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Aligning Value Stream Mapping with Current Good Manufacturing Practice (cGMP) Requirements in Pharmaceutical Production Environments

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ABSTRACT

The pharmaceutical industry operates under tight controls of current Good Manufacturing Practice (cGMP). The application of lean principles under such circumstances often becomes more complicated than may appear at first glance. In this study, a lean compliance-focused Value Stream Mapping approach was designed and implemented with the aim of ensuring process improvement while maintaining regulatory compliance. Based on the results of a single-case study of the State Company for Drug Industries Samarra suspension line, the pre- and post-implementation performance was measured using operational KPIs, compliance metrics, process mapping and internal audit results. Compliance-oriented lean interventions included introduction of checkpoints according to cGMP regulations, setup reduction, queue management, digital support for batch record, and quality-assurance batch release process logic. As a result of intervention, lead time decreased by 28.2%, throughput increased by 29.3%, Overall Equipment Effectiveness was improved by 19.7% and defect rate dropped by 34.4%. At the same time, the time required to obtain batch release from quality assurance, close deviations and documentation errors were also reduced significantly. This study demonstrates that compliance activities do not have to be considered wasteful in the context of lean improvement projects.

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1. Introduction

The pharmaceutical industry operates within regulatory regimes designed to safeguard patient safety and to ensure consistent product quality throughout manufacturing and release. The current Good Manufacturing Practice (cGMP) requirements enforced by agencies such as the U.S. FDA and EMA impose extensive documentation, process-control, validation, and quality-assurance obligations across the product lifecycle [1]–[3]. Although indispensable, these requirements often lengthen batch-release cycles, increase compliance overhead, and constrain process redesign, especially in legacy facilities such as the State Company for Drug Industries (SDI) in Samarra, Iraq.

While the concepts of lean manufacturing are broadly applied, they are even more challenging to implement in a pharmaceutical setting than in discrete industries. Standard Value Stream Mapping (VSM) [4], [5] largely ignores compliance-driven steps, such as batch record review, equipment qualification, and Quality Assurance (QA) checkpoints,

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which represent significant and unavoidable steps in a classical lean tool set. Nonetheless, it is necessary to remove as many non-value-added activities as possible, which is sometimes in conflict with regulations, because some actions must be carried out by law, without being value-added.

Integrating the flow-based principles of value stream management with cGMP facilitates process flow optimization without sacrificing regulatory adherence. Value stream maps that contain value and compliance checkpoints enable pharmaceutical manufacturers to redesign the workflow so as to reduce the lead time, remove unnecessary paperwork, and enhance utilization of equipment while ensuring and maintaining complete end-to-end information tracing and validation integrity [6]–[8]. Such integration links lean operational excellence to the Quality by Design framework, which underpins modern cGMP initiatives.

However, despite increasing attention paid to lean–pharma integration, it remains extremely rare to see compliance-related activities explicitly incorporated into the process map. As can be seen, there are plenty of research works in which the authors emphasize the efficiency aspect but fail to incorporate regulatory checks into their frameworks; there are also many papers that tackle the concept of compliance and do not go further than that [9], [10]. It is precisely this problem that will be tackled in the current research. This paper proposes a systematic methodology for aligning VSM with cGMPs and applies it to SDI Samarra to evaluate operational and regulatory performance metrics.

This study aims at estimating the magnitude of the improvement in operations management that could be realized from the adoption of the proposed integrated approach in terms of compliance. In light of this, the research is guided by these research questions: What is the optimal way of embedding compliance-oriented practices within process mapping not to hamper flow optimization? Given full cGMP compliance, what measures can be taken to improve lead time, work-in-progress, and batch release time? Which of the operations and compliance indicators would best measure the dual lean-compliance impact of the proposed approach?

2. Literature Review

It is widely accepted that lean manufacturing has expanded beyond its roots in the automobile industry and is now used as a worldwide approach to eliminate wastes and improve effectiveness [10]. However, the application of this principle in the pharmaceutical industry is limited, mainly because of the rigorous regulation favoring patient safety and product quality above speed [11]. Some other regulatory demands, such as batch documentation, deviation handling, and process validation, which cannot be ignored and simplified under cGMP conditions, are by definition non-value-adding activities [5], [12].

One of the most well-known structured tools for tracking material and information flows, eliminating waste, and creating future-state processes is still the VSM [13], [14]. It has been used across a range of pharmaceutical contexts to remove waste, shorten lead times, and improve equipment utilization [15]. Even so, classical VSM does not, on the whole, account explicitly for regulatory checkpoints, because conventional process maps merely reproduce, or rather mimic, processes as they occur in practice [16], [17]. To address this limitation, researchers have proposed hybrid approaches in which compliance steps are incorporated into lean redesign initiatives [11].

Current cGMP guidelines have focused on systematic risk management, traceability, and validation of processes throughout their lifecycles [2]. Since quality-by-design is inherently designed to integrate regulatory requirements into process development, it is feasible to reconcile the goals of compliance with lean methodologies, as long as process knowledge, risk management, and documentation are embedded in the system [18], [19]. In other words, documentation and validation procedures need to be standardized, digitized, and mistake-proofed, and not viewed - too easily, perhaps - as inevitable waste [20].

Empirical research into the integration of lean redesign and digitalization in the pharmaceutical industry suggests that compliance gates could be transformed into control gates instead of being seen as obstacles outside of the process [21]-[25]. The use of such enabling technologies as Manufacturing Execution Systems (MES), Electronic Batch Records (EBR), and Industry 4.0 systems allows for faster reviews, improved traceability, and consistent execution; however, there is limited case evidence on how digital technology could contribute in the developing country and state-owned sectors [26]. This is where the research at hand fills the gap.

