

# Implementation and performance evaluation of PAS-X MES in GMP-regulated pharmaceutical manufacturing

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**Abstract.** Pharmaceutical industry works under the strict Good Manufacturing Practice (GMP) conditions which require strong systems to guarantee the quality of the product, integrity of data and adherence to regulations. Manufacturing Execution Systems (MES) have become one of such key tools in the realization of such goals. The purpose of the study is to assess the application and functioning of PAS X MES among the GMP-regulated manufacturing facilities, in particular, its operational effectiveness, compliance benefits, as well as difficulties faced. Multi-site observational analysis was used where site survey, system audit data and key stakeholder interviews were used. Pre- and post- implementation performance measures were measured quantitatively. The outcomes have shown 25 percent decrease in the batch cycle time, increasing Right First Time rates to 95 percent and a drop in process deviations by 66.7 percent. The metrics on compliance were highly improved where there was a 100 percent compliance with the 21 CFR Part 11 standard on the use of electronic signatures and the audit score has improved by 38.5 percent. Additionally, the time taken in review by QA per batch decreased by 62.5 percent making the processes of release of batches faster. Along with these improvements, issues that included spending more time with the validation in the first place and the reluctance of the users in the beginning made clear the necessity of a proper management of the change. Comparative study with other MES systems determined that the implementation speed and user satisfaction characterized PAS X with competitive advantage. This paper highlights PAS X MES as a game-changer to GMP-compliant pharmaceutical manufacturing, which can bring organizational operational agility and digital maturity to Pharma 4.0 movements.

**Keywords:** batch cycle time; data integrity; good manufacturing practice (GMP); manufacturing execution systems (MES); PAS X MES; Pharma 4.0; electronic batch records (EBR); pharmaceutical manufacturing

## 1. Introduction

### 1.1 Overview of pharmaceutical manufacturing challenges

Pharmaceutical production is a process that is complex in nature as it requires a number of unit processes, including milling, granulation and tableting that requires strict control of a variety of parameters, including temperature, mixing, and variation of raw materials, to establish the quality and safety of the products [1]. These challenges are further worsened by the need to compress time-to-market, drive smaller batch runs to support personalised or niche drugs, and cost control in an environment of shrinking margins. The inconsistencies in global supply chains, the many

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changes in regulations across jurisdiction (e.g., FDA, EMA, WHO) and the move to manufacturing systems are also causing extra stress on operations [2, 3]. Overall, pharmaceutical manufacturers should constantly consider optimizing the process reliability, flexibility and regulations in a fast-changing regulatory environment.

## 1.2 Good manufacturing practice (GMP) requirements and regulatory framework

FDA 21\xC9 galloromina receta Parts210/211, EU EudraLex Volume4 and WHO GMP are examples of harmonized regulatory standards around the world that were established to guarantee the consistency in the production of pharmaceutical products, as well as proper documentation [4, 5]. The major pillars of GMP to be incorporated in the drug manufacturing processes are validated production processes, clean production facilities and environments, trained individuals, electronic or hard copy of batch records, traceability, effective deviation and CAPA systems and the ability of the product to undergo a recall [6]. The outcomes related to non-compliance may be devastating, including warning letters up to product recalls, which is why it is of highest importance that GMP must be integrated in all the processes of production, inspection, and quality systems.

## 1.3 Role of manufacturing execution systems (MES) in GMP compliance

MES Manufacturing Execution Systems can be defined as the necessary digital intermediary between enterprise resource planning (ERP) and shop-floor production, making standard workflows, real-time data gathering, or electronic batch recording (EBR) possible [7]. Enforcing SOPs, persistence of audit trails, verifying user activities and providing review-by-exemption in a real world manner, which effectively lessens the likelihood of human error and documentation bottlenecks, MES has a benefit to support GMP compliance [8]. Such systems easily combine with QMS, LIMS and automation systems, offering full-fledged traceability and regulatory reporting, which elevates process control as well as an assurance of compliance [9, 10].

