Level Best

An embedded quality management system using Lean Six Sigma can drive operational excellence and continuous improvement for contract manufacturers. Ensuring buy-in across the value chain, this approach goes above and beyond the periodic monitoring called for in regulatory guidance

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Recent changes in contract development and manufacturing are keeping many industry players on their toes. The patent cliff, for example, has triggered fierce generic competition which, in turn, opens doors for contract manufacturers. New opportunities have surfaced, including a steady increase in pharmaceutical supply regulation in areas such as counterfeit drug prevention, as well as patient safety demands through innovations like automatic dose counting. At the same time, dynamic mergers and acquisitions activity has added focus on maintaining margins in a cost-competitive environment during periods of major organisational change management.

In order to compete in this changing landscape, it is vital for contract manufacturing organisations (CMOs) to provide a clear strategy and prioritise human resources, capital and operational expenses in the right areas. This is crucial to finding the appropriate balance between quality, service and cost for growing successful business partnerships. Embedding an effective quality management system (QMS) can assist companies with this strategy development, operational prioritisation and execution.

While there are regulatory requirements around QMS for contract manufacturers to maintain current Good Manufacturing Practice (cGMP), these only provide a guide to the minimum industry standards. Going above and beyond by adopting a Lean Six Sigma approach can drive operational excellence in safety, quality, service and cost, augmenting business growth. Although this kind of solution is often seen in manufacturing within the automotive or aerospace industries, it has not been used as widely in pharma.

Understanding QMS

A QMS is an essential business requirement, especially in pharma and healthcare, and is expected by regulators and customers of CMOs. However, its implementation in the industry can vary significantly, while still working within the framework of regulations and guidance.

To understand what is meant by QMS, it is important to define the terminology. QMS guidance for pharmaceuticals is provided within the ICH Q10 and FDA Q10 documents, which are similar in nature and essentially outline the same points. The requirements, based on Good Manufacturing Practice regulations, cover the whole product lifecycle, from product conception to routine commercialisation.

Effective Guidance?

The Q10 guidance documents highlight that a QMS must:

- Include knowledge management and quality risk management
- Enable the product to be released so it does not stop or unduly hinder manufacturing
- Allow the establishment and maintenance of a state of control through each stage, and help facilitate continual improvement

The last point means that corrective and preventive action must be integrated within the QMS. Change management and reviews should also be included, as well as monitoring of key quality performance indicators, as the Q10 guidance emphasises management responsibility. Quality objectives should be supported at all levels of the organisation, and there should be a clear documented communication process to ensure flow of information.

However, while this is all good advice, the mechanics of putting everything into place are not well-defined, and implementation in the real world can vary considerably. This is demonstrated by the guidance calling for "periodic reviews". Because no recommended review interval is specified, many contract manufacturers may only carry out quarterly or monthly reviews.

There can also be a less routine approach to data collection and monitoring of key performance indicators, resulting in potential delays to corrective actions. In some cases, this can lead to bigger issues resulting from a lack of pace to respond in a timely manner.