In light of these observations, the proposed conceptual integration of VSM with cGMP compliance is set out in Figure 1. It shows how operational drivers and regulatory constraints are integrated into a systematic improvement process, connecting lean redesign phases with both operational and regulatory Key Performance Indicators (KPIs).

2.1 Summary of Literature Gaps

The integrated framework (see Figure 1) embeds compliance checkpoints into VSM stages to ensure regulatory compliance while targeting lean process efficiency improvement. Far fewer studies offer rigorous empirical support for integrated methods, particularly in the context of developing economies and brownfield pharmaceutical sites.

As can be seen in Figure 1, the proposed model illustrates the transformation of operational drivers and regulatory constraints through a structured VSM-cGMP process into enhanced operational and regulatory KPIs, being underpinned by a digital and cultural enabler.

3. Methodology

3.1 Research Design

The current study applies a mixed-method embedded case study design to explore the impact an integrated VSM-cGMP framework has on improved operational performance within a regulated pharmaceutical setting [27]. It should be mentioned that our selected case study is SDI Samarra, which is the biggest public sector manufacturer of pharmaceuticals in Iraq. This is because of the aged technology base, high documentation requirements, and the need for a more advanced process. The rationale behind choosing such an interesting case for analysis lies in its unique features: old equipment, extensive documentation needs, batch production, and QA release. It is important to mention that this paper is not concerned about statistical generalization across the whole pharmaceutical industry but rather with its transferability to other pharmaceutical production facilities that comply with cGMP regulations. This paper unfolds through three stages of analysis: i) Diagnostic stage - process flow and compliance mapping of current state; ii) Design stage - creation of future-state VSM that will take into account cGMP requirements; and iii) Validation stage - evaluation of the model through KPIs and compliance audits.

3.2 Production Line Description

The production line chosen for consideration in this case produces oral liquid suspensions in batches. Some of the main processes involved in this production line include weighing of raw materials, mixing of wet dispersion, hydration and stabilization, homogenization, filling, packaging, and release. In this regard, process control in a batch, batch recording, and QA approval are done based on cGMP. In addition, equipment qualification, including IQ, OQ, and PQ, as well as periodic validation, makes it more difficult to make changes to the production process, something that is intended.

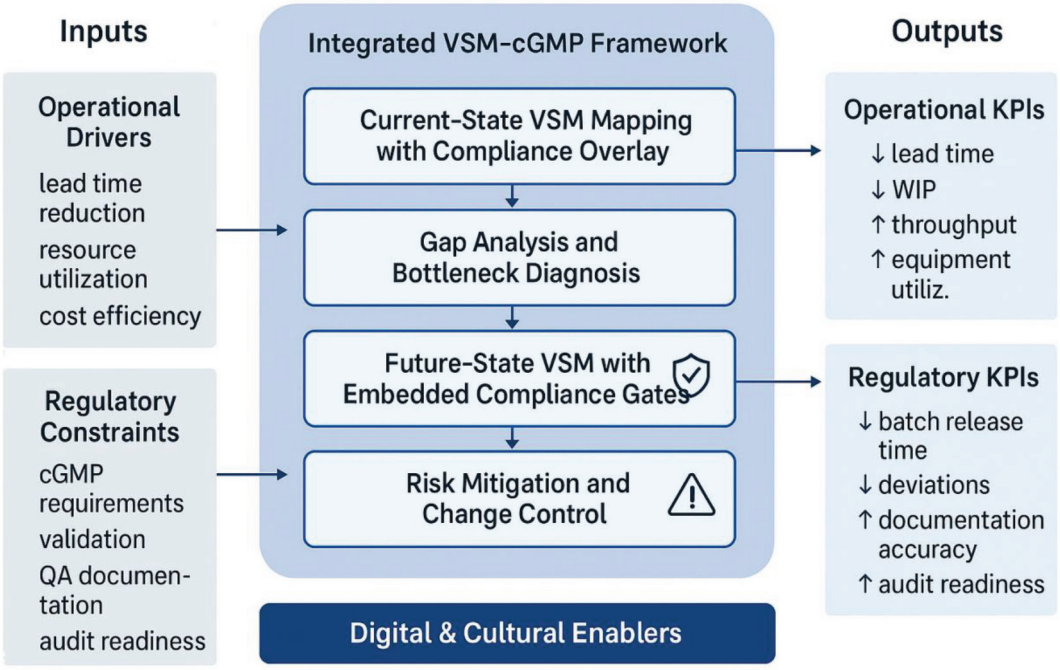


Figure 1. The conceptual framework integrating VSM with cGMP compliance

3.3 Data Collection and KPI Definition

The data sources are categorized as below:

I. Direct observations and time studies of production operations, recorded using digital chronometers and standardized worksheets.
II. Document analysis of Batch Manufacturing Records (BMRs), deviation logs, and validation reports to map compliance-driven activities.
III. Structured interviews with production supervisors, QA/QC officers, and maintenance engineers to identify operational bottlenecks and regulatory pain points.
IV. Historical production data from SDI Samarra's ERP and quality management systems to establish performance baselines.

Also, the KPIs are listed as:

- Operational KPIs: lead time, work-in-process (WIP), cycle time per operation, throughput rate, equipment utilization, and specific energy consumption per batch.
- Regulatory KPIs: batch release time, deviation closure rate, documentation error frequency, and audit readiness score.

Concerning the comparison of operational KPIs, data collected prior to and after the intervention were paired on the basis of equal production periods, allowing for statistical testing based on matching operations rather than comparing unrelated batches of data [28]. A two-tailed paired t-test was performed on pairs of data illustrated in Table 1, whereby the effect size was determined through confidence intervals and the calculation of an effect size. Therefore, the results are described based on matched production periods rather than unmatched batch trends.

