RESEARCH ARTICLE

INNOVATION AND EMERGING TECHNOLOGIES

Digitalisation in European pharmaceutical manufacturing: Towards an operational blueprint

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Digitalisation has become a strategic priority across European pharmaceutical manufacturing, yet many initiatives remain fragmented and poorly embedded in routine practice. Drawing on academic, regulatory and industry literature, this study develops a five-dimension provisional conceptual framework (PCF) and uses it to inform a questionnaire completed by 51 practitioners from 35 pharmaceutical organisations. Structured responses were analysed descriptively, while open-text responses were examined thematically. The findings indicate that digitalisation outcomes were shaped less by technology availability than by integration, data quality, governance, ownership, validation readiness and adoption support. Respondents associated digitalisation with stronger visibility, traceability, coordination and compliance support, but these benefits depended on digital systems becoming trusted and usable in daily workflows. These insights allowed the PCF to be developed into an operational blueprint for pharmaceutical digitalisation, sequencing prerequisites, aligning functions around inspection-ready digital routines and diagnosing implementation breakdowns. The findings will be of interest to researchers examining digitalisation in industry contexts and to practitioners in the pharmaceutical manufacturing sector charged with overseeing digitalisation projects.

Keywords: **Pharmaceutical Industry; Digitalisation; Operational Blueprint; Barriers; Success Factors.**

INNOVATION

This article introduces a practitioner-informed blueprint for examining the routinisation of digitalisation in Good Manufacturing Practice (GMP)-relevant pharmaceutical manufacturing. The blueprint frames digitalisation as a set of interdependent conditions that may need to be diagnosed and stabilised before digital systems become trusted, usable and inspection-ready in routine work. Existing maturity and technology-adoption frameworks often focus on digital capabilities but give less guidance on why digital tools often remain fragmented, hybrid or weakly trusted after implementation. This article addresses that gap by linking literature-informed dimensions with practitioner evidence and translating the findings into five priority activity areas: strategic direction and sequencing; governance, compliance and controlled change; digital foundations, integration and record trust; adoption and operating-model alignment; and routinisation and value evidence. The blueprint offers a structured lens for establishing prerequisites before scaling and alignment across different functions, whilst addressing implementation breakdowns and leadership capabilities. The practical value of the blueprint lies in supporting the transition from a technology deployment orientation to a focus on stable, integrated, inspection-ready digital routines.

INTRODUCTION

The pharmaceutical industry is deploying a range of information systems and digital tools to improve efficiency, quality, compliance, resilience and time-to-market[1–3]. The core information systems include enterprise resource planning (ERP) systems, manufacturing execution systems (MES), laboratory information management systems (LIMS), electronic batch records systems and quality management systems (QMS), whilst digital technologies focus mainly on analytics, artificial intelligence (AI), Internet of Things (IoT) and blockchain. However, progress remains uneven. The main issue is not simply technology availability, but whether digital technologies become integrated into core information systems and incorporated within stable, connected and compliant routine work under Good Manufacturing Practice (GMP) procedures and regulations. In this context, digital technologies must support manufacturing and quality workflows to facilitate records security, audit trails, exception

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Received 15 June 2026; accepted 16 June 2026; published online 16 July 2026; doi: 10.1142/S2737599426500064

handling, batch record reviews and release-related decisions that remain inspection-ready[4].

Some organisations may appear digitally active yet still depend to some degree on spreadsheets, emails, screenshots, manual reconciliation and even paper records, as well as digital applications that may be used in parallel[4,5]. In GMP-relevant manufacturing, 'value' can be conceptualised as a combination of stronger traceability, fewer manual reconciliations, more reliable batch review, faster investigation closure, improved audit readiness, reduced compliance risk and greater confidence in release-related work, rather than short-term financial return. These benefits are difficult to realise if systems remain fragmented, ownership is unclear, data are inconsistent or users are reluctant to transition to new digital processes.

This article focuses on the European pharmaceutical manufacturing ecosystem, particularly GMP-relevant manufacturing and closely related manufacturing-quality interfaces. It covers inbound supply chain, manufacturing operations, quality assurance and quality control, engineering and technical operations, and information technology/operational technology (IT/OT) integration, but excludes research and development, clinical trials, regulatory submission strategy, commercial marketing, sales and downstream distribution strategy. The focus is on operational areas where digital systems must become part of validated routine work and where inadequate technology integration can undermine data continuity, quality oversight, compliance evidence and day-to-day manufacturing control[6].

The study addresses a gap in the academic literature and a critical area of operational practice. Existing digitalisation and maturity frameworks assess readiness, levels of technology adoption and digital capability, but often give less guidance on how digital tools can most effectively be embedded in routine GMP-governed work. The study proposes an operational blueprint, based on literature-informed conceptual development and practitioner evidence, as a framework for planning and assessing digitalisation in pharmaceutical manufacturing.

More specifically, the study addresses two research questions (RQs):

RQ1. What are the main barriers and success factors that impact digitalisation outcomes in the European pharmaceutical manufacturing ecosystem?

RQ2. What blueprint and associated guidance can support the successful transition to digitalised operations in European pharmaceutical manufacturing?

Following this brief introduction, section 'Research Methods' outlines the research methods used in the study. Section 'Relevant Literature and Provisional Conceptual Framework' then reviews relevant literature which is used as the basis for the development of a provisional conceptual framework (PCF) for the primary research phase. Section 'Results' presents the findings and blueprint from the primary research analysis, and section 'Discussion' discusses some emergent issues in more detail. Finally, section 'Conclusion' concludes with contributions, limitations and future research directions.

RESEARCH METHODS

Study design

An interpretivist stance underpinned this exploratory, practitioner-informed study by treating participant responses as situated reflections on how digitalisation challenges are experienced, interpreted and addressed in GMP-relevant manufacturing and quality-system contexts. The study aimed to investigate the necessary conditions for practitioners to successfully go beyond fragmented digital tools deployment towards connected, digitally enabled, inspection-ready routine work. The research was conducted in three phases: literature review and PCF development; practitioner questionnaire data collection; and data analysis with blueprint development and member-checking refinement.

Literature review and PCF development

Phase 1 involved an integrative literature review rather than a systematic review, relevant literature being dispersed across a range of academic, regulatory and industry-facing sources. Searches were conducted through Scopus, Web of Science, ScienceDirect, IEEE Xplore and PubMed databases and via the Google Scholar search engine, supported by targeted searches of regulatory and professional sources, including EU GMP guidance, EMA and FDA materials and ISPE publications. Search terms combined 'digitalisation', 'digitalization', 'digital transformation', 'Industry 4.0', 'Pharma 4.0' and 'smart manufacturing' with 'pharmaceutical manufacturing', 'biopharmaceutical manufacturing', 'GMP manufacturing' and 'regulated manufacturing'. Additional searches combined 'pharmaceutical manufacturing' with 'MES', 'LIMS', 'ERP', 'electronic batch records', 'IT/OT integration', 'process analytical technology', 'digital twin', 'artificial intelligence', 'advanced analytics', 'data integrity', 'computerised system validation', 'audit trail', 'barriers', 'challenges', 'critical success factors', 'implementation', 'adoption', 'governance' and 'change management'.

The review prioritised peer-reviewed English-language publications from 2019 to 2025, while retaining earlier foundational sources where needed to define established concepts, discuss widely used frameworks or clarify GMP-relevant requirements. Sources were included where they addressed digital technologies, implementation conditions, reported impacts, barriers, success factors, maturity or adoption frameworks, or regulatory and operational issues relevant to pharmaceutical manufacturing. Sources which focused mainly on R&D, clinical trials, regulatory submission strategy, commercial marketing, sales or downstream distribution logistics were excluded unless they had a clear link to GMP-relevant manufacturing or quality-system work.

The review informed the PCF, which grouped the main conditions shaping digitalisation into five dimensions: Technological Deployment, Organisational Structuring, Regulatory Compliance, Process Reengineering, and External Environment and Stakeholders. The PCF informed questionnaire design and provided an initial structure for interpretation, while the empirical themes were developed from participant responses rather than imposed as predefined categories.

Questionnaire design and data collection

Phase 2 used a questionnaire to gather the perspectives of practitioners involved in, or directly supporting, GMP-relevant digitalisation in pharmaceutical manufacturing. The questionnaire included both structured items and open-text questions. Structured items captured respondent background, organisational and technical context, impacts, barriers, success factors and value indicators. Open-text questions provided deeper insight into digitalisation initiatives, practical constraints, enabling conditions, integration issues, role-specific examples and framework development. This was deemed appropriate as digitalisation in pharmaceutical manufacturing is shaped not only by technology but also by governance, validation, data integrity, operating-model alignment and day-to-day practice[7,8].

The questionnaire was mainly administered through Google Forms, with a Word version available where company IT restrictions prevented access. Materials were shared only after participants had opted in. Most questions were optional to reduce forced or speculative responses. Minor wording refinements after the first five pilot completions improved clarity without changing the instrument's structure, core constructs or analytic role; these responses were retained. The Checklist for Reporting Results of Internet E-Surveys[9] (CHERRIES) was used as a guideline for the questionnaire analysis.

Participant recruitment and sample profile

Participants were recruited through purposive LinkedIn outreach and were considered eligible if their roles related to manufacturing, supply chain, quality, engineering, IT/OT, digital transformation, validation or adjacent ecosystem activities within appropriate business sectors.

Table 1 Sample profile by organisation type, role category and region.

Category	*n*	%
Organisation type		
Pharma/biopharma manufacturers	31	60.8
CDMO/contract manufacturers	2	3.9
Specialist biotech/specialty manufacturers	6	11.8
Ecosystem and adjacent organisations	12	23.5
Role category		
IT/Digital	17	33.3
Supply chain	12	23.5
Production/operations	7	13.7
Quality/regulatory	5	9.8
Other	5	9.8
Unspecified	3	5.9
General management/cross-functional leadership (function not specified)	2	3.9
Region grouping		
German-speaking Europe (Germany + Switzerland)	30	58.8
Nordics (Denmark + Sweden)	6	11.8
Benelux (Belgium + Netherlands)	4	7.8
Southern Europe (France + Italy + Spain)	4	7.8
British Isles (UK + Ireland)	3	5.9
Eastern Europe (Poland + Hungary)	2	3.9
Other (India + unknown)	2	3.9

Notes: Base = *N* = 51 eligible participants. Percentages are based on participant counts and rounded to one decimal place. Role categories were coded to one primary category; 'Unspecified' indicates no usable role description. 'Other (India + unknown)' includes one participant located in India, retained because the individual's work directly affected European pharmaceutical manufacturing and met the inclusion criteria, and one respondent whose location could not be verified.