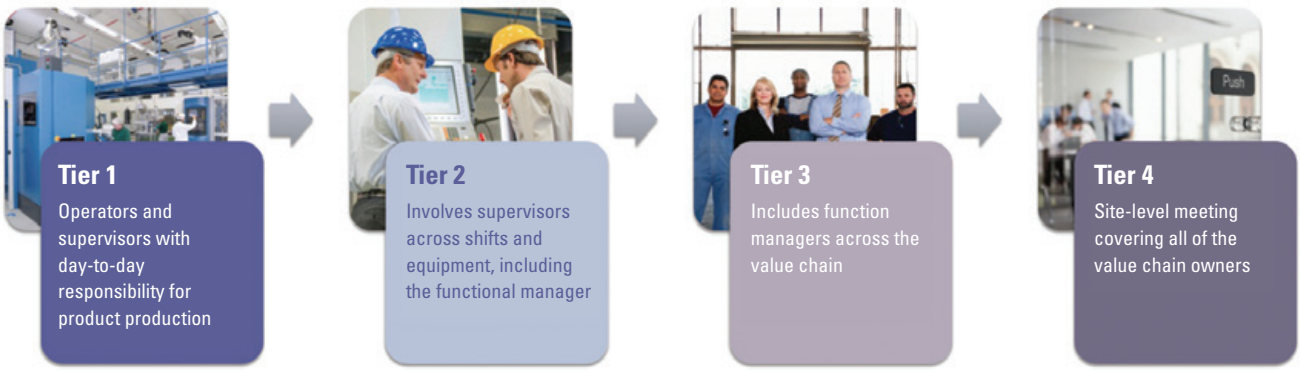

Figure 1: Four-step tier process

Embedded System

To avoid these kinds of problems, an embedded QMS can be adopted. It is different to a standard QMS in that the embedded system ensures effectiveness in delivering operational excellence by leveraging principles of Lean Six Sigma – helping to drive the right behaviours in factories and create a culture of continuous improvement.

Providing the mechanism to actually achieve the intent of the Q10 guidance, an embedded QMS gives visibility of key performance metrics and issue management, which can be escalated within the organisation and to customers in rapid response. Such visibility can improve compliance and foster prioritisation for better shopfloor execution, resulting in better service.

In order to effectively link Lean Six Sigma management and QMS in practice, a significant mindset change is required for those involved in quality management who determine what time interval is acceptable for monitoring, reporting and correcting problems found.

Four-Tier Process

To achieve an embedded QMS, a four-tier process within Lean Six Sigma can be used to involve everyone in the cross-functional value chain and integrate experience across the whole facility (see Figure 1):

- Tier 1 includes operators and supervisors with day-to-day responsibility for production and meeting the schedule. The team leader of the area heads meetings for Tier 1, which take place on the factory floor and should not exceed 20 minutes
- Tier 2 involves the next-level supervisors across shifts and equipment, and includes the functional manager. This tier is led by the supervisor
- Tier 3 includes the function manager, supervisor and the cross-functional value chain team, including quality. This is led by the value stream manager
- Tier 4 is a site management level meeting covering all value chains, quality and safety, led by the plant manager

Using this system, each tier has its own key reporting metrics covering safety, quality, service, cost and engagement. Only three metrics are monitored at each level, and these are different at each tier. This review process allows progress checks and escalation of any issues, as well as the status of corrective action from previously identified concerns. The escalation goes up from Tier 1 to 3 until it is resolved; any unresolved or critical issues are escalated to Tier 4 at the management level. These meetings take place daily at a set time and are cascaded in order to allow a flow of information through the tiers.

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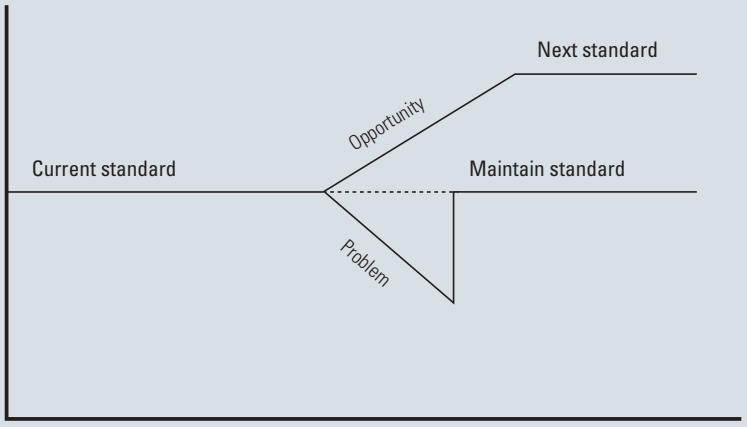
Daily Accountability

Monitoring is, of course, a key part of this process. A daily accountability board exists for each tier, ensuring all required information is available and visible to the whole team, and that action owners are identified (see Figure 2). This board places a focus on telling the story through the use of performance charting of key agreed metrics, looking at trends and noting the impact of actions taken. Any issues across each of the focus areas are raised, and actions are agreed with a clear resolution owner across all teams. Having cross-functional teams discuss the issue and possible solution moves away from the blame culture that can exist within some organisations.