3.4 Value Stream Mapping as a Diagnostic Tool

The material and information flows over the SDI Samarra suspension line were captured in a present-state process flow map that included lead-time, delay, and WIP metrics derived from VSM. The map documented each processing step, together with waiting time, WIP accumulation, and compliance checkpoints, including QA sign-offs and batch-record review. In this way, the hybrid representation allowed bottlenecks to be identified simultaneously from operational and regulatory standpoints.

Building on this diagnostic baseline, a future-state process flow map was developed so as to incor-

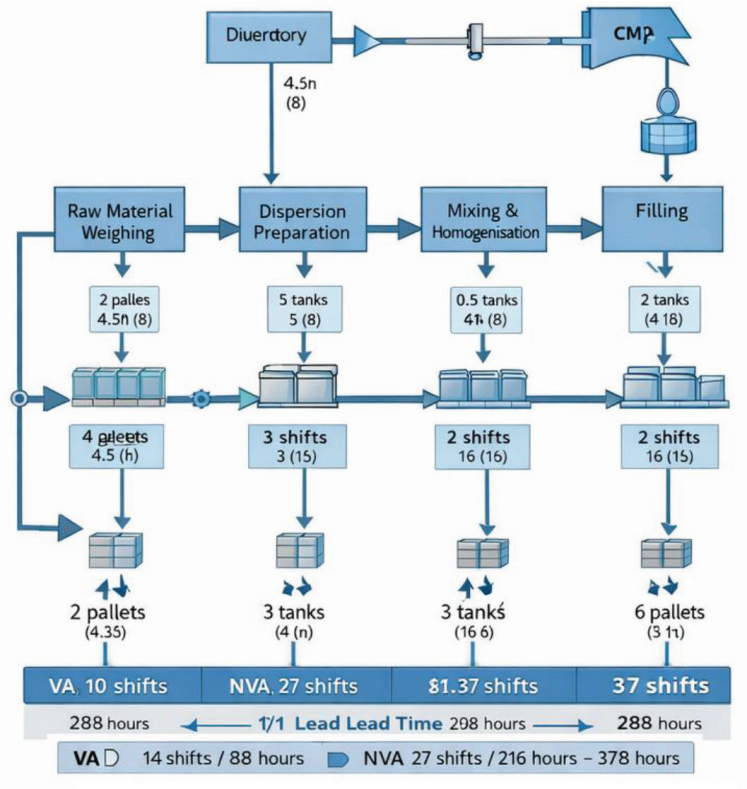


Figure 2. Current-state process flow map of the SDI Samarra suspension production line with integrated lead-time, WIP, and compliance metrics.

porate targeted lean interventions whilst remaining fully compatible with cGMP requirements. Digital batch records, setup reduction, and queue management were built into standardized compliance gates, such that efficiency gains could be pursued without any weakening of QA control or the integrity of documentation. Figures 2 and 3, accordingly, present hybrid process maps that combine VSM-style performance metrics with explicit regulatory checkpoints.

The current-state map sets out the baseline operational and regulatory workflow, from raw-material weighing through to final QA release. It brings into view long lead times, high WIP, prolonged waits, and unnecessary loops in documentation. Compliance checkpoints - including QA approvals and batch-record reviews - are shown within the flow, making clear, and clear enough, how regulatory obligations shape process complexity and create operational bottlenecks.

The future-state map sets out the revised flow once lean practices and compliance gates had been incorporated. The revised configuration is intended to reduce lead time and WIP, increase throughput and Overall Equipment Effectiveness (OEE), and strengthen digital traceability and regulatory confidence.

3.5 Research Procedure

The procedure of the current study was structured into five main steps. First, current-state mapping was conducted by documenting the end-to-end flow of materials and information using process-flow symbols, supplemented by annotations relating to lead time, Work-In-Process (WIP), and compliance. QA approvals, validation steps, and document reviews were subsequently overlaid to illustrate how regulatory activities shape and, at certain points, constrain process flow. Second, bottleneck identification was performed by analyzing cycle-time and waiting-time data using Pareto logic, while interviews and document reviews were used to identify compliance-related pain points. Third, future-state design involved the development of a cGMP-aligned future-state map in which compliance gates, documentation controls, and validation requirements were integrated directly into the redesigned process flow rather than treated as external constraints. Fourth, scenario evaluation was conducted using Excel to calculate time-based KPIs, aggregate queue and waiting-time data, and compare current- and future-state operating scenarios. EES was used exclusively for specific energy-consumption calculations and associated deterministic engineering balances and was not em-

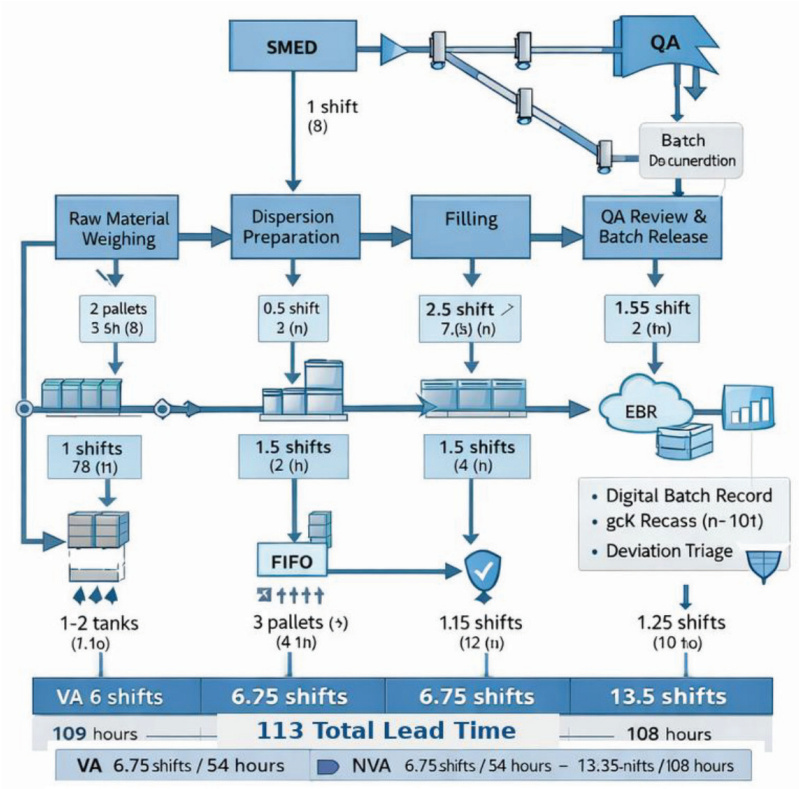


Figure 3. Future-state process flow map of the SDI Samarra suspension production line with cGMP-integrated compliance gates.