The sample included pharmaceutical and biopharmaceutical manufacturers, contract development and manufacturing organisations (CDMOs), specialist biotech manufacturers, and a smaller number of ecosystem or adjacent regulated organisations whose activities directly interfaced with GMP-relevant manufacturing or quality systems. Data collection took place between May and November 2025. After screening for eligibility and duplicates, the final dataset comprised 51 eligible respondents from 35 organisations. **Table 1** provides an overview of the sample profile.

The sample was a purposively recruited cross-functional practitioner sample from the European pharmaceutical manufacturing industry. Most participants were based in Europe, with the largest share located in German-speaking Europe. The findings are therefore presented as practitioner-informed insights rather than statistically representative sector-wide evidence.

Data analysis and blueprint development

Phase 3 involved descriptive and thematic analysis of the questionnaire data and blueprint development. Questionnaire responses were exported from Google Forms and imported into NVivo. Structured responses were analysed to identify organisational context, commonly reported barriers, prioritised success factors and selected indicators of perceived impact. No inferential statistics were conducted. Structured questions that were not central to the main findings were used to provide context, support traceability or inform supplementary interpretation. Missing responses were reported using valid-n counts and were not estimated or replaced.

The open-text responses formed the main analytic material and were analysed in NVivo through a two-layer thematic process combining PCF-informed indexing with inductive interpretation of participant responses[10]. In the first layer, responses were indexed according to reported impacts, implementation challenges, success factors and material relevant to the blueprint. Where appropriate, they were also indexed against the five PCF dimensions covering technology, organisation, compliance, process redesign and external stakeholders. This first-layer indexing helped maintain a clear link between individual responses, the questionnaire topics, the PCF and the article's RQs. In the second layer, the indexed material was reviewed again to identify broader themes across roles, organisations and recurring implementation issues. Initial themes were then refined by checking whether they overlapped, contained different issues, or did not explain the responses clearly. The themes were developed through comparison of recurring patterns in participant responses and were not designed to reproduce the PCF dimensions.

The thematic analysis generated seven cross-cutting themes representing conditions under which digitalisation progressed, stalled, remained hybrid or became more routine in practice. These themes captured the empirical patterns identified in the open-text responses. The digitalisation blueprint, presented in section 'RQ2: What Operational Blueprint and Guidance Can Support the Successful Transition to Digitalised Operations in European Pharmaceutical Manufacturing?', was then developed as the practical output of the study by translating these themes into five priority activity areas (PAAs). The move from seven empirical themes to five blueprint PAAs involved grouping related themes where the data showed that they operated together as linked implementation conditions.

Member checking, ethics and trustworthiness

After completion of the thematic analysis and development of the draft digitalisation blueprint, a purposive maximum-variation sub-sample of ten participants reviewed the draft blueprint and completed a short-structured feedback questionnaire as part of the member-checking process. The reviewers represented different functional perspectives, including IT/OT, supply chain, CSV, operations/manufacturing, QC, digital transformation, engineering and consulting. The purpose was to assess whether the blueprint reflected participants' practical experience and whether it was clear and usable in GMP-relevant settings. Their feedback was used to refine the wording, structure and presentation of the blueprint, particularly around validation, controlled change, adoption support and operational specificity. Member checking was therefore treated as a credibility and usability review, not as external validation or evidence of effectiveness.

Across the primary research phases, participation was voluntary and based on informed consent. Participants received an information sheet before completing the questionnaire; responses were allocated to appropriate respondent codes, and findings are reported in anonymised form. Data were handled in accordance with institutional requirements and GDPR-compliant principles. Trustworthiness was supported through cross-functional sampling, systematic coding, PCF-to-questionnaire traceability, member checking and an audit trail covering recruitment, eligibility screening, coding, theme development and blueprint refinement[11].

RELEVANT LITERATURE AND PROVISIONAL CONCEPTUAL FRAMEWORK

This section reviews the academic, regulatory and industry-facing literature on digitalisation in pharmaceutical manufacturing, encompassing implementation challenges, enabling conditions and relevant frameworks. Available literature supports the view that digitalisation in this sector cannot be understood as technology deployment alone but rather depends on the interaction of digital tools, validated processes, data integrity,

governance, workforce capability and cross-functional coordination under GMP requirements. This perspective supported the development of the PCF, which guided questionnaire design and interpretation.

Digitalisation in pharmaceutical manufacturing

The terms digitisation, digitalisation and digital transformation are often used interchangeably, but they refer to different levels of change. In pharmaceutical manufacturing, digitisation usually means converting paper-based or analogue records into digital form, for example through electronic documents, electronic batch records, digitalised standard operating procedures (SOPs) or laboratory data capture. Digitalisation goes further by embedding digital tools, data flows and analytics into routine workflows, so that execution, monitoring, review, exception handling and decision-making can be supported digitally. Digital transformation refers to broader organisational change in which digital technologies alter how work is organised, governed and improved across functions and sites. Vial[12] emphasises that digital transformation involves organisational change triggered by combinations of information, computing, communication and connectivity technologies.

This broader understanding is important in pharmaceutical manufacturing because the value of digital tools depends not only on their technical deployment but also on whether they are embedded in controlled, auditable and usable routines. Digital technologies such as IoT/IIoT (Industrial Internet of Things) sensors, AI, machine learning, advanced analytics, digital twins, robotics, cloud platforms, edge computing and blockchain-based applications can support stronger visibility, process control, improved traceability, quality monitoring and supply-chain coordination[5,13–15]. However, these benefits are conditional. Digital technologies create sustained value only when they are connected to reliable data, interoperable systems, validated workflows and decision routines that are usable in practice and defensible under GMP[2,5,13].

This distinction is central to the present article. Pharmaceutical manufacturers may appear digitally active while still relying on paper, spreadsheets, screenshots, emails, manual reconciliation or informal workarounds. In such cases, digitalisation remains incomplete because it is not central to the trusted way work is executed, reviewed, investigated or released.

Implementation challenges and enabling conditions

The literature identifies multiple challenges that affect the implementation and scaling of digitalisation in pharmaceutical manufacturing. These challenges are strategic, technical, regulatory, financial, organisational and ecosystem-related, and they often reinforce one another.

One major challenge is the lack of a clear digital strategy. Many organisations launch digital projects without a clearly defined target state, roadmap or sequencing logic. This can lead to isolated pilots, local tool adoption, duplicated initiatives and weak alignment between digital projects and business or quality-system priorities[2,16,17]. This is especially problematic in pharmaceutical manufacturing because digital tools must work within validated processes, controlled change, data-integrity rules and quality oversight.

Another major challenge concerns legacy systems and weak interoperability. Pharmaceutical manufacturers often operate complex system landscapes that include ERP, MES, LIMS, QMS, electronic document management systems (EDMS), supervisory control and data acquisition (SCADA) systems, distributed control systems (DCS), programmable logic controllers (PLCs) and 'data historians', which record and retrieve time-stamped data from SCADA, MES, PLCs and other control systems. Some of these systems may be based on modern technology, while others are older, site-specific or difficult to integrate. Legacy architectures and proprietary interfaces can make end-to-end data flow difficult, especially between enterprise systems and shop-floor operational technology[6,15]. Where systems do not communicate reliably, teams often compensate through manual reconciliation, duplicate data entry or spreadsheet-based controls. This weakens trust in the digital record and limits the feasibility of advanced analytics, digital twins and review-by-exception.

A third challenge is data governance. Digitalisation depends on reliable master data, consistent data definitions, controlled metadata, clear ownership and traceable data flows. Inconsistent data formats, unclear source-of-truth rules, weak master-data governance and fragmented repositories can make it difficult to trust the output of digital systems[2,5]. In a GMP context, poor data governance is not only an efficiency problem. If data are inconsistent, incomplete or difficult to trace, teams may struggle to reconstruct events, investigate deviations, review batches, justify release decisions and provide reliable evidence during inspections.

A fourth challenge relates to regulatory compliance and validation. Digital systems in pharmaceutical manufacturing must operate within requirements for computerised system validation, audit trails, electronic records, electronic signatures, controlled access, data integrity and lifecycle management. EU GMP Annex 11 and related electronic-record regulations are particularly relevant because they shape how computerised systems must be validated, controlled and documented[4,13,18,19]. These requirements are essential for patient safety and product quality. However, implementation can be delayed when validation, data-integrity checks, audit-trail requirements, access controls and documentation are considered only after the digital system has already been designed or configured.

A fifth challenge concerns people, culture and skills. Digitalisation requires operators, supervisors, engineers, quality teams, IT/OT specialists, validation teams and managers to adopt new ways of working. Skills gaps in data science, automation, analytics, cybersecurity, validation and digital process ownership can limit adoption and increase reliance on external vendors[5,20]. Resistance to change may also emerge where users do not trust the system, do not understand the new workflow, or continue to find informal workarounds easier than the formal digital process.

These challenges point to a set of recurring enabling conditions. Successful digitalisation requires strategic leadership, clear governance, workable decision rights, adequate resourcing, manageable IT/OT architecture, reliable data governance, early quality and validation involvement, role-based training, adoption support and credible evidence of value. A step-by-step approach can help organisations reduce risk before scaling. It allows teams to test whether systems connect properly, workflows work in practice, users can adopt the new process and the required validation evidence can be produced[5,21]. However, phased implementation should not mean running isolated pilots that cannot be scaled. A pilot is useful only if it tests the main conditions needed for wider rollout, including data quality, system integration, validation approach, user support, operational ownership and evidence of value.

Value evidence is particularly important in regulated manufacturing. Digitalisation should not be evaluated only through short-term cost reduction or immediate return on investment (ROI). Value may also appear through reduced deviation burden, more predictable batch review, stronger traceability, improved audit readiness, faster investigation closure, more reliable release-related work and reduced compliance risk. These forms of value are central in GMP-relevant settings because the benefits of digitalisation often appear first in quality control, quality assurance and routine operational stability before they appear in financial metrics.

