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Quality Reborn

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Abstract

It is time for Quality leaders to not only fulfill the traditional role of ensuring cGMP compliance within the company but also take the Quality profession to the level of business leadership like Deming did in Japan after World War II. FDA has recently stated that they have low confidence in quality management maturity of the pharmaceutical industry.

For quality leaders to also become good business leaders we must educate them in ways that are different from what we currently do. The education should be in the 6 areas

- Visibly Demonstrating Responsibility of Quality
- Risk-Informed Decision Making and Communication
- Engaging Employees to Continually Improve
- Integrating Quality into the Company Strategy
- Making Quality Operations a Financial Value
- External Global Quality Leadership.

The benefit of this for companies will be that quality becomes a financial competitive advantage with more predictable performance, cost reductions over time, and employees that are engaged and focused on both patients and continual improvement opportunities.

1. What Happened to Quality Business Leadership?

After World War II, Japan rebuilt their industry. The progress was so significant that over time the Japanese car industry outcompeted their American counterpart. Behind this was an American Quality leader, Edward Deming. At the core was a focus on quality and on employee engagement in continual improvement activities to reduce failures and variability, thus making quality a competitive business advantage.

Fast forward to present day, the FDA has stated they have low confidence in quality management (*OPQ, CDER, FDA, White Paper: Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals, April, 2022*). What happened since Deming, and how can we get to a state where Quality leaders are not only ensuring current Good Manufacturing Practice (cGMP) compliance, but are also effective business leaders?

It is time to expand the Quality leader's role beyond cGMP compliance and reacting to issues, to becoming more proactive, integrated into the overall company strategy and business operations, and an active facilitator of employee engagement and continual improvement. To achieve this, we must educate Quality leaders in a very different way. In other words, Quality reborn.

2. Traditional Role of Quality

Quality Assurance (QA) plays a critical role in the final disposition of medicine batches before distribution to patients. Additional responsibilities include approving all quality and cGMP documentation such as deviations, changes, CAPAs, and batch records. They are also final decision makers on cGMP compliance matters.

Many see the role of the Head of Quality to be mainly that of ensuring compliance with legal requirements and current GMP expectations. Some experience Quality as a policing function that

decides right from wrong with zero risk tolerance. My experience as a senior Quality leader and final Quality decision-maker across multiple global organizations is that the Quality organization and its leaders are often under multi-directional pressure. Examples include time pressure to review and decide on deviations so batches can be released, coercion on what is acceptable for approval vs. not, and working with supply chain to avoid drug shortages. The company internal pressure keeps many Quality leaders mostly in a reactive mode with no or very limited time to proactively drive strategic improvements or actively contribute to greater public health topics even in their area of expertise. Instead, they leave this to other company functions with less direct expertise in quality-related matters.

The rapid growth and eventual superiority of the Japanese automotive manufacturing industry was not built on reactivity and compliance; it was an enterprise-driven effort built on a systems approach, employee engagement, and continual improvement. So how can the more traditional role of the Quality leader be developed to incorporate the important role of also being a business leader? Before we get to that, let's first discuss the work of some of the leading Quality thinkers and how the world has changed since the GMPs were first introduced around 50 years ago.

3. Learning from Leading Quality Thinkers

Deming (1900-1993), the father of quality, is known for his systems approach to quality defined in his 'system of profound knowledge' (*W. Edwards Deming, The New Economics*), which builds on his 14-points of management and his many years of experience of what works when it comes to quality. Deming emphasized the importance of training, education, inclusion, and the role of management. Deming's 14 points of management was discussed in the article '*Deming, Finally!*' by A. Vinther and C. Schillinger and posted on LinkedIn.

Other leading quality thinkers include: Shewhart (1891-1967), known for statistical quality control including the Shewhart control chart and use of the Plan-Do-Check-Act quality improvement cycle; Juran (1904-2008) who promoted the Pareto 80:20 principle and the Juran trilogy of

planning, control, improvement; Ishikawa (1915-1989), known for the Ishikawa or fishbone diagram, the 5Ms of root cause analysis and Kaizen; and Crosby (1926-2001), who promoted Right First Time and zero defect.

As an industry we have done a better job at implementing many of the tools developed by these leading quality thinkers than we have at applying their teachings on systems thinking and the softer skills of leading organizations and engaging employees. Operational Excellence originated within Quality, but in most organizations it has transitioned away and primarily become a short-term cost-cutting exercise. Deming advocated for a focus on quality first and cost reduction would follow. The opposite approach rarely results in quality improvements. As an example, I've experienced Procurement being incentivized to procure cheaper raw materials, while manufacturing were to be blamed for a higher product defect rate caused by the cheaper (with lower quality) raw material.