ployed as a discrete-event simulation platform. Finally, stakeholder validation was carried out through cross-functional workshops involving production, QA, and engineering personnel to verify that the redesigned process remained operationally beneficial while maintaining consistency with cGMP requirements.

3.6 Analytical Tools

The analytical tools utilized in the current study comprised five main categories. First, statistical analysis was performed using descriptive statistics, paired t-tests, and confidence intervals to assess process performance and quantify differences between the evaluated states. Second, Root Cause Analysis was conducted using Fishbone diagrams and the 5-Whys method to identify the underlying causes of documentation delays and process variation. Third, process risk assessment was performed through Failure Mode and Effects Analysis (FMEA) to evaluate regulatory and operational risks associated with proposed process changes. Fourth, visualization tools, including Pareto charts, control charts, and VSM of the current and future states, were employed to clearly illustrate process performance and the resulting improvements. Finally, scenario-based engineering evaluation was conducted using Excel for deterministic calculations of efficiency, waiting time, throughput, and cost impacts derived from the mapped process states, while Engineering Equation Solver (EES) was used specifically to calculate energy consumption per batch. Accordingly, the study employed deterministic, scenario-based engineering evaluation rather than a formal discrete-event simulation approach.

3.7 Validation Measures

To ensure the credibility and robustness of the study, several validation measures were implemented. First, data triangulation was achieved by integrating quantitative data, qualitative insights, and relevant regulatory documentation, thereby enabling findings to be examined from multiple perspectives. Second, cross-verification of data was performed by comparing information obtained from ERP production logs, batch records, and on-site observations to enhance the reliability and consistency of the collected evidence. Finally, internal compliance-audit checks were conducted to verify that the proposed process improvements remained aligned with cGMP expectations and did not introduce any identified non-conformities within the scope of the case study review.

3.8 VSM-cGMP Alignment Framework

3.8.1 VSM in cGMP Compliance Integration

The future-state Value Stream Map presented in this alignment framework illustrates how lean principles were targeted within a regulated pharmaceutical environment. Real-world application of mapping compliance obligations to processes shows how regulatory obligations were embedded directly into the process flow, implementing standardized "compliance gates" at key stages - raw material release, wet dispersion preparation, mixing and homogenization, filling, final QA approval, etc.

While the current-state VSM identified long lead times, unnecessary documentation cycles, and siloed information flows; the future-state VSM highlights an ideal flow enabled by digital tools such as EBR and MES. This change is evidence of a two-pronged success story - not only an operational one (lower lead time, WIP, and defect rates) but also a regulatory one (shorter QA release cycles and fewer documentation errors). As shown previously in Figures 2 and 3, the transition between the current-state and future-state VSM provides a diagrammatic abstraction of the main contribution of this study; namely that lean redesign is possible in conjunction with, alongside compliance, and with cGMP requirements in pharmaceutical production.

3.8.2 Mapping Compliance-Critical Steps

VSM-for-cGMP alignment begins with an identification of the compliance-critical points where regulatory controls intersect with production flows. Revisions to the current state (VSM) at SDI Samarra overlap with documented evidence of inspections, such as BMR, deviation logs, and QA inspections (i.e., documentation reviews, equipment validation (IQ/OQ/PQ), and batch record approvals). What are often treated as non-value-adding checkpoints are here re-described as indispensable safety nets for QA [5], [23].

3.8.3 Compliance Gates in Future-State Maps

Within the future-state map, cross-functional compliance gates remain embedded at each critical stage: raw material release, wet dispersion preparation, post-mixing review, filling, and final batch acceptance. They weren't removed. Rather, their sequence, timing, and approval criteria were standardized, so validation, documentation, and QA review could

proceed with fewer avoidable interruptions to cycle time, and with lower process variability [20], [24].

3.8.4 Combination with Digital Tools

In the entire value chain, the digital enablers are realized using MES, EBRs, IoT-enabled data collection, and KPI dashboards. In the suggested architecture, shop floor data are collected at the point of execution and are synchronized with the batch identity, followed by role-based approvals, and are finally stored in timestamped audit trails [20], [24], [25], [26]. For SDI Samarra, the digitization journey is not seen as an abrupt shift from current practices; rather, it is a gradual strategy meant to speed up batch record reviews, reduce transcription errors, improve deviation analysis, and gain insight into machine utilization.

3.8.5 Change Control and Risk Mitigation

Lean redesign initiatives were evaluated based on official change control systems to avoid having any improvement measures affect validation status or regulatory compliance. All changes recommended following the mapping process were screened for FMEA, reviewed by QA, and integrated with ICH Q9 risk management guidelines before being put into practice [2]. In terms of methodology, setup reduction and queue management initiatives focused on optimizing sequencing, handoff, and setup steps without compromising any cleaning, clearance, in-process control, or approval criteria.

In Figure 4, the *"walk down"* process of the alignment that has been proposed is shown visually, wherein compliance gates and virtual traceability methods are included in the VSM process, thus connecting the two together.