Existing frameworks

Several existing frameworks help explain important aspects of digitalisation, but each has limitations when applied to GMP-relevant pharmaceutical manufacturing. Industry 4.0 maturity and readiness models help organisations assess how prepared they are for digitalisation, examining technology, processes, skills, governance, data use and organisational capability to assess how an organisation can move towards more advanced levels of digital integration[22]. In pharmaceutical manufacturing, digital maturity is not only about having advanced digital tools or systems but also depends on whether those systems are validated, connected to

other systems, trusted as reliable records and consistently used in daily GMP-relevant work.

Technology adoption frameworks also help explain why organisations and users decide to adopt digital tools. The Technology–Organisation–Environment (TOE) framework shows that adoption is influenced by three areas: the available technology, the organisation's internal capabilities and external pressures such as regulation, competition or partner requirements. The Technology Acceptance Model (TAM) focuses more on the user perspective, especially whether users see a system as useful and easy to use[23–26]. These perspectives are useful, but they do not fully explain how digital tools become embedded in validated workflows over time, especially where audit trails, change control, data integrity and release-related decisions are involved.

Change-management frameworks add a further perspective by focusing on how people adopt and sustain new ways of working. The Awareness, Desire, Knowledge, Ability, and Reinforcement (ADKAR) framework is based on the premise that change is more likely to be successful when users understand why change is needed, want to support it, understand the new ways of working, are able to apply them in practice, and receive reinforcement and support over time[27]. Integrated business process management approaches connect digital tools deployment to the redesign and control of business processes, requiring digital systems to be implemented with clearer workflows, defined responsibilities, measurable process performance and mechanisms for continuous improvement[28,29]. These frameworks are valuable because digitalisation often fails not at the moment of technical deployment, but during operational embedding. They help explain how users adopt new ways of working and how digital tools can be connected to redesigned processes. However, they do not fully address the specific constraints of pharmaceutical manufacturing, where digital workflows must also meet requirements for validation, data integrity, audit trails, controlled change and inspection readiness.

Pharma-specific frameworks provide stronger links to regulatory and quality requirements. For example, Pharma 4.0 and smart-factory frameworks show how technologies such as cyber-physical systems, process analytical technology (PAT), digital twins, automation and advanced data systems can support pharmaceutical manufacturing. They also emphasise that these technologies must be connected to data integrity, quality systems, validation and compliance-by-design[13,14,30]. The 5Ps of GMP – people, process, procedures, premises and equipment, and products – also provide a useful quality-oriented lens because they connect digitalisation to validated practice, workforce capability and patient safety[5]. However, pharma-specific frameworks often focus on technologies, quality principles or specific use cases rather than on the full set of conditions needed to embed digital tools across functions in routine GMP-governed work.

In summary, many frameworks are technology-centred and explain what tools can do, but less clearly how those tools become integrated across functions and embedded in routine work. Second, governance and operating-model issues are often underdeveloped, especially around decision rights, ownership, resourcing, cross-functional coordination and controlled change. Third, the sequencing and interdependencies are often not sufficiently clearly articulated. Frameworks may list relevant dimensions, but they do not always show what must be stabilised before advanced applications can scale. Fourth, evidence and measurement remain difficult because many benefits of digitalisation are delayed, indirect or compliance-related rather than immediately financial. These gaps suggest that digitalisation in pharmaceutical manufacturing needs to be understood not only through technology, maturity or adoption lenses, but also through the conditions that allow digital systems to become stable, connected, trusted and inspection-ready in practice.

Provisional conceptual framework

The PCF to guide the empirical research was developed based on the analysis of the extant literature reported above. The PCF was used as an organising framework to bring together the main conditions that shape digitalisation in European pharmaceutical manufacturing. These conditions are detailed in **Fig. 1** and are grouped under the five main change

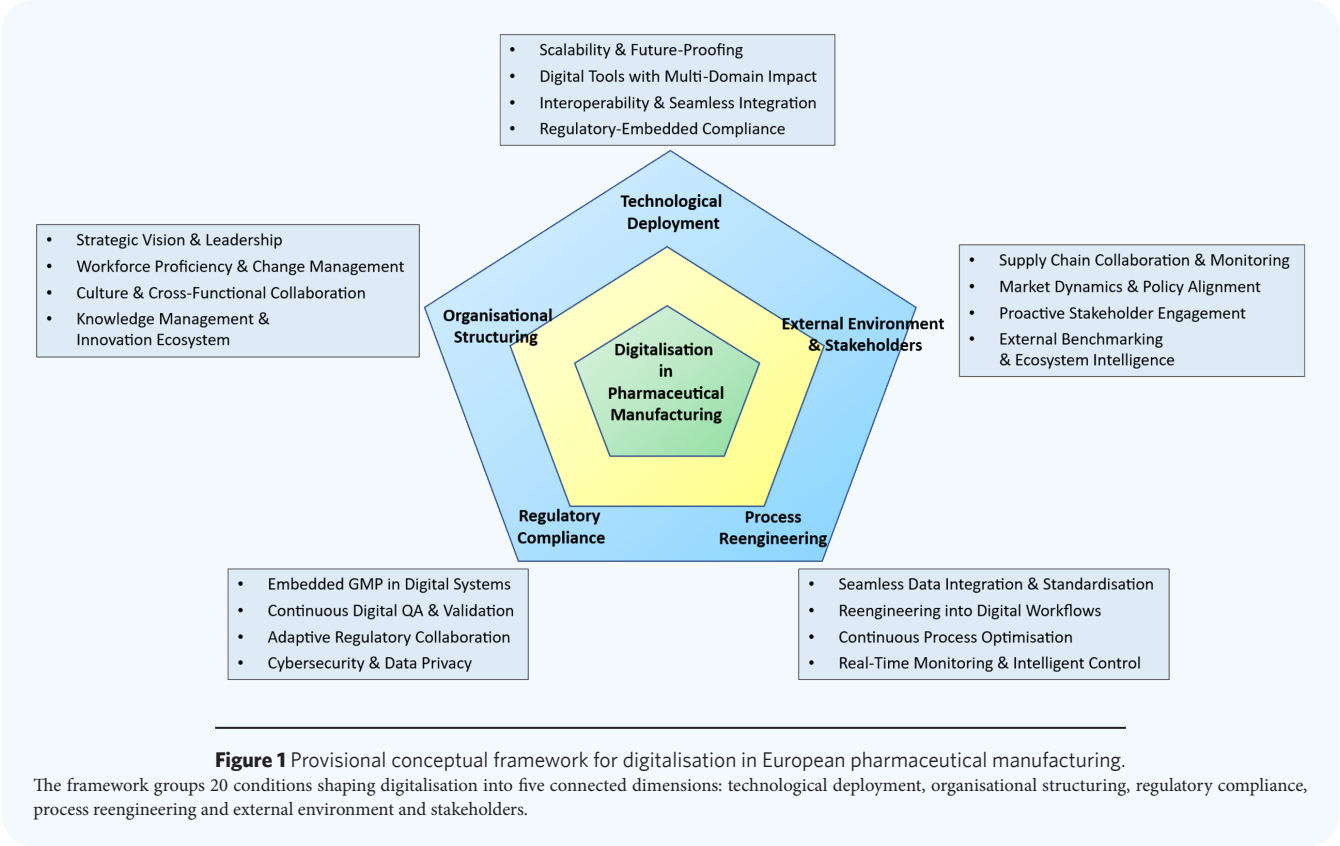

Figure 1 Provisional conceptual framework for digitalisation in European pharmaceutical manufacturing.
The framework groups 20 conditions shaping digitalisation into five connected dimensions: technological deployment, organisational structuring, regulatory compliance, process reengineering and external environment and stakeholders.

dimensions: technology, organisational structure, regulatory compliance, process redesign and external stakeholders.

Technological deployment refers to the tools, platforms, infrastructure and data architecture used to generate reliable data, integrate systems and support workflow continuity in regulated settings. Organisational structuring covers the strategic, leadership, governance, resourcing, skills, cultural and knowledge-management conditions that shape whether digital tools become routine. Regulatory compliance refers to the GMP, validation, data integrity, cybersecurity, documentation and inspection-readiness requirements that structure digital system design, implementation, change control and use. Process reengineering concerns the redesign and embedding of workflows, including execution, review, escalation, exception handling, review-by-exception, release-related work and the retirement of unnecessary hybrid controls. External Environment and Stakeholders covers suppliers, CDMOs, CROs, technology partners, regulators and external data-exchange requirements that affect traceability, quality oversight and GMP-relevant handovers.

These five dimensions represent distinct but connected aspects of digitalisation identified in the literature. Supplementary Information S1–S4 provide further detail on the framework dimensions, the literature-to-PCF mapping, the PCF-to-questionnaire mapping, and the translation of empirical themes into blueprint PAAs.

RESULTS

This section presents the findings in relation to the two RQs.

RQ1. What are the main barriers and success factors that impact digitalisation outcomes in the European pharmaceutical manufacturing ecosystem?

Within the dataset, the most frequently selected barriers were resistance to change, legacy-system incompatibility, data standardisation issues, skills gaps and budget constraints. The success factors most often assigned Priority 1 were leadership and executive sponsorship, change management and workforce development, cross-functional governance, data standardisation and digital quality assurance and clear KPI and metric frameworks. These findings suggest that respondents viewed digitalisation less as a technology deployment process but more as a wider implementation, governance, integration and operating-model challenge. **Table 2** summarises the most frequently reported barriers and the success factors most often assigned Priority 1 by respondents.

The barrier results show that implementation difficulties were rarely straight-forward. Resistance to change, the most frequently selected barrier, was not presented simply as user reluctance to engage in new digital systems. Open-text responses linked it to weak user ownership, insufficient involvement of senior management, poor communication and limited reinforcement after go-live. For example, R49 stated that organisations should 'involve all stakeholders from the beginning and maintain a communicative culture throughout the entire digitalisation process'. R21 similarly argued that 'change management is key to success, as is the development of employees' technical skills'. This suggests that adoption problems were not simply behavioural, but were linked to how well users were involved, prepared, supported and reinforced during and after implementation.