Remarkably, all the leading quality thinkers developed their quality tools and processes in the last century. It is also striking that no significant new quality thinking has been broadly implemented over the past 25 years, and the industry remains compliance-focused rather than quality-focused.

4. 50 years of GMPs in a Faster Changing World

The first GMPs were introduced over 50 years ago. Many guidance documents have been introduced over the years to reflect cGMP expectations for new technologies and further detail out national expectations for GMPs, but there have been no fundamental changes to the principles of GMP.

While the GMPs have stayed practically the same, our world has changed drastically over the past 50 years, and the pace of change is accelerating exponentially. Relevant examples include:

- New manufacturing, analytical testing, and drug delivery technologies
- Reduced risk to patient safety through new knowledge and better technologies

- Increased understanding of diseases and the application of diagnostic tools for targeted treatment
- The way we learn has changed to be less reading and instruction-based
- The supply chain and reporting requirements have become increasingly complex
- Drug shortages have become common and continue to be on the rise.

Adapting to a world of fast and accelerating change requires us to not look at the future through yesterday's lens but instead find new ways of working. In our companies we need to replace wordy SOPs with instructions through videos, micro-learnings, flow diagrams, checklists, etc. The regulatory framework needs to become agile to allow for the approval and implementation of changes within days or weeks, not months and years.

The Quality leader has a central role in enabling real-time continual improvements that match the pace of advancements in technology, knowledge, medicines, and information sharing.

5. Expectations of Great Quality Business Leaders

For the Head of Quality to not only ensure cGMP compliance but also demonstrate great business leadership, it's important to first discuss the unique role a Quality Head has, and then identify how that role can be applied from a business perspective to help achieve company objectives and strategic goals.

The Quality leader obviously must fulfill the role as defined in the cGMP regulatory framework. This requires expert knowledge of the GMPs including emerging trends. Decisions should never put company cGMP compliance at risk. Sometimes that requires the Quality leader to take an unpopular stand with authority. Non-compliance in operations should never be accepted. While the traditional Quality role is often reactive, the Quality business leader identifies risks to compliance, patient safety and drug supply, and mitigate these before they become an issue.

Being proactive benefits the business because issues such as drug shortages and correcting failures can be costly.

It takes everyone involved to produce a successful batch, and only one person to cause a batch to fail. Thus, it is important that every employee is proficient at their job tasks and has the right quality mindset. While the traditional Quality leader is often focused on training completion and assignment of employees to various projects, the Quality business leader is focused on employee proficiency, on-the-job continual education opportunities, and providing opportunities for voluntary engagement of every employee in continual improvement projects.

While the traditional Quality role builds and maintains the company's PQS to ensure cGMP compliance, the Quality business leader uses the PQS as an engine to drive overall business improvements making it a financial competitive benefit. To be able to do so the Quality business leader needs to be financially savvy and be able to translate quality improvements into financial terms.

Quality senior leaders rarely have the capacity to lead quality related topics beyond their company and leave that to regulatory agencies with non-expert company colleagues engaging in the public dialog. Quality business leaders on the other hand, lead public healthcare dialog on topics where they are experts and have an interest. Examples of this include changing the regulatory framework to incentivize continual improvements and the implementation of new technologies, harmonizing and standardizing quality requirements globally (rather than being nationally driven), and driving inspections with quality improvement (vs. a compliance) focus.

These expectations of the Quality business leader are very different from the traditional Quality role. It requires Quality leaders to unlearn certain things that they currently do and instead get educated and developed differently. The areas of focus for their education are

- Visibly Demonstrating Responsibility of Quality
- Risk-Informed Decision Making and Communication

- Engaging Employees to Continually Improve
- Integrating Quality into the Company Strategy
- Making Quality Operations a Financial Value
- External Global Quality Leadership.

The remainder of this article describes steps to educate Quality business leaders based on my own Quality leadership experience in small and large companies, in different cultures, with companies at different levels of cGMP compliance and quality maturity, and drawing on what I have learned from world class leaders in change management.