This may be described as a model where the flow of information and material from TP through a series of manufacturing phases such as material release, wet dispersion formation, mixing and homogenization, and packing takes place within defined validation points in an integrated process where MES, EBR, IoT, and KPI dashboards are synergized. It is important to state that VSM-cGMP convergence includes standard compliance process, traceability process, and change management process.

4. Results

4.1 Quantitative KPI Comparison: Before and After

The reported results in Table 1 compares the operational KPIs before and after implementation of the VSM-cGMP procedure. Results shows that the lead time decreased by 28.2% (from 1,240 ± 115 min to 890 ± 95 min), throughput increased by 29.3%, and equipment utilization improved by 19.7%. These shifts show that the redesigned flow reduced non-value-adding delay while preserving the compliance controls embedded in the process.

Figure 5 shows the distributional shifts in performance. As seen from the boxplot, there is clearly a downward shift in lead time and upward shifts in throughput and equipment utilization. The additional squeeze in variability signals an even higher degree of operational stability and business predictability.

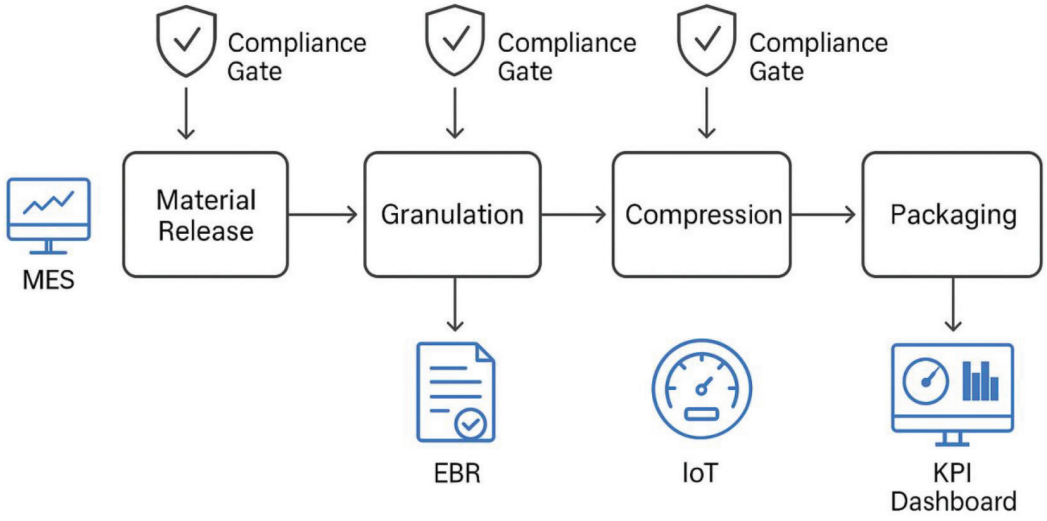


Figure 4. The mini diagram of compliance gates and digital tools placed in the VSM flow

Table 1. Pre- and post-intervention operational KPI comparison for the VSM-cGMP alignment framework (matched pre/post production windows; paired t-test basis).

KPI	Pre-VSM (Mean ± SD)	Post-VSM (Mean ± SD)	% Improvement	p-value (α=0.05)
Lead Time (min)	1,240 ± 115	890 ± 95	28.2% ↓	<0.001
Cycle Time per Station (sec)	185 ± 21	145 ± 18	21.6% ↓	0.002
Value-Added Time (min)	470 ± 40	515 ± 35	9.6% ↑	0.015
Waiting/Queuing Time (min)	320 ± 60	180 ± 40	43.8% ↓	<0.001
Throughput (units/hour)	410 ± 25	530 ± 30	29.3% ↑	<0.001
OEE (%)	62.5 ± 4.2	74.8 ± 3.9	19.7% ↑	0.004
Defect Rate (%)	3.2 ± 0.6	2.1 ± 0.4	34.4% ↓	0.021
WIP (units)	4,200 ± 500	2,950 ± 420	29.8% ↓	0.006
Changeover Time (min)	95 ± 12	62 ± 9	34.7% ↓	<0.001
Equipment Utilization (%)	62.5 ± 4.2	74.8 ± 3.9	19.7% ↑	<0.001

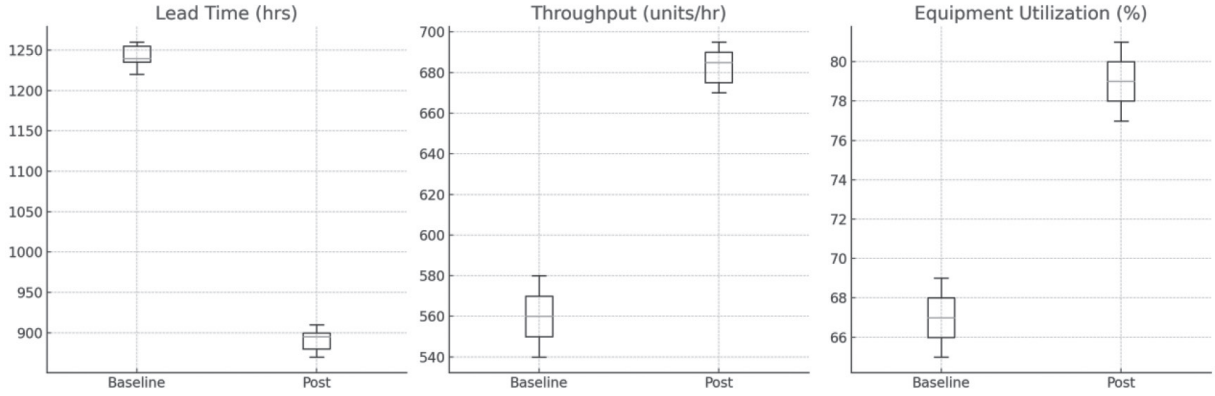


Figure 5. Boxplots between lead time, throughput and equipment utilization- baseline Vs Post-VSM

4.2 Compliance Impact (Quality & Validation Integrity)

The compliance-related KPIs (shown in Table 2) were used to evaluate the compliance-based assurance impact of the framework, in addition to operational performance. So, it appears that efficiencies were obtained with adherence to cGMP compliance as evidenced by these metrics.

