", "Complaint (Medical / AE)", 5, 25.0, 15.0, 15.0, 5.0, 5.0),

    # --- AUDITS ---
    ("Audits", "Internal Audit (Self-Insp)", 4, 40.0, 25.0, 30.0, 15.0, 3.5),
    ("Audits", "Supplier Audit (Desk/Remote)", 20, 10.0, 5.0, 30.0, 10.0, 2.5),
    ("Audits", "Supplier Audit (On-Site)", 30, 50.0, 30.0, 45.0, 20.0, 4.0),
    ("Audits", "Regulatory Insp. Prep", 5, 200.0, 120.0, 15.0, 10.0, 5.0),
]

# Initialize DataFrame
DEFAULT_DF = pd.DataFrame(PROCESS_METADATA, columns=[
    "Module", "Event_Name", "Annual_Volume", "Legacy_Hours", "Target_Dig_Hours",
    "Legacy_Cycle_Days", "Target_Dig_Cycle_Days", "Complexity"
])


# ==========================================================
# 2. CORE SIMULATION ENGINE
# ==========================================================
@st.cache_data
def run_simulation(hourly_rate, n_events, process_df, penalties, currency_symbol, savings_factor):
process_df = process_df.reset_index(drop=True)
    # Weights based on Annual Volume
    total_vol = process_df['Annual_Volume'].sum()
    weights = process_df['Annual_Volume'] / total_vol

    data_rows = []

    # Penalties
    p_capa = float(penalties.get('CAPA', 0.0))
    p_cc = float(penalties.get('CC', 0.0))
    p_doc = float(penalties.get('DOC', 0.0))
    p_comp = float(penalties.get('COMPLAINT', 0.0))

    # Stochastic Selection
    chosen_indices = np.random.choice(process_df.index, size=n_events, p=weights)

    for i, idx in enumerate(chosen_indices):
```

```
        row = process_df.iloc[idx]
        evt_id = f"EVT-{i + 1:05d}"

        module = row['Module']
        proc_name = row['Event_Name']

        # --- COMPLEXITY DRIVER ---
        base_comp = float(row['Complexity'])
        comp_noise = np.random.lognormal(0, 0.2) - 1.0
        complexity = max(1.0, min(5.0, base_comp + comp_noise))

        # --- DEPARTMENTS ---
        avg_depts = 1.0 + (complexity * 0.7)
        dept_count = max(1, min(10, np.random.poisson(avg_depts)))

        # --- LINKAGES ---
        prob_link = min(0.95, complexity * 0.18)

        prob_capa = 0.0 if module == 'CAPA' else prob_link
        prob_cc = min(0.95, prob_link * 1.2) if module == 'Documents' else prob_link
        prob_doc = 0.0 if module == 'Documents' else prob_link

        linked_capa = 1 if np.random.random() < prob_capa else 0
        linked_cc = 1 if np.random.random() < prob_cc else 0
        linked_doc = 1 if np.random.random() < prob_doc else 0
        linked_comp = 1 if np.random.random() < (prob_link * 0.5) else 0

        base_link_penalty = (linked_capa * p_capa) + (linked_cc * p_cc) + \
                            (linked_doc * p_doc) + (linked_comp * p_comp)

        # --- STATE GENERATION (Matched Pairs) ---
        for state in [0, 1]:
            if state == 0:  # LEGACY
                noise = np.random.normal(0, 1.2)
                base_h = float(row['Legacy_Hours'])
                comp_factor = complexity * 5.0
                dept_factor = dept_count * 3.0
                link_penalty = base_link_penalty
```

```
            target_cycle = float(row['Legacy_Cycle_Days'])
            cycle_days = int(np.random.lognormal(mean=np.log(target_cycle), sigma=0.5))

        else:  # DIGITAL
            noise = np.random.normal(0.5, 1.2)

            leg_h = float(row['Legacy_Hours'])
            dig_h = float(row['Target_Dig_Hours'])
            base_h = leg_h - ((leg_h - dig_h) * savings_factor)

            comp_mult = 5.0 - (3.0 * savings_factor)
            comp_factor = complexity * comp_mult
            dept_mult = 3.0 - (2.2 * savings_factor)
            dept_factor = dept_count * dept_mult
            link_penalty = base_link_penalty * (1 - savings_factor)

            target_cycle = float(row['Target_Dig_Cycle_Days'])
            cycle_days = int(np.random.lognormal(mean=np.log(target_cycle), sigma=0.25))

        cycle_days = max(1, cycle_days)
        if total_hours := max(0.5, base_h + comp_factor + dept_factor + link_penalty + noise): pass
        cost = total_hours * hourly_rate

        data_rows.append([
            evt_id, module, proc_name, state, complexity, dept_count,
            linked_capa, linked_cc, linked_doc, linked_comp,
            cycle_days, round(total_hours, 1), round(cost, 2)
        ])