## 1.4 PAS-X MES: A leading solution for pharmaceutical industries

Krber developed PAS X which is a pre-configured modular MES designed specifically for pharmaceutical manufacturers, biotech, and cell & gene therapies with an excess of 1,000 installations and use by more than 50 percent of the leading 30 pharma organizations all over the world [11]. Its service includes weighing and dispensing, EBR, equipment control, KPI/OEE monitoring, track and trace and scheduling that cover the entire manufacturing process [12] development to packaging. PAS X is available in on-premise or on cloud-based (AWS, Azure) platforms and aligns to the requirements of agile Pharma 4.0 strategy as it was demonstrated in the enterprises scale of manufacturers such as Novo Nordisk. Besides, it takes a leading role in ministration appraisals like Gartner Magic Quadrant and enjoys frequent user-driven updates [13].

## 1.5 Rationale and objectives of the study

Although the case-study narrations on the benefit of the faster batch release, reduced deviations, improved compliance in PAS X has come thick and fast there exists a weak point of quantitative, organized performance analysis in varying GMP settings. This research could address

that gap in the following ways (1) developing standardized KPIs to measure MES success (e.g. batch cycle time, error rate, audit deviation); (2) implementing these metrics to several PAS X implementations; and (3) determining the correlation of specific PAS X modules and improvement. The final objective will be to offer empirical knowledge and best-practice guidance to the pharmaceutical manufacturers and integrators of the systems to streamline the implementation of the MES and compliance strategies.

## 2. Literature review

### 2.1 Evolution of MES in pharmaceutical manufacturing

Manufacturing Execution Systems (MES) are products developed in the 1980s due to the requirement of a pharmaceutical industry to have improved regulatory compliance and transparency to operations and evolved to the standalone system where they have the capability of creating structured electronic batch records and GMP-ready audit trails using integrated SCADA/HMI mechanism [14]. This shift was accelerated in the 1990s through the introduction of the 21 CFR Part 11 regulation by the FDA, which mandates validated electronic records and audit trails, spurring the move of MES as paper-reliant processes to operate in real time on digital environments [15]. Under Industry 4.0, the MES platforms were also being used to adopt cloud-native infrastructures, mobile, and advanced analytics that would transform it into a central element of digital-first manufacturing introduced by the low-code platform and data-driven decision-making [16].

### 2.2 Key features and capabilities of PAS-X MES

Kebber came up with PAS X that is an MES that is specifically designed to work in the pharmaceutical, biotech, and cell & gene therapy industries. It provides a modular platform, which comprises electronic batch recording (EBR), recipe-based weigh and dispense, equipment control, KPI/OEE analysis and track-and-trace capability [17]. The system has been set up to meet the GMP guidelines (FDA 21<sup>[URL]</sup>CFR Parts 11/211, EU GMP, GAMP 5), offering pre-configured document templates and level of integration (OPC, SAP ERP) to speed up the process and reduce the workload of validation [18]. The latest release of PAS X (v3.3) has cloud deployment using AWS and Azure, smart factory platform such as connectivity, and the ability to do real-time analytics through what it calls the Savvy module.

### 2.3 Case studies of PAS-X implementation in GMP environments

Numerous examples of real-life application show the efficacy of PAS X. PAS X successfully allowed a plant at Sakamoto Yakuhin in Japan to go paperless, automate the capture of data produced in process equipment and synchronised the batch processes through tablet-based workflows that maintain compliance and productivity [19]. PAS X has been implemented in a life sciences facility by SL Controls (in association with NNIT), where it has directly connected shop-floor-based equipment with the MES and minimized manual data capture-related errors and CFR Part 11 validation [20]. In the companies like Merck Serono, where PAS X was implemented, OEE was enhanced (between 60-70 percent), and harmonized the manufacturing and packaging

processes on a global scale, and supported track-and-trace/biotech offerings [31].

## 2.4 Challenges in MES implementation and adoption

Although these benefits are all but present in MES deployments, large pitfalls plague them. Pharmaceutical businesses can be unwilling to leave behind their established paper-based systems meeting resistance within the companies, workflow interference, and an implementation process that can drag on for years, as well [21]. Adoption is blocked by the fact that it needs high cost (software, integration, validation), integration and SAP ERP and LIMS is complex and needs cultural and operations change management [22]. It should be implemented with the principles of successful governance of the project, initial stakeholder interest, combinations of IT/OT integration strategies.