For instance, the QA batch release decision time-to-target was reduced from 18-24 hours to 10-14 hours at most production lines as a result of enhanced access to digitalized batch records and alignment on pre-approvals. By drastically reducing transcription and manual entry in the documentation process, batch quota documentation errors were reduced by nearly 70%. The same was true for deviation closure cycles, which exhibited a nearly 50%

Table 2. Compliance-related performance indicators before and after VSM–cGMP alignment (same matched production context as the operational comparison).

Compliance KPI	Baseline (Pre-VSM)	Post-VSM Implementation	Improvement
QA batch release decision time	18-24 hrs	10-14 hrs	~ 35-40% faster
Documentation errors per batch record	4-6 findings	1-2 findings	~ 60-70% reduction
Deviation closure cycle (days)	12-15	6-8	~ 45-50% shorter
Audit readiness score (internal QA)	Medium (incomplete records, redundant checks)	High (standardized, digital support)	Substantial increase
Change control turnaround (days)	10-12	6-7	~ 40% shorter

reduction, thereby avoiding time wasted on addressing quality concerns and ensuring their remedy was properly handled through controls applied to deviation management.

This idea starts to become a reality as illustrated in Figure 4, where the compliance gates (validation, documentation, QA release, etc.) are integrated into the value stream and digitally enforced in real-time via MES dashboards and IoT checkpoints. This visualization provides a high-level view of how the new process adds to our existing one and complies with validation integrity and auditing readiness.

4.3 Critical Path Enhancements (Stage-Specific Contributions)

Stage-level analysis was used to identify which process segments contributed most to the total lead-time reduction. The largest gains were associated with changeover reduction in mixing and homogenization, followed by shorter filling queues, improved preparation allocation, and fewer packaging stops, as summarized in the Pareto chart (Figure 6).

4.4 Visualization of Gains (Boxplots, Pareto, Correlation)

Beyond descriptive comparisons, the analysis also examined correlations to clarify the likely sources of improvement. Figure 7 shows a correlation heatmap in which equipment utilization is strongly and positively associated with throughput ($r \approx +0.76$), whereas throughput is negatively associated with waiting time ($r \approx -0.73$). Lead time is inversely related to utilization ($r \approx -0.74$), and defect rate is positively related to waiting time ($r \approx +0.68$). These relationships support the interpretation that reducing waiting and improving equipment availability contributed jointly to higher output and more stable quality.

4.5 Synthesis

The VSM-cGMP integrated framework yielded tangible and statistically significant benefits (Table 1; Figures 5-7). The results of this study show that lean redesign in regulated systems:

- Enhances operational KPIs (lead time, cycle time, throughput, utilization).
- It also reduces the rate of defects without compromising on compliance.
- The organization drives impact through selective bottleneck interventions with digital tools and compliance gates in a structured manner.

However, at resource-poor pharmaceutical settings such as SDI Samarra, compliance-integrated lean strategies seem most appealing due to this dual focus on enhancing operational excellence while providing assurance to the regulatory agencies.

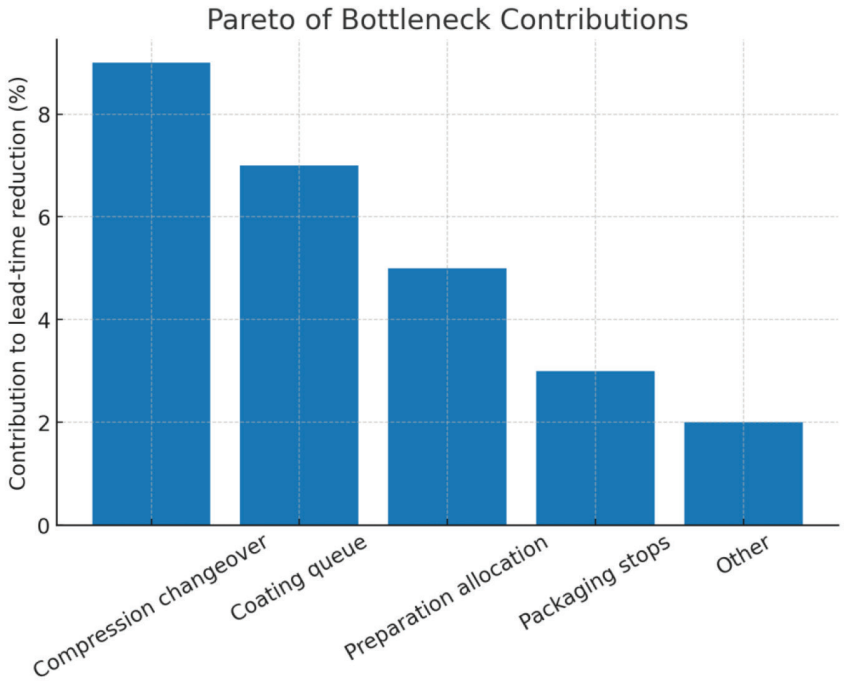


Figure 6. Pareto chart of stage-specific contributions to lead-time reduction.