Legacy-system incompatibility and data standardisation issues were also seen as problematic. Respondents described older systems, weak interfaces, poor synchronisation, inconsistent data formats and unclear source-of-truth rules as obstacles to reliable digital work. R30 explained that 'older systems were often built as standalone solutions and are not designed to communicate easily with modern digital tools, cloud platforms, or IoT devices'. R5 summarised the issue as 'data format and mapping, outdated system, lack of support from vendors in terms of adapting legacy systems to new tools'. These responses illustrate that integration problems are not only technical system issues but also involve data consistency, workflow reliability and trust in the digital record.

Skills gaps, budget constraints and ROI expectations also impacted the digitalisation process. Respondents linked weaker progress to training that was poorly timed, insufficiently promoted, or not connected closely enough to real workflows. For example, R29 noted that 'training is sometimes not aligned with go-live dates'. Financial justification was also difficult where the benefits were delayed, indirect or compliance-related. R36 stated that 'often the business case is not clear: what problem are we trying to solve, and what benefits do we expect to realise'. Foundational work related to, for example, data governance, system integration, validation readiness and change support, may struggle to receive sufficient resources when its value is not clearly defined or measured.

Other reported barriers emphasised the interrelationship and complexity of digitalisation projects. Cross-functional communication problems showed the need to 'create interdisciplinary teams to bridge people, process, technology and data' (R5). Lack of top management support pointed to the need for 'clear top-to-bottom directives with

Table 2 Barriers and success factors assigned the highest priority for digitalisation implementation.

Most Frequently Reported Barriers	*n*	% Valid Respondents (*n* = 48)	Success Factors Assigned Priority 1	*n*	% of *N* = 51
Resistance to change	29	60.4	Leadership and executive sponsorship	26	50.9
Legacy-system incompatibility	27	56.2	Change management and workforce development	18	35.3
Data standardisation issues	26	54.2	Cross-functional governance	14	27.5
Skills gap	22	45.8	Data standardisation and digital quality assurance	13	25.5
Budget constraints	21	43.8	Clear KPI and metric frameworks	12	23.5
Cross-functional communication	16	33.3	Advanced technologies and analytics adoption	8	15.7
Lack of top management support	16	33.3	Cybersecurity and data integrity measures	6	11.8
Regulatory validation delays	14	29.2	Supply-chain digitisation and end-to-end traceability	6	11.8
Limited adaptability to change	11	22.9	Modernised IT infrastructure and legacy upgrades	6	11.8
Cybersecurity concerns	7	14.6	Incremental/phased implementation	5	9.8

Notes: Barriers were captured through a multi-select item and are reported against valid responses only (*n* = 48); percentages may exceed 100% because respondents could select up to three barriers. Success factors are reported as items assigned Priority 1; percentages are based on *N* = 51. Because respondents could assign Priority 1 to more than one success factor, these figures indicate strongest emphasis in the sample rather than a mutually exclusive rank order.

accountability for failure and success' (R2). Regulatory validation delays were linked to the difficulty of changing systems already embedded in validated processes, where changes may require 'extensive revalidation, documentation, and regulatory scrutiny' (R30). Cybersecurity measures, although less frequently identified, were nevertheless viewed as part of the cost of maintaining safe and compliant digital operations.

The success factor assessments reinforce the view implementation success is not primarily dependent on technology deployment. Leadership and executive sponsorship were assigned Priority 1 by 26 of 51 respondents. Respondents saw leadership as necessary for converting digitalisation from isolated local initiatives into an aligned roadmap with ownership, priorities and accountability. R29, for example, noted that organisations should 'have the top management empowered to align on a roadmap, which can be used to break down goal settings to individual business units/areas'. R2, a production/operations respondent, similarly called for 'clear top-to-bottom directives with accountability for failure and success'. These responses indicate that executive sponsorship mattered not only as visible support but also as a mechanism for aligning direction, resources and cross-functional execution.

As regards adoption capability, change management and workforce development were assigned Priority 1 by 18 respondents, reflecting the importance of preparing people to use digital systems reliably in routine GMP work. R21 argued that 'change management is key to success, as is the development of employees' technical skills', while R49 emphasised the need to 'involve all stakeholders from the beginning and maintain a communicative culture throughout the entire digitalisation process'. Resistance to change was not seen as only individual reluctance but as a consequence of whether users were involved early, trained appropriately, and supported during and after implementation.

Cross-functional governance, data standardisation and digital quality assurance, and clear KPI frameworks were assigned Priority 1 by 14, 13 and 12 respondents respectively. Respondents called for 'interdisciplinary teams to bridge people, process, technology and data' (R5), while integration and data-quality barriers were linked to 'data format and mapping, outdated system, lack of support from vendors in terms of adapting legacy systems to new tools' (R5). At the same time, R36 noted that 'often the business case is not clear: what problem are we trying to solve, and what benefits do we expect to realise'.

The questionnaire responses highlight the imperative of the alignment of strategic direction, digital governance, data management, adoption support and value evidence in digitalisation projects in pharmaceutical manufacturing.

RQ2: What operational blueprint and guidance can support the successful transition to digitalised operations in European pharmaceutical manufacturing?

Across the open-text responses, seven recurring themes were identified (**Fig. 2**). These are outlined below.

Strategic direction and future-state alignment highlighted the importance of defining the target end-to-end way of working prior to the deployment of tools. R8 summarised this as the need to 'focus on solving the right problems' and to ensure 'a clear scope and strategy'. *Governance, leadership and portfolio decision-making* emphasises that governance is necessary but has to remain workable. R35 noted, 'governance models are complex - sometimes too much governance can hinder progress and prevent fast decision making'. *People readiness, culture and adoption capability* reflected the importance of training, ownership, reinforcement and post-go-live support. Respondents showed that adoption depended not only on formal training, but also on whether support was timed and reinforced in practice. In this context, R29 commented that 'training is sometimes not aligned with go-live dates, so knowledge may already be lost by then or may not have been built up sufficiently'. *Operating model and ecosystem orchestration* highlighted the need to coordinate responsibilities, handovers and data exchange across functions, sites and external partners. R48 described this as the need for 'securing and standardising data exchange with external partners such as CMOs, CDMOs, and CROs'. *Establishing digital foundations and integration preconditions* was strongly linked to weak interfaces and loss of trust in the digital record. R14 explained that 'the ERP system would not display updated quantities that had already been recorded in the MES system…that generates confusion and a lot of investigation'. *Operational digitalisation in practice* focused on whether digital workflows operated end-to-end without manual breaks. R25 stated that 'the challenge is always to implement end-to-end workflows without any breaks in between'. *Value realisation, metrics and risk trade-offs* showed that value was understood not only in financial terms, but also in terms of compliance, assurance, operational continuity and risk reduction. R22 argued that projects needed for 'regulatory compliance and cyber security' should be recognised as 'the cost to keep the business running'.

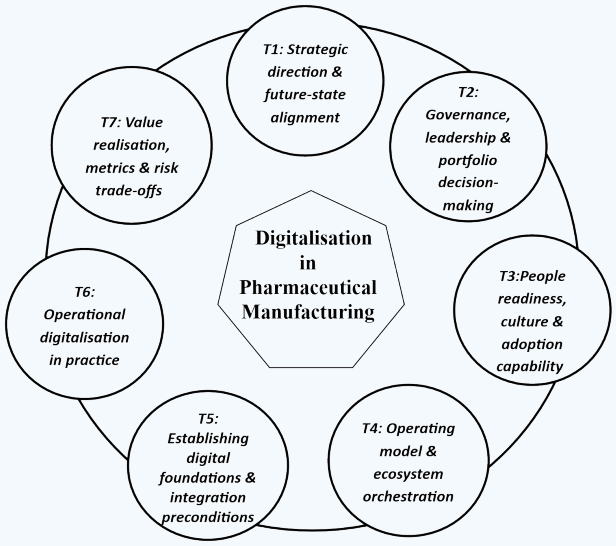

Figure 2 Digitalisation in pharmaceutical manufacturing: key themes in questionnaire responses.

Some respondents also described more mature digitalisation states. R1, for example, identified 'MES and EBR [Electronic Batch Recording] with full concept of Review by Exception and Release by Exception' as a potential benefit. On the other hand, other respondents warned that excessive governance or digitising unstable processes could exacerbate current problems. Overall, responses underlined the need for stability, consistency and alignment of governance, workflow design and technology adoption conditions.

The seven empirical themes were used as the basis for the definition of five interconnected stages that constitute a blueprint for digitalisation in pharmaceutical manufacturing. Themes were merged where they addressed related implementation problems, involved overlapping organisational actors, or pointed to the same practical stabilisation activity. The PCF was literature-derived, the themes were developed from questionnaire responses, and the blueprint translated these themes into PAAs (**Table 3**).

Stages A, B and C mainly correspond to one theme each. Stage D combines people readiness with operating-model orchestration because both concern the alignment of roles, ownership, handovers, sites and partners around new digital routines. Stage E combines operational digitalisation with value evidence because routine use and credible evidence for scaling were treated as mutually dependent in the data. The resulting blueprint structure is shown in **Fig. 3**.

Table 3 Translation of empirical themes into blueprint priority activity areas (PAAs).