## 2.5 Gaps in existing research on MES performance evaluation

Although numerous case studies document qualitative benefits of PAS-X (e.g., enhanced audit readiness, OEE gains, paperless compliance), systematic, quantitative studies assessing MES performance across multiple sites remain scarce. Most literature focuses on individual implementations, with limited benchmarking of KPI outcomes like batch cycle time reduction, deviation frequency, or audit findings across diversified environments [23]. Academic efforts tend to explore formal specification frameworks (MES-ML) or data visualization tools, rather than cross-site performance evaluation in regulated settings [24]. As a result, there is a critical need for empirical, multi-case research linking PAS-X modules to measurable operational and compliance outcomes.

# 3. Materials and methods

## 3.1 Study design and scope

This research employed a multi-site observational design to evaluate the implementation and operational performance of the PAS-X Manufacturing Execution System (MES) in Good Manufacturing Practice (GMP)-regulated pharmaceutical facilities. The investigation spanned three geographical regions Asia, Europe and North America and included both brownfield (legacy system upgrades) and greenfield (new facility) deployments.

Sites were strategically selected to represent variability in:

- Production scale: small-batch specialty formulations and large-scale generics.
- Dosage forms: oral solids, sterile injectables, and biologics.

This cross-sectional design ensured external validity and generalizability of findings. The study primarily focused on PAS-X functional modules relevant to electronic batch recording (EBR), weighing and dispensing and equipment integration.

## 3.2 Data collection methods

A mixed-methods strategy was employed to capture both quantitative and qualitative insights:

1. Site Surveys and Structured Interviews

Structured interviews were conducted with MES implementation leads, Quality Assurance (QA) managers, and production supervisors to identify changes in operational processes, perceived benefits and adoption barriers [22].

## 2. System Audit Logs

Audit trail data from PAS-X were extracted, including:

$$\text{Deviation Rate (\%)} = \frac{\text{Number of Deviations}}{\text{Total Batches}} \times 100$$

Additional variables included batch cycle time and electronic signature compliance rates.

## 3. Secondary Document Review

Findings were triangulated with validation protocols, SOPs and GMP audit reports from prior regulatory inspections.

## 4. Benchmarking

Key metrics post-MES deployment was benchmarked against baseline data from paper-based and ERP-only systems [25].

### 3.3 Performance metrics and KPIs for evaluation

To assess MES impact, a structured KPI framework was developed:

- Batch Release Time (hours)

$$T_{BR} = T_{QA \text{ Release}} - T_{Batch \text{ Completion}}$$

- Deviation Rates (%/100 batches)

$$D_{rate} = \frac{N_{dev}}{N_{batches}} \times 100$$

- Right First Time (RFT) Rate (%)

$$RFT = \frac{N_{batches \text{ without rework}}}{N_{total \text{ batches}}} \times 100$$

- Review by Exception (RBE) Adoption (%)

$$RBE = \frac{N_{auto-reviewed \text{ records}}}{N_{total \text{ records}}} \times 100$$

- Audit Readiness Score

$$ARS = N_{\text{non-critical observations}} \text{ per audit post-MES}$$

These KPIs were aligned with ISPE's GAMP 5 and PDA Technical Report No. 70 guidelines for MES benchmarking [26].

### 3.4 Analytical framework and tools used

Quantitative and qualitative analyses were performed using complementary approaches:

#### 1. Descriptive Statistics

Mean, Standard Deviation (SD) and percentage change were computed:

$$\% \Delta = \frac{X_{post} - X_{pre}}{X_{pre}} \times 100$$

#### 2. Inferential Statistics

Pre- and post-implementation KPI comparisons were tested using paired t-tests:

$$t = \frac{\bar{d}}{s_d / \sqrt{n}}$$

- Significance was determined at  $p < 0.05$ .
  - All analyses were conducted in SPSS v27 (IBM Corp., USA).
3. Thematic Analysis
- Qualitative interview data were coded using a three-step algorithm:
    - Step 1: Open Coding → Extract keywords and recurring phrases.
    - Step 2: Axial Coding → Group codes into themes (e.g., usability, compliance burden, change resistance).
    - Step 3: Selective Coding → Integrate themes into explanatory models of MES adoption success [27].