Figure 2: A daily accountability board exists for each tier, ensuring all required information is available and visible for the whole team



While this daily accountability board is a simple approach, it is essential that the right people are engaged in the discussion. With everything visible, everyone is accountable for the process and knows the issue, who is responsible for it, when it will get done, and the status of any other concerns.

Each action that needs follow-up is clearly recorded and made visible using the board. Progress against each action item then forms part of the next day's review. Any issues that cannot be resolved or managed by the tier team are escalated up to the next-level tier review meeting for resolution. Feedback from each review meeting is passed up and down the adjacent tiers. This approach confirms that all stakeholders are fully engaged at every level within the process and all actions are directly linked to the business objectives around safety, quality, service (and customer), costs and engagement.

A critical factor to success of this process is allowing people time for tier meetings and follow-up actions. Diary time should be protected for a set period of each day to allow the meetings to take place with full attendance and engagement, and for any corrective action to be processed before the next day. Without a culture that gives this time to resolve quality issues, problems may continue without being addressed or until they have more severe consequences.

Company Impact

One may wonder how this approach is different from just complying with the Q10 guidance for QMS as it is written, and whether it really provides the business benefits compared to the time invested. In reality, many companies have suffered problems, despite complying with the QMS guidance.

We have all heard of recent issues around the supply of pharmaceutical products where regulators have revoked manufacturing licences or quality incidents have resulted in product recalls. These actions have a significant adverse impact on the business, leading to customer dissatisfaction and a loss in sales revenue. There will also likely be increased costs at the manufacturer's expense in order to resolve and put in place robust corrective action.

Beyond these hurdles, any regulatory actions can impact the morale of the

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workforce and may result in difficulty recruiting or retaining a suitable calibre of staff. This, in turn, may have a harmful impact on brand reputation and future sales.

Real-Time Monitoring

The approach outlined here differentiates itself by bringing focus to real-time monitoring. The team ensures regular monitoring and has a simple route to highlight and resolve issues within normal daily operations. It is important to keep hourly production running according to plan; if it is not, then the team identifies the issue and fixes it.

In addition, the team understands that by tackling the small things at source, their time is freed up to work on the bigger concerns. If the team misses one hourly metric, but resolves the issue by the end of the day, they are back on track. Time must be made to resolve issues so that they do not carry over into another day or escalate.

Finally, teams are not left running around during the last few days of each month trying to hit their end-of-month metrics (as is the case in many organisations). By this stage, it is already understood exactly where teams are tracking, relative to objectives and metrics. It is also clear where there are still problems and who is responsible for delivering a solution. The organisation exhibits full visibility, so expectations can be managed both internally and externally with customers.

Using this system, continuous improvement is no longer a special project to be carried out periodically: the embedded QMS and Lean Six Sigma approach ensures it is constant and addressed as part of the normal operations flow. By having a cross-functional team tackling the problem, new ideas can be stimulated and collective solutions found. Everyone is empowered and feels accountable, so they want to contribute to raising issues and finding answers.

Furthermore, if the monitoring metrics are regularly 'green' – meaning that everything is running smoothly – then this gets challenged. No organisation is perfect: if everything is green, then you may be monitoring the wrong thing or have the wrong targets. Metrics and targets can then be adjusted to focus on areas for further improvement; 'green' can be turned back to 'amber' and 'red' until these parts of the organisation are made even better.

All Inclusive

Linking Lean Six Sigma to a QMS can bring a positive cultural change across the business. This approach is in stark contrast to the culture and behaviours that have been observed with traditional monthly or quarterly monitoring QMS.

Using a traditional system, many other tasks take priority between review meetings, leading to a mad frenzy trying to remember problems and find quick fixes prior to the next review. If there is not time to progress the fix, then it may be reported as 'work in progress' and forgotten – either until the next meeting or until it causes a major customer incident or stops production.

However, with an embedded QMS, the right behaviours are driven to ensure product quality and customer services meet the highest standards. Everyone has a common goal and is aligned in its delivery; everyone feels accountability through joint ownership; and everyone is encouraged to raise their hand if they have an issue – and to be part of the solution.

About the authors

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