Empirical Themes (T1–T7)	Key Issue Identified in the Findings	Blueprint Priority Activity Area
T1 Strategic direction and future-state alignment	Digital tools were weaker where the target workflow, scope, sequencing and future state were unclear.	A. Strategic direction and sequencing
T2 Governance, leadership and portfolio decision-making	Progress depended on decision rights, ownership, prioritisation, validation involvement and workable governance.	B. Governance, compliance and controlled change
T5 Digital foundations and integration preconditions	Weak interfaces, poor data continuity and unclear source-of-truth rules reduced trust in digital records.	C. Digital foundations, integration and record trust
T3 People readiness, culture and adoption capability	Adoption was weaker where training, ownership, reinforcement and post-go-live support were insufficient.	D. Adoption and operating-model alignment
T4 Operating model and ecosystem orchestration	Digitalisation was harder where partner handovers, external data exchange and cross-site responsibilities were unclear.	D. Adoption and operating-model alignment
T6 Operational digitalisation in practice	Digitalisation became stronger where end-to-end workflows operated without manual breaks or parallel workarounds.	E. Routinisation and valuable evidence
T7 Value realisation, metrics and risk trade-offs	Value needed to include compliance, assurance, risk reduction and routine stability, not only short-term ROI.	E. Routinisation and valuable evidence

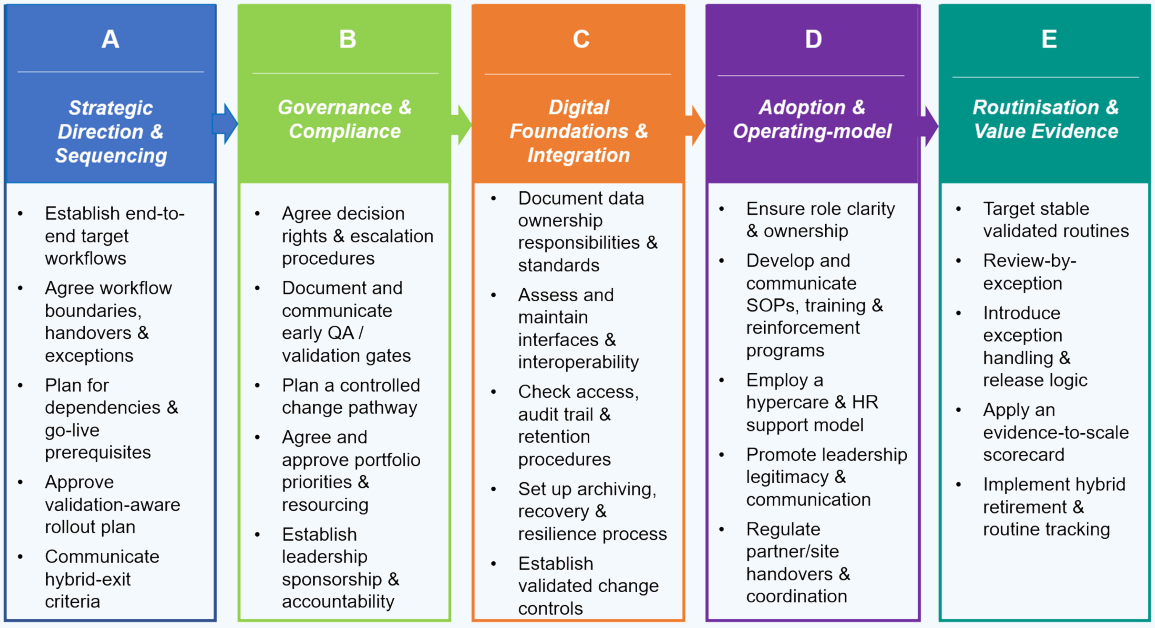

Figure 3 The operational blueprint for digitalisation in pharmaceutical manufacturing.
The blueprint translates the empirical themes into five priority activity areas (A–E). It includes key actions for each PAA and is intended as a diagnostic, sequencing and cross-functional alignment tool for GMP-relevant digitalisation programmes.

The blueprint is intended to provide a structured diagnostic lens for examining where digitalisation may be breaking down, which conditions may need stabilisation before scaling, and which functions may need to be involved. For example, in an ERP–MES–LIMS record mismatch, a batch may be executed in MES, test results generated in LIMS, and material movements recorded in ERP, but the records do not align. The visible symptom may be delayed batch review, while the underlying causes may include unclear source-of-truth rules, weak interface design, insufficient exception handling, late QA/validation involvement or lack of agreed evidence for release-related review. The blueprint therefore encourages attention to move from the mismatch as a narrow system defect to the linked conditions that may allow it to persist. Practical actions may include mapping system handovers, defining data ownership for critical fields, testing exception paths, clarifying QA evidence requirements and prioritising the highest-risk breakpoints before scaling. The fully worked version is provided in Supplementary Information S5.1, alongside further illustrative scenarios on stalled change requests, post-go-live workarounds, weak foundational preparation and invisible value, and system outage, archiving or retention failures. These scenarios illustrate how the blueprint can support diagnosis, sequencing and cross-functional discussion.

Participants involved in member checking judged that the blueprint broadly reflected real-world GMP digitalisation challenges and was relevant and usable for day-to-day implementation practice. Their suggestions, particularly around validation, controlled change, adoption support and practical use, informed the final wording and presentation.

Member checking was used as a credibility and usability review rather than as a systematic validation.

DISCUSSION

A number of emergent issues merit further discussion. First, the benefits of digitalisation appear to be conditional rather than automatic. Participants associated digitalisation with stronger visibility, traceability, coordination, control and compliance support. However, these benefits were strongest where digital systems were embedded in connected workflows, supported by trusted records, and usable in daily GMP-relevant work. Where workflows remained fragmented, data were inconsistent or records were not trusted, digitalisation produced weaker and less stable benefits. This supports the view that value in regulated manufacturing should not be assessed only through short-term financial return. Important benefits may first appear through stronger traceability, fewer manual reconciliations, more predictable batch review, improved audit readiness, lower compliance risk and more reliable release-related work. These forms of value are critical, but they can be difficult to capture through conventional ROI measures.

Second, the findings help explain why hybrid work can persist after digital tools have been deployed. In this context, hybrid work means that digital systems are used alongside informal or manual controls, such as paper records, Excel trackers, screenshots, emails, duplicate data entry or manual reconciliation. These workarounds can become normal practice when digital ambition is not supported by reliable integration, clear ownership, trusted data, workable processes, timely quality involvement and sufficient adoption support. Although such practices may keep operations moving in the short term, they increase effort, reduce trust in the digital record, weaken evidence of value and make scaling harder.

Third, the blueprint can be used as a diagnostic and planning tool. It provides a structure for looking beyond visible symptoms and asking whether a problem reflects unclear strategy, weak governance, limited integration, poor data foundations, late QA/validation involvement, insufficient adoption support or weak evidence of value. It is also intended to support sequencing and cross-functional alignment by giving Quality, Operations, Engineering, IT/OT, Supply Chain, Validation and Leadership a common structure for discussion.

Taken together, these implications shift attention from technology availability to operational reliability. Digitalisation creates sustainable value when digital systems become the normal basis for execution, review, exception handling and decision-making in GMP-relevant work. Operational routinisation therefore extends sociotechnical and process-oriented views of digital change into pharmaceutical manufacturing by showing how digital investment depends on trusted, auditable and repeatable routines for execution, review, exception handling and release-related work (see Supplementary Information S1–S2).

CONCLUSION

This article examined digitalisation in the European pharmaceutical manufacturing ecosystem, with particular attention to GMP-relevant manufacturing and quality-system interfaces. The findings show that digitalisation becomes more effective when digital systems are not only deployed but also embedded into stable, connected and inspection-ready routine work. Participants associated successful digitalisation with clear strategic direction, workable governance, reliable digital foundations, cross-functional coordination, adoption support and credible evidence of value. Where these conditions were weak, digitalisation was more likely to remain fragmented, hybrid and difficult to sustain.

The article contributes to digitalisation research by positioning pharmaceutical digitalisation as a challenge of operational routinisation rather than tool deployment. The study identifies the necessary conditions which practitioners associated with the transition from fragmented digital activity to reliable GMP-relevant digital routines. The operational blueprint translates these conditions into a diagnostic and planning heuristic for examining where hybrid work, manual reconciliation, weak record trust or poor cross-functional alignment may prevent digital routines from becoming embedded. The PCF provided the literature-derived starting point, the themes captured patterns in the questionnaire data, and the blueprint translated these findings into practical PAAs.

The study has its limitations. The sample was purposively recruited to capture relevant practitioner insight rather than statistical representativeness, and recruitment through LinkedIn and professional networks may have favoured more digitally engaged or visible practitioners, with stronger representation from German-speaking Europe. The study was based mainly on questionnaire responses, but there was no systematic application or validation of the framework, although member checking strengthened credibility and usability. Because data collection took place between May and November 2025, the findings reflect practitioner experience during a specific period of rapid technological and regulatory development. As digital manufacturing technologies, AI governance, validation approaches and regulatory expectations continue to evolve, some findings may require reassessment in future contexts.

Future research could apply and test the blueprint in real digitalisation programmes, rather than only assessing it conceptually. Longitudinal and multi-method studies could examine how the blueprint is used over time, how teams interpret implementation problems through it, and whether its use is associated with improved sequencing, alignment, and routine stability. Comparative studies across different organisation types, regions, product categories and manufacturing settings would also help determine which implementation patterns are broadly transferable and which need to be adapted to local contexts.

DECLARATIONS

Acknowledgments: The authors thank all practitioners who participated in the questionnaire study and the member-checking review for sharing their time, experience and reflections. Their contributions were essential to the development and refinement of the operational blueprint.

Authors' contributions: Conceptualisation, C.F.; methodology, C.F., M.W. and J.A.; software, C.F.; validation, C.F., M.W. and J.A..; formal analysis, C.F.; investigation, C.F.; resources, C.F.; data curation, C.F.; writing—original draft preparation, C.F. and M.W.; writing—review and editing, C.F., M.W. and J.A.; visualisation, C.F., M.W. and J.A.; supervision, M.W. and J.A.; project administration, C.F., M.W. and J.A. All authors have read and agreed to the published version of the manuscript.

Sources of funding: The authors received no financial support for the preparation, research, authorship and/or publication of this manuscript.

Declaration of competing interests: The authors do NOT have any potential conflicts of interest with respect to this manuscript.

Ethical statement: This study involved a questionnaire of adult professional practitioners and did not involve patients, vulnerable participants, clinical intervention, biological samples or identifiable patient data. Under the applicable University of Gloucestershire research ethics procedure, formal ethical approval was not required for this professional-practitioner questionnaire study, and no ethics approval number was issued. Participants received study information in advance and provided informed consent before completing the questionnaire. Responses were pseudonymised, any follow-up contact details were stored separately from questionnaire data, and findings are reported only in aggregated or de-identified form. Data handling followed EU GDPR, UK GDPR and institutional requirements.

Human rights statements and informed consent: All participants received study information in advance and provided informed consent before completing the questionnaire. The submitted manuscript contains no information that can be used to identify individual participants.