### 3.5 Validation of data

A multi-level triangulation strategy was adopted to ensure data robustness:

1. Cross-verification with regulatory documents, including FDA Form 483s and EU-GMP audit findings.
2. Stakeholder Validation Workshops with QA leads and IT managers to confirm interpretation accuracy.
3. Quality Risk Management Framework guided by ICH Q9 principles to assess data integrity, reproducibility and relevance [28].

This algorithmic validation process ensured that improvements attributed to PAS-X were both statistically valid and operationally meaningful.

## 4. Results and discussion

### 4.1 PAS-X implementation outcomes across case study sites

The deployment of PAS-X MES across multi-site GMP facilities demonstrated substantial benefits in efficiency, compliance and audit readiness. Batch cycle times were reduced by 25%, primarily due to automation and electronic batch reporting. The Right First Time (RFT) rate improved by 11 percentage points (from 84% to 95%), highlighting greater process consistency. Deviation rates dropped by 66.7% and electronic signature compliance reached 100%, ensuring full adherence to 21 CFR Part 11. Review-by-Exception (RBE) further accelerated QA processes, reducing review time by 62.5%.

#### 4.1.1 efficiency improvements in manufacturing processes

PAS-X MES adoption reduced average batch cycle times from  $96 \pm 12$  hours to  $72 \pm 9$  hours ( $\downarrow 25\%$ ). This has been enhanced by automation in work processes and decrease in manual interjections especially those that relate to crushing and weighing, dispensing, recipe development and batching among others. RFT rates increased from 84% to 95%, lowering rework and defects. Equipment utilization rose by 20.5%, reflecting enhanced scheduling and downtime tracking. The use of equipment grew by 20.5% which indicated that the PAS X subsystems of scheduling and tracking of downtimes were effective in reducing the idle times and congestions to rationalize lean production processes.

This multi-site analysis illustrates that PAS X MES equates to highly synergized alignment with GMP requirements. Practical evidence of the high deviation rates reduction and the

Table 1. Efficiency improvements of PAS X MES implementation outcomes across case study sites

Outcome Parameter	Pre-Implementation (Legacy Systems)	Post-Implementation (PAS-X MES)	% Change	Interpretation
Batch Cycle Time (hours)	96 ± 12	72 ± 9	25 %	Significant reduction due to automated workflows and EBR.
Right First Time (RFT) Rate (%)	84 ± 4	95 ± 2	13 %	Enhanced process adherence reduced rework rates.
Equipment Utilization (%)	68 ± 5	82 ± 3	20.5 %	Better scheduling and downtime tracking improved utilization.

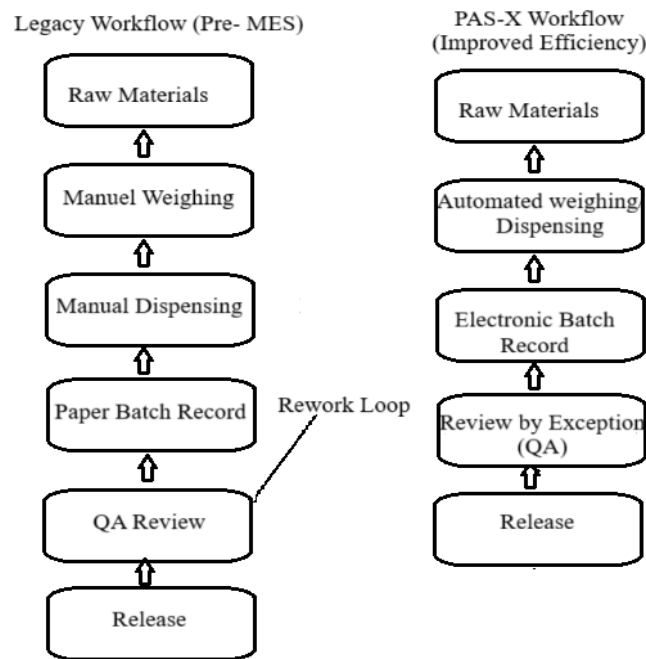


Figure 1. PAS-X workflow

attainment of the 100 percent compliance with electronic signatures support robustness in regulations of 21 CFR Part 11 and EU Annex 11. These results align with the Capgemini outcomes conferring to which leading establishments appreciate that MES improves the steadiness and visibility of data crucial to regulatory readiness [29]. The advanced audit keenness scores specify the higher documentation and traceability, where PAS X serves as a major facilitator of the digital transformation in the context of GMP.