6. Visibly Demonstrating Responsibility of Quality

The Quality business leader demonstrates ownership of quality matters and ensures that everyone in the company operate within a cGMP compliant framework. This extends to the oversight of contract manufacturing organizations for outsourced production or QC testing. Although meeting cGMP compliance expectations seems to be a low bar, it starts with exactly that. The majority of companies ensure they are cGMP compliant, but a small fraction do not. This small fraction of companies unfortunately provides the reason for FDA to state that they have low confidence in quality management maturity in the pharmaceutical industry. The Quality business leader needs to demonstrate through actions that non-compliance is not acceptable, and deliberate failures to meet cGMP and company quality requirements are acted upon promptly.

As a business leader it is important to partner with other functions within the company particularly Manufacturing Operations and the C-suite. Although there should be no doubt that the Head of Quality is the final decision maker on all quality matters, doing the right thing in terms of quality should be owned by all functions and at all levels. The Head of Quality job becomes

much easier when everyone in the company owns quality and always do the right thing for patients and cGMP compliance.

My experience is that it is particularly important that the CEO in their words and actions demonstrate sponsorship of and support for the Quality Head and the Quality function. The Head of Quality should have regular meetings with the CEO, the CEO should attend Management Reviews, and at best the Head of Quality should report directly to the CEO. I have had both good and bad experiences in this regard and know that if the CEO is not fully supportive of the direction for Quality in the company, it becomes almost impossible for the Quality Head to perform their duties as the Quality responsible. Working with a Head of Manufacturing who is more interested in meeting the supply schedule than supplying quality medicine is a particular challenge, that should be escalated to the highest level of company leadership for resolution.

The Quality business leader should ensure that employees are well-trained and implement tools developed by the leading quality thinkers such as the Plan-Do-Study-Act, control charts, fishbone diagrams etc. Applying these tools will not only keep processes in control but also continually improve them.

Although the pharmaceutical industry is heavily regulated, and some might think too restrictive, it is important to remember that the GMPs resulted from failures, some of which were fatal. The Quality business leader must be capable of translating cGMP language into practical terms and activities with a science and data-based approach, thus making it meaningful and relevant for the employees. Lessons learned after a failure, is a great way to discuss the GMPs and the company's PQS framework (discussing not only the what but also the why) and together look for improvement opportunities.

The expectations of the PQS are outlined in ICH Q10 and in the regulatory framework and focus on meeting cGMP expectations along with defining senior management's role. The Quality

business leader expands the PQS to also include the 7 ISO9001 quality management principles, which includes customer (patient) focus, engagement of people and relationship management.

7. Risk-Informed Decision-Making and Communication

One of the most important skills of the Quality business leader is to master decision-making, weighing benefits vs risks. One extreme is taking an approach of no or very low risk tolerance, which could lead to drug shortages, even for minor issues that pose no risk to patients. The other extreme is to accept a non-compliance that could lead to patient harm.

When making quality decisions I have always kept the patient in mind. What would be the right decision for patient safety and medicine availability?

Decisions should be data and science-driven, evidence-based, and risk-informed. Sometimes decisions are not easy to make. As an example, let's imagine that you have a lifesaving drug product on the market with a shelf life of 36 months. You found out that one of the stability batches showed an OOS at 36 months but was within specifications at 30 months. You don't know if other batches might be OOS at the 36-month time point. The 36-month OOS has no impact on safety or efficacy. If you recall the drug product you will stock out at patient level. What will you do? It depends on the situation, but here is one approach. You start by contacting the regulatory agency in the country where the product is on the market. Maybe you agree with the agency that the next batches will be short-dated with 30-month shelf life and the current batches will remain on the market. You agree on a timeline for solving the issue at which time you can get back to the 36-month shelf life. In this case you avoided stock out at patient level (there was no patient safety impact) and you have a time-bound plan for solving the issue. In situations like these you should always contact your regulatory agency for a conversation.

The decision above is just an example and different Quality business leaders might come to different decisions, but they should all be based on data, science, compliance, and a documented benefit-risk analysis. It should also be informed, *i.e.* the Quality business leader should always seek different views from experts and other people with experience to gather all the information and knowledge needed to make the right and timely decision.

I have found that one more thing is important for decision making and it is often not given adequate time and attention. Sharing your thoughts and rationale for making the decision, things that weighed in favor of or against, benefits vs risks, data considered, experts solicited etc. are excellent points to teach others in the organization the skill of risk-informed decision making. This practice is particularly helpful when one needs to deviate from normal practice. In such cases I spend more time discussing how risks will be mitigated/managed and the benefits of the decision.