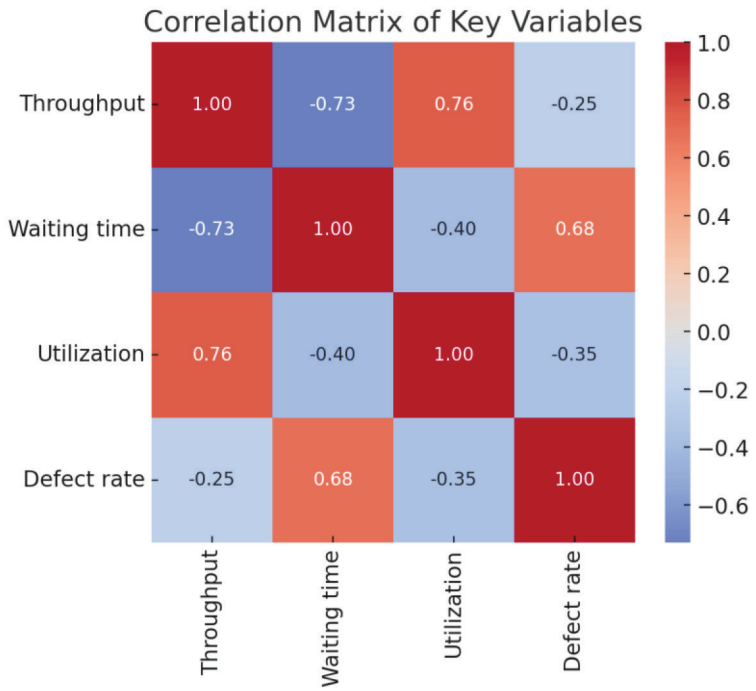


Figure 7. Correlation matrix of key operational and compliance-critical variables.

5. Discussion

5.1 Theoretical implications

Our findings reaffirm that lean equipment, and mainly VSM, can be included with strict pharmaceutical guidelines, provided that such an intervention is framed within a Pharmaceutical Quality System (PQS) and that the guiding ideas include hazard-based thinking. This case empirically justifies the "compliance-aware Lean" paradigm by illustrating how the *"waste-reduction"* activities aligned with cGMP regulatory requirements (e.g., documentation, validation, and QA release) in the provided case, rather than enforcing a trade-off between speed and assurance [28]. More specifically, the SDI Samarra intervention incorporated cGMP checkpoints as official nodes on the value stream (e.g., batch record review, line clearance, and deviation triage). Therefore, regulatory "constraints" were converted to flow conditions rather than to bottlenecks, which is aligned with the spirit of ICH Q10 (integrated PQS enabling continual improvement) and the revised ICH Q9 (R1) focus on risk-based decision-making and manufacturing risk "early warning" initiatives [15].

Conceptually, the SDI results show that the seven wastes can be re-specified in pharma as *"regulated wastes"* (e.g., avoidable waiting due to preventable documentation rework) without diluting compliance; the observed improvements in lead time, WIP, and throughput were achieved while strengthening traceability and deviation close-out discipline (see Results, Table 1 and Table 2; Figures 4 and 5).

This is important because it indicates a trend. It is here that the largest gains have been made in the areas of wait times and queues and QA-related release delays, while the value-added process times showed little variance [18], [23]. Altogether, the results point toward a system whereby improved performance comes from reducing unnecessary downtime, decreasing document handling, and coordinating the transfer from the production line to QA. These gains did not come about by shortening vital processes within the factory or by loosening regulatory oversight.

5.2 Managerial insights

From a managerial perspective, three practices proved decisive at SDI Samarra. First, designing the VSM with cGMP gates built in from the outset reduced the back-and-forth with QA and curtailed non-value-added documentation touches (Results 5.2; Figure 4). Secondly, digital enablers - batch genealogy capture, e-logs, and straightforward KPI dashboards - shortened the feedback loops between production and QA, thereby supporting right-first-time documentation and quicker deviation triage (Results 5.1-

5.3; Figure 5). Thirdly, the risk-based prioritisation of bottlenecks (for example, suspension filling and packaging) focused changeover and line-clearance improvements where they mattered most for the critical path (Results 5.3). Taken together, these choices produced the KPI shifts summarised in Tables 1 and 2 without eroding validation rigour or expectations of data integrity.

Managers should therefore institutionalize: i) a VSM-PQS handshake (that is, mapping each flow step to its controlling SOP or validation artefact), ii) visual controls for compliance readiness (for example, release checklist status), and iii) tiered metrics pairing flow KPIs (lead time, WIP, throughput) with compliance KPIs (batch record error rate, deviation closure time, on-time QA release). These practices align with the FDA's cGMP expectations under 21 CFR Parts 210/211 and with ICH Q10's call for structured change management and knowledge management.

5.3 Comparison with global literature

International experience now increasingly indicates that Lean can coexist with - and may even strengthen - regulated quality systems when it is deliberately architected around risk-based controls. Case studies of VSM in pharmaceutical production and logistics report substantial reductions in lead time and inventory, provided that documentation and validation are re-engineered rather than simply bypassed; those patterns are consistent with the evidence from SDI Samarra (cf. our Table 1 and 2; Figure 5).

Recent syntheses concerning Lean/Industry 4.0 (Lean 4.0) further indicate that digital traceability (MES/eBMR, IoT sensing) can strengthen both flow and compliance by reducing human error and enabling near-real-time checks of release readiness - again, very much in keeping with SDI's digital supports embedded along the value stream (Figure 4) [20]. At the same time, the ICH Q9 (R1) revision (effective with 2023-2025 updates across jurisdictions) explicitly foregrounds chance signals associated with manufacturing and supply continuity, which rather underlines the value of quicker, more tightly controlled flows achieved through Lean-based redesign [23].

Beyond sterile manufacturing, meta-analyses of pharmacy operations also report sizeable gains from Lean Six Sigma without any compromise to safety, lending support to the wider generalizability of the compliance-aware Lean pattern beyond our own case [14].

5.4 Practical guidelines for cGMP-aligned VSM in pharma

Drawing on the SDI Samarra case and the surrounding guidance landscape, we propose the following actionable steps for firms seeking to implement VSM whilst ensuring cGMP alignment:

I. Start with a compliance-critical map - Construct the current-state VSM so that it explicitly overlays: i) required records (for example, BRR/eBMR fields), ii) validation dependencies, and (c) QA decision points. Use colour-coded "compliance gates" (release, line clearance, deviation triage) and tie each to the governing SOPs. (See our Figure 4 for a template.)