Disclosure of the use of generative AI and AI-assisted technologies: Goblin Tools Formalizer was used during manuscript preparation for language refinement and stylistic improvement. No AI tool was used to generate data, conduct analysis, interpret findings or produce scientific conclusions. All scientific content, analysis, interpretation and final wording were reviewed and approved by the authors, who take full responsibility for the manuscript.

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REFERENCES

1. Heesakkers, H. *et al*. Applying holistic control strategy in Pharma 4.0™. *Pharm. Eng.* **40**, 30–37 (2020). https://ispe.org/pharmaceutical-engineering/january-february-2020/applying-holistic-control-strategy-pharma-40
2. Miozza, M., Brunetta, F. & Appio, F.P. Digital transformation of the pharmaceutical industry: A future research agenda for management studies. *Technol. Forecast. Soc. Change* **207**, 123580 (2024). doi: 10.1016/j.techfore.2024.123580
3. Seo, I., Yang, H.K., Seo, M.J., Kim, S.H. & Hong, J.T. Digital transformation shift in global pharmaceutical industry going through the COVID-19 pandemic era. *Asian J. Innov. Policy* **12**, 54–74 (2023). https://accesson.kr/ajip/assets/pdf/42590/journal-12-1-54.pdf
4. European Commission. EudraLex Volume 4: EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Annex 11: Computerised Systems. (https://health.ec.europa.eu/system/files/2016-11/annex11_01-2011_en_0.pdf, 2011).
5. Hole, G., Hole, A.S. & McFalone-Shaw, I. Digitalization in pharmaceutical industry: What to focus on under the digital implementation process? *Int. J. Pharm.: X* **3**, 100095 (2021). doi:10.1016/j.ijpx.2021.100095
6. Ehie, I.C. & Chilton, M.A. Understanding the influence of IT/OT convergence on the adoption of Internet of Things in manufacturing organizations. *Comput. Ind.* **115**, 103166 (2020). doi:10.1016/j.compind.2019.103166
7. Braun, V., Clarke, V., Boulton, E., Davey, L. & McEvoy, C. The online survey as a qualitative research tool. *Int. J. Soc. Res. Methodol.* **24**, 641–654 (2021). doi:10.1080/13645579.2020.1805550
8. Creswell, J.W. & Creswell, J.D. *Research Design: Qualitative, Quantitative, and Mixed Methods Approaches*, 5th ed., (Sage, Los Angeles, CA, 2018).
9. Eysenbach, G. Improving the quality of Web surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J. Med. Internet Res.* **6**, e34 (2004). doi:10.2196/jmir.6.3.e34
10. Braun, V. & Clarke, V. Using thematic analysis in psychology. *Qual. Res. Psychol.* **3**, 77–101 (2006). doi:10.1191/1478088706qp063oa
11. Lincoln, Y.S. & Guba, E.G. *Naturalistic Inquiry*, (Sage, Newbury Park, CA, 1985).
12. Vial, G. Understanding digital transformation: A review and a research agenda. *J. Strateg. Inf. Syst.* **28**, 118–144 (2019). doi:10.1016/j.jsis.2019.01.003
13. Arden, N.S. *et al*. Industry 4.0 for pharmaceutical manufacturing: Preparing for the smart factories of the future. *Int. J. Pharm.* **602**, 120554 (2021). doi:10.1016/j.ijpharm.2021.120554
14. Chen, W. *et al*. Pharmaceutical industry: Challenges and opportunities for establishing Pharma 4.0. In Sharifzadeh, M. (ed.) *Industry 4.0 Vision for the Supply of Energy and Materials: Enabling Technologies and Emerging Applications*, 313–337 (Wiley, Hoboken, NJ, 2022). doi:10.1002/9781119695868.ch12
15. Ntamo, D. *et al*. Industry 4.0 in action: Digitalisation of a continuous process manufacturing for formulated products. *Digit. Chem. Eng.* **3**, 100025 (2022). doi:10.1016/j.dche.2022.100025
16. Debnath, B. *et al*. Assessing the critical success factors for implementing Industry 4.0 in the pharmaceutical industry: Implications for supply chain sustainability in emerging economies. *PLoS One* **18**, e0287149 (2023). doi:10.1371/journal.pone.0287149
17. Dhiman, A. & Madan, P. Revolutionizing pharma: Prioritizing Industry 4.0 implementation challenges in the Indian pharmaceutical landscape through analytical hierarchy process analysis. *J. Pharm. Innov.* **19**(4), 1–12 (2024). doi:10.1007/s12247-024-09849-3
18. Doyle, F., Carvalho, S., Kovács, Z. & Cosgrove, J. Application of digitalisation in regulated environments for predictive failure modelling. *IFAC-PapersOnLine* **58**, 222–227 (2024). doi:10.1016/j.ifacol.2024.08.124
19. Rezepa, S. & Pekar, J. Strategy and planning and implementation and impact for the pharmaceutical industry with and by Industry 4.0 (2021). ISBN:978-80-572-0111-3. Language Competence as Part of Lifelong Learning Book of Scientific Articles. Available at SSRN: https://ssrn.com/abstract=3955697
20. Johnson, T.L., Fletcher, S.R., Baker, W. & Charles, R.L. How and why we need to capture tacit knowledge in manufacturing: Case studies of visual inspection. *Appl. Ergon.* **74**, 1–9 (2019). doi:10.1016/j.apergo.2018.07.016
21. Heeren, E., Wassink, A.J., Nalluri, V.R. & Niederhauser, S. Methodology to define a Pharma 4.0™ roadmap. *Pharm. Eng.* **43**, 56–63 (2023). https://ispe.org/pharmaceutical-engineering/may-june-2023/methodology-define-pharma-40tm-roadmap
22. Schumacher, A., Erol, S. & Sihn, W. A maturity model for assessing Industry 4.0 readiness and maturity of manufacturing enterprises. *Procedia CIRP* **52**, 161–166 (2016). doi:10.1016/j.procir.2016.07.040
23. Davis, F.D. Perceived usefulness, perceived ease of use, and user acceptance of information technology. *MIS Q.* **13**, 319–340 (1989). doi:10.2307/249008
24. Venkatesh, V., Morris, M.G., Davis, G.B. & Davis, F.D. User acceptance of information technology: Toward a unified view. *MIS Q.* **27**, 425–478 (2003). doi:10.2307/30036540
25. N'Dri, A.B. & Su, Z. Successful configurations of technology–organisation–environment factors in digital transformation: Evidence from exporting small and medium-sized enterprises in the manufacturing industry. *Inf. Manag.* **61**, 104030 (2024). doi:10.1016/j.im.2024.104030
26. Raj, A. & Jeyaraj, A. Antecedents and consequents of Industry 4.0 adoption using technology, organisation and environment framework: A meta-analysis. *Ann. Oper. Res.* **322**, 101–124 (2023). doi:10.1007/s10479-022-04942-7
27. Hiatt, J.M. *ADKAR: A Model for Change in Business, Government and Our Community*, (Prosci Learning Center Publications, Loveland, CO, 2006).
28. Butt, J. A conceptual framework to support digital transformation in manufacturing. *Designs* **4**, 17 (2020). doi:10.3390/designs4030017
29. Picado Argüello, B. & González-Prida, V. Integrating change management with a knowledge management framework: A methodological proposal. *Information* **15**, 406 (2024). doi:10.3390/info15070406
30. Cullen, M., Calitz, A.P. & Mugwagwa, B. A model for smart factories in the pharmaceutical manufacturing industry. In *Proceedings of the 16th International Business Conference*, 24–27 (Swakopmund, Namibia, September 2023). https://internationalbusinessconference.com/a-model-for-smart-factories-in-the-pharmaceutical-manufacturing-industry/

SUPPLEMENTARY INFORMATION

Supplementary Information accompanies this article and includes selected framework-mapping tables, a questionnaire overview and PCF mapping, theme-to-blueprint traceability, illustrative worked scenarios, and a CHERRIES-style reporting summary.

S1: SELECTED FRAMEWORK FAMILIES RELEVANT TO PHARMACEUTICAL DIGITALISATION

Framework/Lens	Main Strength	Main Weakness for this Study	What this Article Adds Beyond It
Industry 4.0 readiness/maturity models. (e.g., Schumacher et al.[22])	Clarify readiness dimensions and implementation logic	Often generic; limited GMP-specific attention to validated routine work, record trust, and release-related use	Shifts attention from readiness level to the conditions under which digital systems become usable and defensible in GMP routine work
Integrated BPM/process-oriented change models (e.g., Butt[28])	Make workflow redesign and process embedding more explicit	Less specific on GMP governance, validation burden, and quality-system constraints	Brings process redesign together with GMP-relevant governance, validation, and digital record trust
Change management models (e.g., Hiatt[27])	Explain adoption, reinforcement, and behavioural embedding	Too general to explain integration, data, and compliance constraints in regulated manufacturing	Connects adoption capability to governance, integration, and controlled change in GMP settings
Pharma 4.0/smart factory frameworks (e.g., Arden et al.[13], Cullen et al.[30])	Stronger regulatory and pharmaceutical grounding	Often technology- or capability-centred; less explicit on cross-functional routinisation in day-to-day work	Focuses on how execution, review, exception handling, and release-related work become stable and inspection-ready in practice
Knowledge/change integration approaches (e.g., Picado Argüello & González-Prida[29])	Help explain organisational learning and implementation support	Less specific on manufacturing system integration, data continuity, and GMP operating realities	Adds a manufacturing-centred, GMP-relevant lens linking change, integration, and routine operational use

S2: FROM LITERATURE STRANDS TO PCF DIMENSIONS

Literature Strand	Recurring Issue Identified in the Review	PCF Dimension
Industry 4.0/Pharma 4.0 technology literature	Tool deployment, system capability, interoperability, automation potential	Technological Deployment
Digital transformation/organisational change literature	Governance, ownership, leadership, readiness, capability building	Organisational Structuring
GMP/Annex 11/Part 11/validation/data integrity literature	Validation, auditability, controlled change, record trust, compliance burden	Regulatory Compliance
Process, workflow, BPM, routinisation literature	Workflow redesign, exception handling, handovers, stable routine execution	Process Reengineering
Supply chain/ecosystem/partner coordination literature	External interfaces, partner alignment, regulatory and ecosystem pressures	External Environment and Stakeholders

S3: QUESTIONNAIRE OVERVIEW AND PCF MAPPING

The questionnaire was designed to collect both structured descriptive information and open-text evidence on digitalisation in GMP-relevant pharmaceutical manufacturing. It was informed by the PCF, which helped ensure that the instrument covered technological, organisational, regulatory, process, and ecosystem-related conditions. The questionnaire was intentionally broad because the study examined digitalisation as a cross-functional implementation problem rather than as a single-technology issue.