It is obvious that one should never use quality risk management to justify cGMP non-compliance. cGMP non-compliance is non-compliance and therefore, unacceptable. End of story.

8. Engaging Employees to Continually Improve

When all employees understand the importance of quality and cGMP compliance and they all feel they 'own quality' the work becomes much easier for the Head of Quality. The opposite (employees not feeling quality ownership) is one of the most challenging situations to be in as a Quality leader. Being able to engage all employees is thus, one of the most important skills for a Quality business leader.

According to Daniel H. Pink we are motivated by autonomy, mastery, and purpose (*Daniel H. Pink, Drive).* We are engaged when we are motivated. We are also engaged when we do things because we 'want to 'rather than 'have to' and when leaders speak to and engage not only our head but also our heart. All of this may sound obvious to many, but my experience is that many leaders have yet to learn how to reach the full potential of engaged employees. Creating an environment

that facilitates employee engagement requires certain actions and behaviors demonstrated by the Quality business leader and senior management.

One of the most important things I have learned in my career as a Quality leader is that the management title doesn't automatically make you a great people leader. That is a skill a Quality leader must learn just like getting an education to be a microbiologist, engineer, or computer scientist. Reaching out to, working with, and learning from some of the best in the field of change management and people leadership, have taught me how to successfully lead company culture change and massive quality improvements, that have even been positively acknowledged by the FDA. One example of this is covered in John Kotter's book *Change*.

As a Quality business leader, it is important to create an environment where employees at all levels feel psychologically safe to speak up when they either identify a compliance issue, a quality problem, or an improvement opportunity. In some companies they call this 'see something, say something, do something'. If such an environment does not exist, the Quality business leader needs to create it. There are various ways of doing so, some of which are described by Amy C. Edmondson in her book *'The fearless organization'*.

Now, let's discuss autonomy, mastery, and purpose in relation to the pharmaceutical industry. Many of us chose to work in the industry because we know that the vaccines or drug products we produce save lives, cure diseases, or in other ways improve health for people. That's purpose right there. Keeping the patient in mind in our daily activities make us want to do the right thing be it integrating a chromatogram, adding raw materials into a reactor, or investigating a deviation.

Mastery comes through education and on-the-job experience. Every employee should have a plan and a path to become proficient in their job role. Once proficient, the employee should continue to develop mastery and as a trainer and coach to help grow the proficiency of their colleagues.

The pharmaceutical industry is highly regulated with Standard Operating Procedures (SOPs) instructing on all routine activities related to manufacturing and testing; these must be adhered to and documented. This might suggest that there is little room for making changes. However, employees should be encouraged and incentivized to help continually improve the system and procedures, drive down risks to patients, implement new technologies and better ways of working. A Quality business leader must ensure that the PQS change management system does not become so complicated and onerous that improvements become a hassle.

Providing employees with autonomy doesn't mean that everyone can do what they want as this could lead to non-compliance and unwanted variations. Autonomy can be practiced when employees suggest improvements to the system. Encourage employees to speak up, be part of and maybe even lead continual improvement projects under the PQS. In one of my jobs, I led a change in an organization of 10,000 employees across manufacturing sites on several continents. Once the environment for change was created it was incredible to see the number of improvements made at small and large scale by employees at all levels and across the network. One of the greatest experiences for me as the global Head of Quality was when employees started coming to me excited to share solutions they created for problems I didn't even know existed. That is very different from the traditional experience of 'here is a problem, help us solve it'.

Employee engagement and the results of continual improvements can be difficult to measure. One way is to register how many employees (actual numbers or percentage) are involved in continual improvement projects and how many projects have been initiated and completed.

As a Quality business leader, it is also important to visibly celebrate the creation and progress of these projects, which can have a snowball effect that expands engagement from a select few to the diverse many employees. The collection of improvements it not only becomes a major drive for quality improvements but also creates significant business results and an environment of 'quality owned by all'.

9. Integrating Quality into the Company Strategy

An effective Quality business leader demonstrates quality as a business value in words, actions, and results. Quality should be an integral part of the overall company strategic framework and included in the annual objectives for all key functions and at all levels.

To be successful at the C-suite level the Quality business leader must possess or gain the experience to run a company strategically and tactically at senior management level. Having a compliance and quality background and experience only makes it difficult to be successful beyond an operations organization.

A good place to start integrating quality into the company strategy is to be purposeful about the company Quality Policy, which usually include statements that link it to company values and/or purpose and commitments to cGMP compliance and continual improvement. The Quality Policy can also include statements about reducing risk to supply disruptions and to cGMP non-compliance, as these can have a significant business impact.