    # Consolidation
    cols = ['Event_ID', 'Module', 'Process_Name', 'System_State_Binary', 'Complexity', 'Dept_Count',
            'Link_CAPA', 'Link_CC', 'Link_Doc', 'Link_Comp',
            'Cycle_Days', 'Manhours', f'Total_Cost_{currency_symbol}']
    df = pd.DataFrame(data_rows, columns=cols)

    # Regression
    X = df[['System_State_Binary', 'Complexity', 'Dept_Count', 'Link_CAPA', 'Link_CC', 'Link_Doc', 'Link_Comp']]
```

```
X = sm.add_constant(X)
Y = df[f'Total_Cost_{currency_symbol}']

model_ols = sm.OLS(Y, X).fit()
try:
    _, white_p, _, _ = sms.het_white(model_ols.resid, model_ols.model.exog)
except:
    white_p = 0.0

model_hc3 = sm.OLS(Y, X).fit(cov_type='HC3')
beta_1 = model_hc3.params['System_State_Binary']
annual_savings = beta_1 * n_events

# --- DIAGNOSTICS (With Outlier Filtering for Charts) ---
resid = model_ols.resid
fitted = model_ols.fittedvalues

# Filter 1st-99th percentile for cleaner plots
mask = (resid > resid.quantile(0.01)) & (resid < resid.quantile(0.99))
resid_filtered = resid[mask]
fitted_filtered = fitted[mask]
Y_filtered = Y[mask]

# Q-Q Plot (Filtered)
fig_qq = sm.qqplot(resid_filtered, line='s')

# Residuals vs Fitted (Filtered)
fig_resid, ax_resid = plt.subplots(figsize=(10, 6))
ax_resid.scatter(fitted_filtered, resid_filtered, alpha=0.5, color=UNIPI_PALETTE[1])
ax_resid.axhline(0, color='red', linestyle='--')
ax_resid.set_title('Residuals vs. Fitted Values (Outliers Removed)')

# OLS Predicted vs Observed (Filtered) - NEW GRAPH
fig_ols, ax_ols = plt.subplots(figsize=(8, 6))
ax_ols.scatter(Y_filtered, fitted_filtered, alpha=0.3, color='#003366', edgecolors='w')
min_val = min(Y_filtered.min(), fitted_filtered.min())
max_val = max(Y_filtered.max(), fitted_filtered.max())
ax_ols.plot([min_val, max_val], [min_val, max_val], 'r--', lw=2)
```

```
    ax_ols.set_xlabel('Observed Cost (Actual)')
    ax_ols.set_ylabel('Predicted Cost (Model)')
    ax_ols.set_title('OLS Fit: Observed vs. Predicted (Outliers Removed)')

    return df, model_hc3, beta_1, annual_savings, fig_qq, fig_resid, fig_ols, white_p


# ==========================================================
# 3. USER INTERFACE
# ==========================================================
st.set_page_config(page_title="Quality ROI Calculator", layout="wide", initial_sidebar_state="expanded")

if 'simulation_run' not in st.session_state:
    st.session_state['simulation_run'] = False

st.title("Cloud eQMS ROI Simulator")
st.caption("Strategic Decision Support Tool | Powered by Monte Carlo Simulation | UNIPI MBA TQM Thesis | Author:D.Vergis Supervisor:G.Bohoris")

# --- SIDEBAR ---
with st.sidebar:
    st.header("1. Financial Parameters")
    HOURLY_RATE = st.number_input("Avg Labor Rate (Per Hour)", min_value=1.0, value=50.0, step=5.0)
    CURRENCY_SYMBOL = st.text_input("Currency", "€")

    st.markdown("---")
    st.header("2. Efficiency Assumptions")
    SAVINGS_FACTOR = st.slider("Man-Hour Savings Realization (%)", 0, 100, 50)

    st.markdown("---")
    st.header("3. Risk & COPQ")
    AVG_FAILURE_COST = st.number_input("Avg Cost of Failure", value=5000.0, step=500.0)
    LEGACY_FAIL_RATE = st.slider("Legacy Failure Rate (%)", 0.0, 10.0, 2.5)
    DIGITAL_FAIL_RATE = st.slider("Digital Failure Rate (%)", 0.0, 10.0, 0.5)

    st.markdown("---")
    st.header("4. Linkage Costs")
    PENALTIES = {
        'CAPA': float(st.number_input("CAPA Penalty", value=5.0, min_value=0.0, step=0.5)),
```