The instrument contained 44 questions organised into 12 sections. These included respondent background, governance, digital technologies and systems, integration and data governance, infrastructure and investment, perceived impacts, SOPs and documentation, training and change, challenges and success factors, future digitalisation priorities, role-specific questions, and final reflections. Most questions were optional to avoid forcing speculative responses from participants whose roles did not cover all areas.

The table below provides a condensed overview of the questionnaire structure and its relationship to the PCF. To keep the Supplementary Information concise, the full questionnaire is not reproduced in full, but it can be provided to the editor, reviewers, or readers on reasonable request.

Questionnaire Section	Main Topics Covered	Question Types	Main PCF Dimension(s)	Purpose in the Study
A. General information	Respondent role, department, years of experience, involvement in digitalisation initiatives	Closed questions and open-text prompts	Cross-cutting	To understand respondent background and relevance to GMP-relevant digitalisation.
B. Governance and objectives	Digitalisation strategy or roadmap, dedicated digital transformation team or Centre of Excellence, top digitalisation objectives	Closed questions, ranking, open-text prompts	Organisational Structuring; Regulatory Compliance	To capture strategic direction, governance arrangements, prioritisation, and organisational intent.
C. Digital technologies and usage	Digital tools deployed, platforms and systems in use, cloud/on-premises implementation, frequency and purpose of use	Multi-select, structured fields, open-text prompts	Technological Deployment	To identify the technologies and systems used and understand whether they were part of routine work.
D. Integration and data governance	Interoperability with enterprise systems and shop-floor/OT infrastructure, integration challenges, data governance frameworks, relevant regulations and standards	Rating scales, multi-select, open-text prompts	Technological Deployment; Regulatory Compliance	To examine integration maturity, data standards, interoperability, source-of-truth issues, and regulatory alignment.
E. Infrastructure and investment	Infrastructure adequacy, constrained resources, planned upgrades, IT/digitalisation investment priorities and budget allocation	Rating scales, multi-select, open-text prompts	Technological Deployment; Organisational Structuring	To assess whether technical and financial foundations were perceived as sufficient to support digitalisation.
F. Impact and benefits	Perceived impact on manufacturing efficiency, batch release, quality control, supply-chain resilience, workforce productivity, compliance, and ROI	Likert-scale items, multi-select, open-text prompts	Process Reengineering; Regulatory Compliance	To capture perceived operational, quality, compliance, and value-related effects of digitalisation.
G. SOPs and process documentation	Access to digital SOPs and documentation, ease of locating current versions, documentation challenges	Multi-select, rating scale, open-text prompts	Regulatory Compliance; Process Reengineering	To examine whether digital documentation supported controlled, usable, and inspection-ready ways of working.
H. Training and change	Digital-skills training, training delivery methods, frequency and effectiveness of training	Multi-select, rating scale, open-text prompts	Organisational Structuring; Process Reengineering	To assess workforce readiness, adoption support, and training conditions for routinisation.
I. Challenges and success factors	Main barriers to digitalisation, prioritised success factors, recommended best practices	Multi-select, ranking, open-text prompts	Cross-cutting across all PCF dimensions	To identify reported implementation barriers, enabling conditions, and practical lessons from respondents.
J. Strategic blueprint and future	Technologies to prioritise, future digitalisation expectations, organisational and cultural changes needed, emerging technology plans, AI governance readiness	Multi-select, rating scale, open-text prompts	Cross-cutting across all PCF dimensions	To capture forward-looking views and suggestions relevant to blueprint development and refinement.
K. Role-specific questions	Supply chain, production, QA/regulatory, IT/digital transformation, and executive perspectives	Open-text prompts	Depends on role; mainly Technological Deployment, Regulatory Compliance, Process Reengineering, and External Environment and Stakeholders	To collect function-specific examples of impacts, barriers, integration issues, compliance challenges, and strategic priorities.
L. Final comments	Additional reflections, examples, and suggestions for refining the blueprint	Open-text prompts	Cross-cutting	To allow respondents to add evidence, examples, or concerns not captured elsewhere in the questionnaire.

S4: FROM EMPIRICAL THEMES TO BLUEPRINT PRIORITY ACTIVITY AREAS

Empirical Input	Cross-cutting Theme	Blueprint Priority Activity Areas
Barriers: weak roadmap, fragmented priorities; quotes on target state and sequencing	T1 Strategic Direction and Future-State Alignment	A Strategic direction and sequencing
Success factors: leadership, governance; quotes on decision rights and workable speed under GMP	T2 Governance, Leadership and Portfolio Decision-Making	B Governance and compliance
Barriers: legacy incompatibility, data standardisation issues; quotes on ERP–MES–LIMS breaks and record mismatch	T5 Digital Foundations and Integration Preconditions	C Digital foundations and integration
Barriers: resistance, skills gaps, cross-functional communication; quotes on training, ownership, post-go-live support	T3 People Readiness, Culture and Adoption Capability	D Adoption and operating-model alignment
Quotes on coordination across sites and external partners	T4 Operating Model and Ecosystem Orchestration	D Adoption and operating-model alignment
Quotes distinguishing tool installed from work changed	T6 Operational Digitalisation in Practice	E Routinisation and value evidence
Quotes on ROI, licence-to-operate, scaling evidence	T7 Value Realisation, Metrics and Risk Trade-offs	E Routinisation and value evidence

S5: WORKED SCENARIOS

S5.1: Scenario 1 - Records do not match across ERP–MES–LIMS	
Situation	A batch is executed in MES, test results are generated in LIMS, and material movements are recorded in ERP, but the records do not align. Batch review takes longer because teams must manually prove what happened before QA can rely on the digital record.
What you typically see	• Excel reconciliations, screenshots, and emails added to batch review packages • Repeated investigations caused by quantity, status, time-stamp, or result mismatches • Low confidence in the system record ('the system is wrong') • Review and release are delayed because evidence is scattered across systems and people
Likely upstream cause	The workflow may be digitised in parts, but the end-to-end target workflow, source-of-truth rules, interfaces, and exception paths were not stabilised before go-live. In practice, the problem usually sits across **PAA C (Digital foundations, integration & record trust)**, supported by **PAA A (Strategic direction & sequencing)** and **PAA B (Governance, compliance & controlled change)**.
Where the blueprint points first	**PAA C:** data ownership & standards; interfaces & interoperability; access, audit trail & retention; archiving, recovery & resilience; validated change controls **PAA A:** end-to-end target workflow; workflow boundaries, handovers & exceptions; dependencies & go-live prerequisites **PAA B:** decision rights & escalation; early QA/validation gates
What the team does next (practical actions)	1. Build **breakpoints register** for every ERP↔MES↔LIMS handover: what data moves, when it moves, who owns it, and where it breaks. 2. Define the **source of truth** for each critical field (e.g., consumption, yield, test result, disposition, release status). 3. Fix the **top three mismatch drivers first**, based on pain and frequency. 4. Confirm **business and quality ownership** for master data and critical data corrections. 5. Test the **exception path** explicitly: late result, corrected result, rework, retest, material adjustment, or manual intervention. 6. Agree with QA what evidence must remain inside the workflow so review does not depend on ad hoc reconstruction.
Who needs to be involved	Process owner, QA reviewer, system owner(s), interface owner, master-data owner, validation/CSV representative, and the operational user(s) who experience the mismatch in real work.
Outputs (what you produce)	• System/interface map and owned breakpoints register • Source-of-truth matrix for critical data fields • Updated workflow and exception map • Data ownership and approval rules • Validated change plan for interface or master-data fixes
How you know the issue is stabilising	• Reconciliation steps reduce for the top mismatch drivers • Fewer deviations or investigations are triggered by record mismatches • Batch review time becomes more predictable • QA can answer audit questions from system records and audit trails rather than screenshots and emails
What not to do	• Do not scale the same workflow to more products or sites while the breakpoints remain unresolved • Do not normalise permanent Excel reconciliation as the solution • Do not leave data ownership with IT alone if the data are GMP-relevant

S5.2: Scenario 2 - Change request stuck — validation, approvals, and rework	
Situation	A needed change such as an interface correction, role/access change, workflow update, report change, or software patch remains 'in progress' for weeks or months. QA questions arrive late, documentation loops repeat, and delivery slows down.
What you typically see	• Change requests sit in queues with unclear status • Teams argue about classification, risk, or whether the change is GxP-relevant • QA/validation objections arise late, triggering redesign or retesting • Security/OT constraints block updates because patch windows, segmentation, or vendor dependencies were not planned early • Small changes take almost as long as major ones
Likely upstream cause	The initiative has no clear validated change pathway in day-to-day delivery. Decision rights, QA involvement, change classification, and escalation routes are unclear or arrive too late. The main pressure points are **PAA B (Governance, compliance & controlled change)** and **PAA C (Digital foundations, integration & record trust)**.
Where the blueprint points first	**PAA B:** decision rights & escalation; early QA/validation gates; controlled change pathway; portfolio priorities & resourcing; leadership sponsorship & accountability **PAA C:** validated change controls; access, audit trail & retention; interfaces & interoperability
What the team does next (practical actions)	1. Classify the change clearly: **GxP vs non-GxP**, and minor vs medium vs major, with the validation consequence made explicit. 2. Define who has authority for scope, risk acceptance, testing approval, go/no-go, and final sign-off. 3. Bring QA/validation in **before build or configuration work goes too far**. 4. Create a simple **validated change pathway**: request → assess → classify → test → approve → deploy → verify → close. 5. Agree what evidence is required for each change type, including documentation, test evidence, and release criteria. 6. Where repeated delays reflect a broader weakness, route the issue through **CAPA**. 7. For OT/security/vendor constraints, define patch windows, compensating controls, vendor lead times, and fallback arrangements up front.
Who needs to be involved	Business/process owner, QA, validation/CSV, IT/OT or system owner, cybersecurity/infrastructure where relevant, and approvers with real authority to release or stop the change.
Outputs (what you produce)	• RACI (responsible, accountable, consulted, informed) or decision-rights map • Change-type classification guide with evidence expectations • Validated change playbook • Escalation route for blocked changes • QA/validation touchpoints built into the workflow • CAPA linkage where repeated failure patterns exist
How you know the issue is stabilising	• Fewer back-and-forth review loops • QA objections are raised earlier and are more predictable • Routine changes have shorter and more stable cycle times • Teams can explain the change pathway clearly in an inspection • Fewer delays appear close to deployment
What not to do	• Do not treat QA as a final gate only • Do not let every change default to 'major' • Do not ignore OT/security/vendor realities until deployment week • Do not accept repeated approval delays as normal operational friction