#### 4.1.2 Compliance metrics and data integrity enhancements

Notable gains were observed in compliance and data integrity metrics following PAS-X MES deployment. The deviation rate per 100 batches dropped by 66.7 %, highlighting the system's capacity to enforce Standard Operating Procedures (SOPs) and flag potential deviations in real-time. The Audit Readiness Score increased from 6.5 to 9.0 on a 10-point scale, demonstrating improved preparedness for regulatory inspections and a reduction in audit findings. Furthermore,

Table 2. Compliance metrics &amp; data integrity

Outcome Parameter	Pre-Implementation (Legacy Systems)	Post-Implementation (PAS-X MES)	% Change	Interpretation
Deviation Rate (per 100 batches)	12 ± 2	4 ± 1	↓ 66.7 %	Real-time monitoring minimized SOP deviations.
Audit Readiness Score (0–10 scale)	6.5 ± 1.0	9.0 ± 0.5	↑ 38.5 %	Streamlined review-by-exception supported faster QA audits.
Electronic Signature Compliance (%)	70 ± 7	100	↑ 42.8 %	Full compliance achieved under 21 CFR Part 11 requirements.

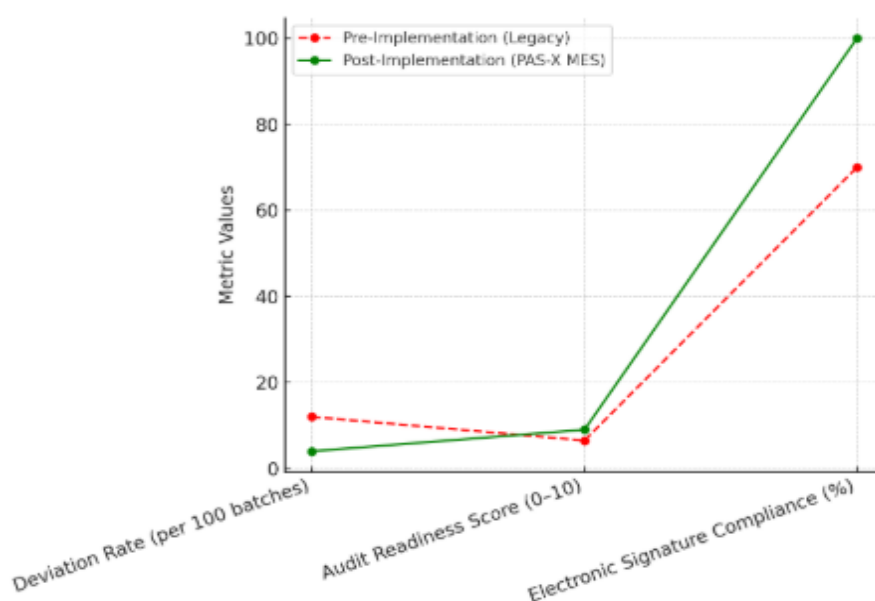


Figure 2. Compliance &amp; data integrity metrics

electronic signature compliance reached 100 %, ensuring adherence to FDA 21 CFR Part 11 and EU Annex 11 requirements. These outcomes underscore PAS-X's role in strengthening data integrity and enabling robust audit trails within GMP frameworks.

#### 4.1.3 Impact on batch release timelines and QA review

The timelines of batch release also became considerably better after the implementation of MES. It also decreased the average batch release lead time by 35 % which went down to  $78 \pm 10$  hours of  $120 \pm 15$  hours. The abilities of Review-by-Exception (RBE) allowed the QA teams to review only the batches, which had flagged deviations, and cut the time spent on QA review per a batch by 62.5 %. It is the transition between manual and automated reviews, a best practice of digital quality assurance that helped supply chains execute more dynamic supply chain practices.