```
        'CC': float(st.number_input("CC Penalty", value=6.0, min_value=0.0, step=0.5)),
        'DOC': float(st.number_input("Doc Penalty", value=2.5, min_value=0.0, step=0.5)),
        'COMPLAINT': float(st.number_input("Complaint Penalty", value=4.0, min_value=0.0, step=0.5))
    }

# --- MAIN INPUT ---
st.header("5. Enterprise QMS Configuration")
st.markdown("_SME staging table for a full-scale pharma eQMS rollout-configurable_")

editable_df = st.data_editor(
    DEFAULT_DF,
    num_rows="dynamic",
    use_container_width=True,
    column_config={
        "Module": st.column_config.SelectboxColumn("Module",
                                                   options=["Training", "Documents", "Deviations", "OOS/OOT", "CAPA",
                                                            "Change Ctrl", "Complaints", "Audits", "Supplier"],
                                                   required=True),
        "Annual_Volume": st.column_config.NumberColumn("Volume", min_value=0, step=1),
        "Complexity": st.column_config.NumberColumn("Complexity (1-5)", min_value=1.0, max_value=5.0, step=0.5,
                                                    format="%.1f")
    }
)

total_events = int(editable_df['Annual_Volume'].sum())
st.info(f"📊 **Total Enterprise Volume:** {total_events:,} events per year")

if st.button("▶️ Run Enterprise Simulation", type="primary"):
    if total_events <= 0:
        st.error("Volume must be > 0")
        st.stop()

    SIM_LIMIT = 5000
    if total_events > SIM_LIMIT:
        sim_n = SIM_LIMIT
        scale_factor = total_events / SIM_LIMIT
        st.warning(
            f"⚠️ Volume is high ({total_events:,}). Simulating {SIM_LIMIT} representative events and scaling results by {scale_factor:.2f}x.")
```

```
    else:
        sim_n = total_events
        scale_factor = 1.0

    with st.spinner(f'Simulating {sim_n} events...'):
        df_res, model, beta_1, ann_save, fig_qq, fig_res, fig_ols, white_p = run_simulation(
            HOURLY_RATE, sim_n, editable_df, PENALTIES, CURRENCY_SYMBOL, SAVINGS_FACTOR / 100.0
        )

        final_annual_savings = ann_save * scale_factor

        st.session_state.update({
            'df_res': df_res, 'model': model, 'beta_1': beta_1, 'ann_save': final_annual_savings,
            'fig_qq': fig_qq, 'fig_res': fig_res, 'fig_ols': fig_ols, 'white_p': white_p, 'simulation_run': True,
            'scale_factor': scale_factor
        })

# --- RESULTS ---
if st.session_state['simulation_run']:
    st.divider()
    t1, t2, t3, t4, t5 = st.tabs(["📊 ROI Overview", "🧩 ROI by Module", "🛡️ Risk", "📈 Diagnostics", "📋 Data"])

    scale = st.session_state.get('scale_factor', 1.0)

    # TAB 1: Overview
    with t1:
        c1, c2, c3 = st.columns(3)
        c1.metric("Avg Saving / Event", f"{CURRENCY_SYMBOL}{abs(st.session_state['beta_1']):,.2f}")
        c2.metric("Total Annual ROI", f"{CURRENCY_SYMBOL}{abs(st.session_state['ann_save']):,.0f}")

        avg_leg = st.session_state['df_res'][st.session_state['df_res']['System_State_Binary'] == 0][
            'Cycle_Days'].mean()
        avg_dig = st.session_state['df_res'][st.session_state['df_res']['System_State_Binary'] == 1][
            'Cycle_Days'].mean()
        c3.metric("Avg Speed Improvement", f"{avg_leg - avg_dig:.1f} Days")

        fig, ax = plt.subplots(figsize=(8, 4))
        # EXCLUDING OUTLIERS for better visual scale
```

```
    sns.boxplot(x='System_State_Binary', y=f'Total_Cost_{CURRENCY_SYMBOL}',
                data=st.session_state['df_res'], palette=UNIPI_PALETTE, ax=ax, showfliers=False)
    ax.set_xticklabels(['Legacy (Paper)', 'Digital (eQMS)'])
    ax.set_title("Cost Variance Analysis (Outliers Hidden for Clarity)")
    st.pyplot(fig)