The Quality business leader has a significant role in identifying supply chain risks and mitigating these as much as possible either through inventory management, second suppliers, or other actions. Missed supply is not only a risk to patients but also to the financial performance of the company. It is recommended to have a formal risk management plan for the supply of drug products.

Many companies establish the PQS around minimum or close to minimum cGMP requirements and do not use it to also drive financial improvements. However, the opportunities to do so are numerous. A few examples are 1) driving to root cause of deviations and implementing corrective actions to reduce recurring deviations and thus save money, 2) identifying risks to supply and

mitigating these before they materialize into supply disruptions, and 3) standardizing key quality activities such as validation across multi-site companies.

10. Making Quality Operations a Financial Value

Quality leaders tend to speak in 'quality and compliance' language like complying with section so and so in the regulations, talking about RPN numbers for quality risks, etc. However, that is usually not a language well-understood by the C-Suite. It is important that Quality business leaders can translate quality and compliance activities into financial terms.

One way of doing so is to introduce a Cost of Quality model. Although it can be difficult to generate accurate estimates of the various preventive and corrective activities, identifying where the money goes and where efficiencies could be gained, is a role the Quality business leader is uniquely positioned to perform. My experience with Cost of Quality models is that they always provide new financial insights. In one case, we found that validation activities were very costly at an aggregate level and the reason was that each site had they own validation approach. The solution was harmonizing validation activities across the company.

A key area to focus on in the Cost of Quality model is the cost of deviations – and particularly those that are recurring. When the cost for these deviations is added up, one often recognized that a) they are significant and b) they provide valuable opportunities for a company to reduce financial cost simply by preventing them from happening again. Yet I have seen repeatedly that companies are willing to pay the money to fix issues (often not knowing the exact cost) but not ready to invest in preventing them from happening in the first place. The reason is that risk prevention is a budget item, whereas fixing issues is a P&L item. The Quality business leader has a role to play in this regard.

Let's take a look at the company's risk register. It usually assesses severity, occurrence, and detectability to arrive at an RPN score for each risk. My experience is that presenting a list of risks

with RPN scores to the CEO doesn't really work well. However, when I added the estimated cost of prevention vs. fixing the issue it changed the dialog entirely because the CEO then had a better and more informed way to make decisions about which risks to mitigate (budget) vs. not.

11. External Quality Leadership

Quality leaders possess certain skills and competencies that are unique, and they should use these to be actively involved outside their company on topics of relevance to these skills and competencies. They are experts in the PQS, they are the final decision makers on company internal quality matters, and they make the final disposition decision for drug product batches to the market. They also have a very detailed knowledge about the supply chain and where the risks to shortage are highest.

Quality business leaders should lead the external dialog and discussion on such topics where they are the experts. Examples of this include changing the regulatory framework to incentivize continual improvements and the implementation of new technologies, harmonizing and standardizing quality requirements globally (rather than being nationally driven), and driving inspections from a compliance to a quality improvement focus. My experience is that when quality leaders speak up about topics they are experts in they are listened to and they can drive significant change for the greater benefit of patients. It is important for the Quality business leader to allocate time for this external work because it can help change the quality and healthcare framework for the better.

12. Conclusion

In this article I have outlined areas that Quality leaders must master to become successful Quality business Leaders. These are

- Visibly Demonstrating Responsibility of Quality
- Risk-Informed Decision Making and Communication
- Engaging Employees to Continually Improve

- Integrating Quality into the Company Strategy
- Making Quality Operations a Financial Value
- External Global Quality Leadership

Quality leaders have traditionally been educated and trained to ensure cGMP compliance within the company but have often been limited to that role. The way they are assessed by regulatory agencies and by company senior leadership often rewards maintaining this cGMP compliance focus. However, to take the Quality profession to the level of business leadership like Deming did with the Japanese automobile industry, requires that we start educating Quality leaders in a new way. The benefit of this for companies will be that quality becomes a financial competitive advantage with more predictable performance, cost reductions over time, and employees that are engaged and focused on both patients and continual improvement opportunities.

Quality Reborn starts here.

QUALITY BUSINESS ADMINISTRATION

About the author: Anders Vinther, Ph.D., is the owner of QBA – Quality Business Administration and SVP of Process Development at Kronos Bio. His experience includes starting companies, merging companies and quality systems, leading culture and compliance turnarounds, and leading industry wide quality initiatives.