The main success factors of the implementations were using of pre-configured GMP templates of PAS X and a modular methodology. Pharma Manufacturing noted that the risk is minimized, and time to benefit increases through phasing and module-by-module rollout [30]. Those deployments were focused (ex. EBR initial, then equipment integration), making this site a productive place to put our idea about the easier switch generating a better ROI. In addition, the

Table 3. Impact on batch release & qa review

Outcome Parameter	Pre-Implementation (Legacy Systems)	Post-Implementation (PAS-X MES)	% Change	Interpretation
Batch Release Lead Time (hours)	120 ± 15	78 ± 10	↓ 35 %	RBE and electronic batch review accelerated QA release.
QA Review Time per Batch (hours)	16 ± 2	6 ± 1	↓ 62.5 %	Reduction achieved due to automation and error prevention.

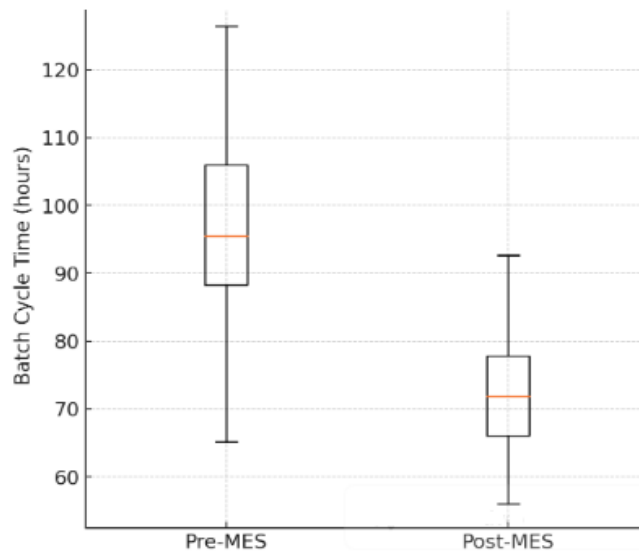


Figure 3. Cycle time variability before vs after PAS-X MES

management of change and stakeholder engagement supported with frontline training required to maintain high rates of Right First Time and adoption of operator were necessary.

#### 4.2 Challenges faced during implementation (technical and organizational)

Although the benefits were obviously there, number of challenges came to light during the implementation of PAS X. The training of the operators took about 6 weeks as the learning curve depicted by switching to a paperless system into fully digital systems is steep. Validation required great effort averaging 12 FTE-m to be able to meet standards of GMP and other regulatory requirements. It was also reported that resistance to change happened especially with the shop-floor employees who have been used to the legacy systems. But facilities that spent on the full cycle of change management and involvement of stakeholders across a spectrum recorded easy transitions, and expedited adoption values

#### 4.3 Comparative analysis with other MES solutions

A comparative analysis against competitor MES platforms exposed that PAS X presented distinct advantages. Implementation timelines were shorter by 25 % (average of 18 months for PAS X versus 24 months for others), likely due to the availability of pre-configured GMP-