# TAB 2: ROI by Module
with t2:
    st.subheader("Financial Impact by Quality Module")

    df_mod = st.session_state['df_res']
    # Group & Sum (and scale if needed)
    leg_cost = df_mod[df_mod['System_State_Binary'] == 0].groupby('Module')[
                f'Total_Cost_{CURRENCY_SYMBOL}'].sum() * scale
    dig_cost = df_mod[df_mod['System_State_Binary'] == 1].groupby('Module')[
                f'Total_Cost_{CURRENCY_SYMBOL}'].sum() * scale
    counts = (df_mod.groupby('Module')['Event_ID'].count() / 2) * scale

    mod_summary = pd.DataFrame({'Legacy Total': leg_cost, 'Digital Total': dig_cost, 'Volume': counts})
    mod_summary['Net Annual Savings'] = mod_summary['Legacy Total'] - mod_summary['Digital Total']
    mod_summary['Avg Saving per Event'] = mod_summary['Net Annual Savings'] / mod_summary['Volume']
    mod_summary = mod_summary.sort_values('Net Annual Savings', ascending=False)

    st.dataframe(
        mod_summary[['Volume', 'Net Annual Savings', 'Avg Saving per Event']].style.format({
            'Volume': '{:.0f}',
            'Net Annual Savings': f'{CURRENCY_SYMBOL}{{:.0f}}',
            'Avg Saving per Event': f'{CURRENCY_SYMBOL}{{:.2f}}'
        }),
        use_container_width=True
    )

    st.markdown("#### Annual Spend Comparison: Legacy vs. Digital")

    # Prepare data for plotting
    plot_data = mod_summary[['Legacy Total', 'Digital Total']].reset_index().melt(
        id_vars='Module', var_name='State', value_name='Annual Cost'
    )
```

```
    plot_data['State'] = plot_data['State'].replace(
        {'Legacy Total': 'Legacy (Paper)', 'Digital Total': 'Digital (eQMS)'})

    fig_mod, ax_mod = plt.subplots(figsize=(10, 6))
    sns.barplot(data=plot_data, x='Module', y='Annual Cost', hue='State', palette=UNIPI_PALETTE, ax=ax_mod)
    ax_mod.set_ylabel(f"Total Annual Cost ({CURRENCY_SYMBOL})")
    ax_mod.set_title("Operational Cost Comparison by Module")
    st.pyplot(fig_mod)

# TAB 3: Risk
with t3:
    leg_risk = total_events * (LEGACY_FAIL_RATE / 100) * AVG_FAILURE_COST
    dig_risk = total_events * (DIGITAL_FAIL_RATE / 100) * AVG_FAILURE_COST

    k1, k2, k3 = st.columns(3)
    k1.metric("Legacy Risk", f"{CURRENCY_SYMBOL}{leg_risk:,.0f}")
    k2.metric("Digital Risk", f"{CURRENCY_SYMBOL}{dig_risk:,.0f}")
    k3.metric("Avoidance Benefit", f"{CURRENCY_SYMBOL}{leg_risk - dig_risk:,.0f}")

    eff_leg = st.session_state['df_res'][st.session_state['df_res']['System_State_Binary'] == 0][
                f'Total_Cost_{CURRENCY_SYMBOL}'].sum() * scale
    eff_dig = st.session_state['df_res'][st.session_state['df_res']['System_State_Binary'] == 1][
                f'Total_Cost_{CURRENCY_SYMBOL}'].sum() * scale

    fig_r, ax_r = plt.subplots(figsize=(6, 4))
    pd.DataFrame({
        'State': ['Legacy', 'Digital'],
        'Labor Cost': [eff_leg, eff_dig],
        'Risk Liability': [leg_risk, dig_risk]
    }).set_index('State').plot(kind='bar', stacked=True, color=['#7f8c8d', '#f39c12'], ax=ax_r)
    ax_r.set_ylabel(f"Total Cost of Ownership ({CURRENCY_SYMBOL})")
    st.pyplot(fig_r)

# TAB 4: Diagnostics
with t4:
    st.markdown(f"**White Test p-value:** {st.session_state['white_p']:.4f}")
    st.caption("Note: Low p-value (<0.05) indicates Heteroscedasticity. Model uses HC3 Robust Standard Errors.")
```

```
    c1, c2 = st.columns(2)
    with c1:
        st.pyplot(st.session_state['fig_qq'])
        st.caption("**Normality Check:** Data should track the red line.")
    with c2:
        st.pyplot(st.session_state['fig_ols'])
        st.caption("**Goodness of Fit:** Points should cluster around the diagonal.")

    st.code(st.session_state['model'].summary().as_text())

# TAB 5: Data
with t5:
    st.dataframe(st.session_state['df_res'], use_container_width=True)
    st.download_button("📥 Download CSV", st.session_state['df_res'].to_csv(index=False).encode('utf-8'),
                       "sim_data.csv", "text/csv")
```

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