S5.3: Scenario 3 - Tool is live, but people still work around it	
Situation	The system is live, but users continue to rely on Excel trackers, paper notes, personal checklists, or informal side channels. The organisation says the workflow is digital, but the real routine still runs partly outside the system.
What you typically see	• Double documentation: system plus paper/Excel • Patchy use: some teams use the tool fully, others only partially • Workarounds become the true routine ('ask X, she has the tracker') • Questions keep returning even though training has already happened • Leadership describes the tool as implemented, but day-to-day execution does not reflect that
Likely upstream cause	The issue is usually not resistance alone. More often, the target workflow, exception routes, role ownership, handovers, and post-go-live support were not made operational. The main pressure point is **PAA D (Adoption & operating-model alignment)**, supported by **PAA A** and **PAA B**.
Where the blueprint points first	**PAA D:** role clarity & ownership; SOPs, training & reinforcement; hypercare & support model; leadership legitimacy & communication; partner/site handovers & coordination **PAA A:** end-to-end target workflow; workflow boundaries, handovers & exceptions **PAA B:** decision rights & escalation; leadership sponsorship & accountability
What the team does next (practical actions)	1. Identify the **top three workarounds** and document where they occur, why they occur, and who depends on them. 2. Separate the causes: usability issue, missing exception path, unclear ownership, insufficient training, missing support, or insufficient leadership reinforcement. 3. Run short **co-design sessions** with real users to fix the most painful points in the workflow. 4. Update SOPs, work instructions, and handover rules so the digital routine replaces the old one instead of sitting beside it. 5. Set up **hypercare** for the first weeks of live use: visible support, fast issue resolution, and a mechanism for prioritising fixes. 6. Define a **hybrid exit plan**: which temporary controls remain, who owns removal, and by when. 7. Clarify where leadership must intervene when users continue to bypass the agreed routine despite the process being workable.
Who needs to be involved	End users, frontline supervisors, process owner, QA where documentation/review is affected, training/change lead, and the business owner accountable for the routine after go-live.
Outputs (what you produce)	• Workaround log with root-cause categories • Updated SOPs and handover definitions • Targeted adoption plan (training, reinforcement, communication, support) • Hypercare model with named owners • Hybrid exit plan with dates and accountability
How you know the issue is stabilising	• Shadow spreadsheets and paper notes reduce and then stop for the targeted workflow • Users follow the exception process inside the workflow rather than through side channels • Fewer deviations arise from missing or unclear documentation steps • The routine remains stable after hypercare, without depending on hero support • Leadership no longer needs repeated intervention to enforce use
What not to do	• Do not blame 'resistance' before checking whether the workflow is actually workable • Do not declare success because the system is installed • Do not allow temporary Excel controls to become permanent • Do not leave ownership ambiguous after go-live

S5.4: Scenario 4 - Too many initiatives, weak foundations, and invisible value	
Situation	Many digital initiatives run in parallel: dashboards, pilots, automation projects, system rollouts, and site-level improvements. Teams are busy, but day-to-day GMP work does not become easier, and leadership starts asking where the value is.
What you typically see	• Too many priorities and slow progress everywhere • Foundations such as interfaces, data ownership, validation approach, and change pathways keep being postponed • Different sites implement similar tools differently • Value remains promised rather than visible in execution, review, release, or exception handling • Projects continue because they are active, not because they are stabilising a routine
Likely upstream cause	The portfolio is being managed as a set of tools or projects rather than as a sequence of workflows that need stable prerequisites before scale. The main pressure points are **PAA A (Strategic direction & sequencing)**, **PAA B (Governance, compliance & controlled change)**, and **PAA E (Routinisation & value evidence)**.
Where the blueprint points first	**PAA A:** end-to-end target workflow; workflow boundaries, handovers & exceptions; dependencies & go-live prerequisites; validation-aware rollout plan; hybrid-exit criteria **PAA B:** decision rights & escalation; early QA/validation gates; controlled change pathway; portfolio priorities & resourcing; leadership sponsorship & accountability **PAA E:** stable validated routine; review-by-exception; exception handling & release logic; evidence-to-scale scorecard; hybrid retirement & routine tracking
What the team does next (practical actions)	1. Stop reviewing the portfolio as a list of tools and reframe it as a set of **priority workflows** that matter most for GMP execution, review, release, or exception handling. 2. Define the **minimum prerequisites** for each workflow before scale: interfaces, data ownership, validation approach, exception handling, support model, and governance. 3. Freeze, stop, or defer work that does not reduce hybrid burden or increase trust in the digital record. 4. Create an **evidence-to-scale scorecard** using three lenses: operational benefit, assurance/risk reduction, and financial value. 5. Protect foundational work through explicit governance and resourcing rather than treating it as work that can wait until later. 6. Standardise what must be common across sites and what may legitimately vary. 7. Track whether hybrid controls are actually being retired rather than assuming routinisation has happened because the tool is live.
Who needs to be involved	Portfolio owner or sponsor, business/process owners, QA, validation/CSV, IT/digital lead, site representatives, and finance or programme governance where resourcing decisions are made.
Outputs (what you produce)	• Sequenced roadmap organised by workflow, not tool • Prerequisite checklist for scaling • Evidence-to-scale scorecard • Portfolio stop/defer/continue decision log • Site rollout pack showing mandatory common elements versus local variation • Hybrid retirement tracker
How you know the issue is stabilising	• Fewer initiatives are running, but completion and stabilisation improve • Foundations improve measurably: fewer breakpoints, clearer ownership, more predictable change control • Hybrid paper/Excel burden shrinks in the selected workflows • Scaling decisions rely on agreed evidence rather than optimism or pressure • Value becomes visible in routine execution and QA reliance, not only in presentation decks
What not to do	• Do not scale a fragile pilot to more sites before the prerequisites are stable • Do not confuse dashboards or activity with routinised value • Do not allow prioritisation to remain political and opaque • Do not keep adding features while the core workflow still depends on manual bridging

S5.5: Scenario 5 - System outage, archiving failure, or retention gap	
Situation	A critical system or interface becomes unavailable, archived records cannot be retrieved reliably, or retained data are incomplete. Teams can continue some work manually, but batch review, release, or inspection readiness is now at risk because the digital record is inaccessible, incomplete, or not trusted.
What you typically see	• System or interface outage interrupts execution, review, or release • Archived or historical records cannot be retrieved quickly or completely • Backup exists, but restore confidence is low or not recently tested • Teams create emergency paper logs, screenshots, or offline trackers • QA cannot confirm whether the record remains complete, contemporaneous, and defensible • Production or release is delayed because evidence cannot be accessed or reconstructed reliably
Likely upstream cause	Record trust was designed mainly for normal operation, not for degraded operation or recovery. Retention, archiving, restore capability, contingency operation, and decision rights during outage were not fully defined or tested. The main pressure points are **PAA C (Digital foundations, integration & record trust)**, supported by **PAA A**, **PAA B**, and **PAA E**.
Where the blueprint points first	**PAA C:** data ownership & standards; access, audit trail & retention; archiving, recovery & resilience; validated change controls **PAA A:** workflow boundaries, handovers & exceptions; dependencies & go-live prerequisites; validation-aware rollout plan **PAA B:** decision rights & escalation; early QA/validation gates **PAA E:** stable validated routine; exception handling & release logic; hybrid retirement & routine tracking
What the team does next (practical actions)	1. Define which records, raw data, metadata, and audit-trail elements are business-critical and GMP-critical, and where each must be retained. 2. Confirm the source of truth for critical records and whether archive and restore arrangements preserve that integrity. 3. Create or update a **BCP/DRP** for the workflow: outage response, degraded-mode operation, restore sequence, decision rights, and maximum tolerable downtime. 4. Define a validated contingency process for temporary manual operation, including who records what, where, how reconciliation is handled, and when the workflow returns to normal mode. 5. Test restore and recovery regularly rather than assuming backup equals recoverability. 6. Add explicit incident/CAPA pathways when data loss, incomplete retrieval, or failed restore creates GMP impact. 7. Clarify retention rules for raw data, reports, audit trails, and supporting evidence so that archive design supports inspection readiness, not just IT storage convenience.
Who needs to be involved	QA, system owner, IT/OT or infrastructure owner, business/process owner, validation/CSV, records/data owner, and operational leads responsible for continuing work during degraded operation.
Outputs (what you produce)	• Retention and archiving matrix (record type, source of truth, retention rule, retrieval method, owner) • BCP/DRP for the workflow or system landscape • Restore-test evidence and frequency plan • Validated degraded-mode/contingency SOP • Incident/CAPA pathway for record-access or retention failure • Escalation map showing QA, IT/OT, Operations, and system-owner responsibilities during outage or archive failure
How you know the issue is stabilising	• Critical records can be retrieved within the defined business and QA time window • Restore tests are passed and documented at planned intervals • Temporary manual controls are defined, controlled, and retired after recovery • QA can explain outage handling and record continuity in an inspection without reconstructing evidence ad hoc • System failure or archive retrieval issues no longer create unplanned release delays or undocumented workaround behaviour
What not to do	• Do not assume backup automatically means usable recovery • Do not leave degraded-mode operation informal or dependent on local heroics • Do not treat archiving as an IT-only storage issue; it is part of GMP record trust • Do not wait for an audit or outage to discover that historical data cannot be retrieved reliably • Do not let emergency spreadsheets, screenshots, or paper notes become the permanent contingency model