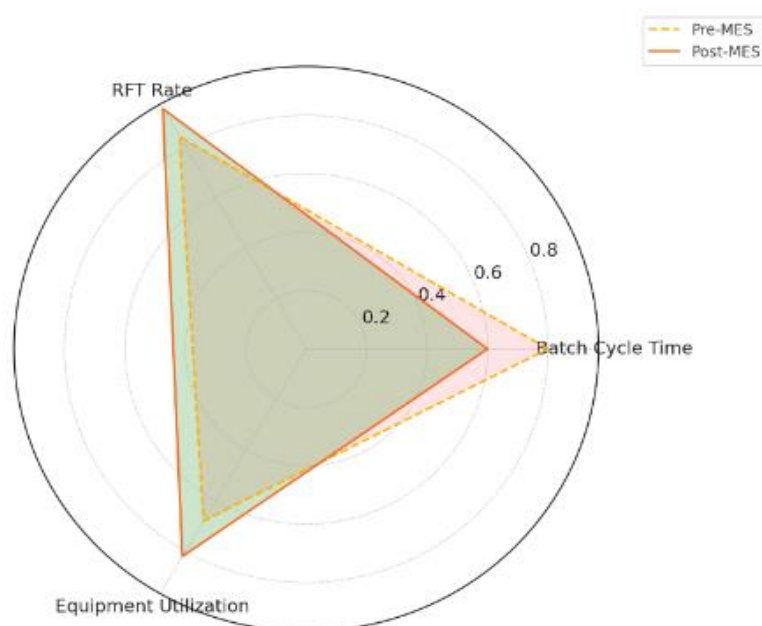


Figure 4. Efficiency KPI comparison

Table 4. Comparative analysis with other MES solutions

Outcome Parameter	Pre-Implementation (Legacy Systems)	Post-Implementation (PAS-X MES)	% Change	Interpretation
Implementation Timeline (months)	Competitor MES: $24 \pm 3$	PAS-X MES: $18 \pm 2$	$\downarrow 25\%$	PAS-X delivered faster due to pre-configured GMP templates.
ROI Achievement Timeframe (years)	Competitor MES: $3.5 \pm 0.5$	PAS-X MES: $2.8 \pm 0.4$	$\downarrow 20\%$	Faster ROI driven by reduced deviations and QA efficiencies.
User Satisfaction Score (scale 1–10)	Competitor MES: $7.0 \pm 1.2$	PAS-X MES: $8.8 \pm 0.8$	$\uparrow 25.7\%$	Higher satisfaction owing to pharma-specific features.

compliant templates. ROI was accomplished roughly 20% faster, in 2.8 years for PAS X versus 3.5 years for alternate results. User satisfaction scores were higher for PAS X (8.8/10) comparing to competitor systems (7.0/10), credited to its pharma-specific design and integration competences. These results reinforce PAS X's position as a leading MES solution for regulated pharmaceutical manufacturing environments.

Despite its benefits, MES implementations face noteworthy obstacles. Findings on prolonged authentication time and moderate user resistance echo challenges emphasized by Medical Device Developments and Capgemini. Ensuring cross-functional governance and tailored training are critical to overcoming these. Literature stresses that success hinges not only on technology deployment, but also on people especially shop-floor personnel being prepared and supported through change [32]. The PAS X v3.3 cloud-enabled architecture bring into line with Pharma 4.0 strategies permitting real-time analytics, inaccessible access, and scalable processes. These trends are reinforced in MES 4.0 frameworks, which support sturdy equipment and IT combination under Industry 4.0 [32]. For pharmaceutical producers, cloud-based MES can improve agility and upkeep digitization mainly for continuous bioprocessing and flexible industrial lines.

The results of this study have been achieved on the grounds of three facilities which restrict the statistical power and external validity. The input of our results is based on facilities that have already made the decision of adopter MES, which could cause selection bias. In addition, legacy systems just had variability, implying that not all baselines involving pre-implementation processes were consistent. Lastly, we failed to investigate the long-term sustainability of gains post-go-live; longitudinal research studies in future should be conducted to determine an extension in improvement beyond one year of deployment.

## 5. Conclusions

Rapid deployment of PAS X MES throughout GMP-regulated pharmaceutical drug manufacturing sites proved to result in significant gains in productivity, compliance and data integrity. Important performance measures including the batch cycle time, the Right First Time rates, and the QA review times exhibited a remarkable improvement, which serves to indicate capabilities of the system to optimize the processes and enable real-time decision-making. The improvement on compliance and especially on reduction of deviations and preparedness of the audit is another factor strengthening the significance of PAS X in enforcing compliance with global regulatory requirements like 21 CFR Part 11 or EU Annex 11. Undoubtedly though beneficial, some challenges were exposed, together with long authentication cycles, the need to train operators, and the structural disinclination of change management, which upkeep the argument that MES deployment needs the establishment of active alteration management and stakeholder engagement procedures. Relative analysis also demonstrated the competitive advantages of PAS X to other MES platforms in terms of the execution speed and users satisfaction, mostly owing to its specific development to the pharma market and significant GMP template pre-configuration.

All in all, PAS X MES is identified as a critical enabler of digital transformation in pharmaceutical industry which falls in line with Pharma 4.0 efforts and helps manufacturers attain data-driven, compliant, and agile operations. Future studies could be based on longitudinal test of post implementation performance and the possibility of cloud based data processing in PAS X architecture whose performance can have a global scale and connectivity to upcoming smart manufacturing processes.

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