II. Design a future-state with digital supports - Where documentation or genealogy interrupts flow, specify digital aids (MES data capture, barcode/RFID, e-logs) to reduce re-entry and transcription errors; and define data integrity checks (ALCOA+) at the point of capture.

III. Embed risk-based change control - For each VSM change (for example, setup reduction or batch size smoothing), conduct a QRM assessment (per ICH Q9 (R1)), update control strategies, and agree acceptance criteria with QA in advance so as to avoid late-stage objections.

IV. Pair Flow and compliance KPIs - Publish a compact tier-1 dashboard that always displays both dimensions together: lead time, WIP, and throughput alongside deviation closure time, first-pass BRR accuracy, and on-time QA release. The SDI experience indicates that these pairings made trade-offs visible and prevented "local optimisations" that generate downstream compliance work (Tables 1–2; Figure 5).

V. Stabilise the critical path first - Focus improvement cycles where delays propagate and cascade (for example, filling and packaging); use regression and correlation evidence to set priorities (Results 5.3).

VI. Institutionalize learning in the PQS - Update SOPs, training, and knowledge-management artefacts so that improved flows are locked into the PQS - consistent, of course, with ICH Q10's continual improvement model.

It can be summarized that the SDI Samarra case study shows that VSM-cGMP alignment can result in tangible benefits for flow efficiency and improved compliance. The achievement is based on considering cGMP gateways as deliberately created checkpoints, utilizing digital technology to mitigate delays in documentation, and managing any improvements via quality risk management within the PQS framework. It should be noted that the model operates via scalability principles rather than strict duplication. The framework, including the mapping process, the two-fold KPI design, and the gating process design, is replicable in other pharmaceutical production lines operating in batch mode. For sterile production lines, continuous manufacturing processes, and fully automated facilities, the criteria must be adjusted accordingly.

6. Conclusions

This study investigated that VSM can be combined with cGMP on a regulated pharmaceutical suspension line. At SDI Samarra (the surveyed case), the revised procedure improved performance without loosening compliance control. Lead time fell by 28.2%; throughput rose by 29.3%; The OEE improved by 19.7%; and the defect rate fell by 34.4% (Results, Tables 1 and 2; Figures 5-7). Yet the operational gains weren't the whole of it: batch-release time, deviation closure time, and documentation quality also improved. Across the operational KPI set, the differences were statistically significant, and the compliance indicators changed in the same direction. These gains, significantly, were made under active cGMP constraints. In the redesign, compliance gates were added, document review was parallelized where permissible, and accountability protocols for material and document hand-offs were tightened. Still, traceability, document control, and QA oversight were preserved. The case therefore supports the view that operational excellence and regulatory assurance can reinforce one another rather than pull in opposite directions, provided the improvement logic is built around the compliance-critical path.

At stage level, the principal drivers of improvement behind the end-to-end lead-time reduction were mixing and homogenization (setup reduction/changeover), filling (queue management/capacity), and preparation (allocation accuracy/digital batch records) - these forming the critical path. These observations sit well with our bottleneck analysis and, just as importantly, provide a practical plan for sustaining the gains.

Although, this study reported promising results, but it faces some limitations. First, this is a single-case, single-line evaluation centered on a pharmaceutical suspension stream at SDI; generalizability to other dosage forms or lines is limited. Second, the primary outcomes reflect a cross-sectional, short-horizon comparison (pre vs. immediate post-VSM); long-term durability and seasonality were not assessed. Third, while the study incorporated compliance gates, it did not quantify risk exposure changes (e.g., via FMEA/RPN) nor did it fully leverage advanced digital instrumentation to continuously verify control/validation status. Finally, although multiple data sources and analyst triangulation were used to strengthen reliability and validity, case-study threats (observer/participant bias, instrumentation drift) cannot be fully excluded.

In the following, to cope the mentioned limitations, some suggestions can be proposed for the future studies. The VSM-cGMP alignment should be extended to oral liquid forms, injectables, and suspensions, with effect sizes and critical-path patterns compared across these differing contexts. In parallel, one might usefully incorporate parallel-processing design options - modular rooms or dividing walls, for instance - where cGMP permits, and quantify their effects on flow and QA cycle time. KPIs, together with deviation and closure metrics, should be tracked over a 6-12-month period, with explicit attention to whether observed gains are sustained through shifts in product mix and demand, whilst on-time batch release and documentation quality are maintained. That matters. It matters especially where operating conditions do not stand still. FMEA/RPN and change-control metrics should be embedded within the future-state map so that risk reduction is quantified alongside waste elimination; in addition, the movement of risk scores under setup reduction, Kanban, and workload levelling should be evaluated. Not simply noted, but evaluated. A discrete-event simulation, or digital twin, of the line should be developed so that it mirrors cGMP gates - validation status, QA queues, and document release - and streams real-time data from MES/IoT to dashboards. The model can then be used to test VSM scenarios virtually, to optimise compliance-throughput trade-offs before any physical change is introduced, and to institutionalise KPI monitoring, including lead time, WIP, OEE, right-first-time, and deviation closures. Given the documentation and allocation constraints already observed, clearer roles are worth trying. Packaging assistants could serve as documentation co-signers, or simply as material handlers. Alongside barcode-

enabled pick and put-away, and tighter allocation logic, that may reduce QA queueing and rework. Those changes should be tied to compliance KPIs, including batch-record error rate and QA review lead time.

Taken together, the SDI case points to performance gains compatible with regulation, with VSM built around compliance-critical checkpoints. Extended through digital verification, formal risk metrics, and longitudinal auditing, the approach should help pharmaceutical manufacturers sustain improvements whilst strengthening cGMP assurance.

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