

21c Quality Management in the Pharmaceutical Industry

The Journey from Compliance to Excellence

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Editio Cantor Verlag Aulendorf (Germany)

Funding for this publication was made possible, in part, by the Food and Drug Administration through grant [1U01FD005675-01]. The views expressed in written materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does any mention of trade names, commercial practices, or organization imply endorsement by the United States Government.

Bibliographic information published by the Deutsche Bibliothek

The Deutsche Bibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <http://dnb.ddb.de>.

ISBN 978-3-87193-457-5

ECV · Editio Cantor Verlag on the internet www.ecv.de

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Cover illustration: Shutterstock Inc., cover design by Text & Grafik, Wolfgang Irmeler, Aulendorf

Typesetting: rdz GmbH, St. Augustin

Printing: druckhaus köthen GmbH & Co. KG, Köthen

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1 Introduction

Thomas Friedli, Prabir K. Basu, and Nuala Calnan

Mere allocation of huge sums of money for quality will not bring quality.
W. Edwards Deming

1.1 From Operational Excellence to Quality Management

After publishing three books on Operational Excellence in the Pharmaceutical Industry (Friedli et al., 2006; Friedli et al., 2010; Friedli et al., 2013) in recent years, we have shifted our attention more and more to the underlying logic of successful and sustainable implementation of Operational Excellence (OPEX). While our first book was simply a status report on the industry (Operational Excellence in the Pharmaceutical Industry), we described OPEX in our 2010 publication as a never-ending journey (Pathway to Operational Excellence in the Pharmaceutical Industry). The following 2013 publication focused on cultural and leadership aspects of state-of-the-art Operational Excellence approaches (Leading Pharmaceutical Operational Excellence). Since then, partly because of severe quality issues and drug shortages, quality has regained center-stage in the pharmaceutical industry due to renewed consideration by the regulators.

In one of our presentations (Basu, 2014), we linked the ICH Q10 model to the St. Gallen OPEX model, focusing on the similar aims and the theoretical overlap of a respective metrics system. While preparing a presentation in 2015, Thomas Friedli (Friedli, 2015), changed the title of his presentation from *OPEX as basis for Quality* to *Quality as basis for OPEX* giving a clear indication how, based on his experience and available data from the St. Gallen OPEX Database, the two topics were intimately interlinked. This connection had always been apparent in the underlying logic of the St. Gallen OPEX model (as in other excellence models). Quality cannot be separated from OPEX. Quality operations lead to quality products. High quality processes result in high quality products, but over time also in higher efficiency. Quality and efficiency are the two sides of the same coin named excellence.

However, as the industry to a high degree still separates quality from OPEX, both organizationally and culturally, the conclusions of this connection have not been drawn adequately in most cases. The same is true in many other industries, as several high-level recalls and quality issues show. We believe that what is needed is a wake-up call, not only for the industry, but also for academia. Colledani et al. (2014) talking about production quality state that: *"traditionally, all these fields have been treated by scientists and industrialists almost in isolation. Yet it is clear that equipment availability, product quality and system productivity are strongly interrelated. As a matter of fact, quality, maintenance and production planning strongly interact and jointly determine those aspects of a company's success that are related to production quality, i.e., the company's ability to timely deliver the desired quantities of products that are conforming to the customer expectations, while keeping resource utilization to a minimum level."*

While the excellence models that were developed in late last century have theoretically solved the underlying problem of separating quality from general management, pushing the attention to the need for integration and stopping the practice of managing quality as a specialized function, this message has obviously not been translated into the day-to-day realities of today's industrial enterprises. In this book, we will make another attempt to contribute to an integrated management of quality. This is in line with the thinking of one of the most prominent quality management gurus, Edwards Deming, who proposed the *theory of profound knowledge* which states that the success of quality management efforts depends on the effective integration of various management subsystems (Deming, 1998). This time we will attempt to integrate quality and OPEX using the data compiled from our extensive research in Operational Excellence over the last twelve years. This does not mean that we will deviate from Operational Excellence, as we still believe that Operational Excellence is the overarching framework embracing and being built on quality. Now, our effort will focus on the attempt to align the quality function with operational excellence. This could become a real competitive advantage for the companies being the first to implement such an integrated approach.

These companies will additionally be the ones to see an opportunity and not a threat in the new regulatory interest in quality management and quality metrics. Therefore, we focused our research over the last two years to develop a complementary model to the well-known and established St. Gallen OPEX model which is the St. Gallen Quality Benchmarking Model. This will hopefully help industry overcome the existing divide between Quality and Excellence. This model is in line with the comment made by Victor Prybutok from the University of North Texas who commented that "*... the future of quality management is dependent on the development of unique and specific quality management models ...*" (Evans, 2013). It additionally highlights the underlying relationships between quality and operational performance, therefore contributing to quality theory addressing an existing gap that had also been identified by Fredendall (Evans, 2013).

The first results of applying this model, together with the interest driven by the FDA's quality metrics initiative, convinced us to write a book about 21st century Quality Management for the Pharmaceutical Industry. Considering the quality issues we have experienced over the last decade from automotive to electronics and from aviation to pharma, we believe that some of the thinking presented in this book could make a difference in other industries too. The winners in tomorrow's business landscape will be the companies who are able to manage from an overall system perspective, not sacrificing long-term success for short term profits.

1.2 Quality in the Spotlight

1.2.1 Quality Issues across Industries

Several high-level recalls and quality issues have brought back quality center-stage in recent years. General Motors, Toyota, Porsche and Baxter to name only a few have made visible that despite decades of improvement in the management of quality, it still seems not or no longer to be mastered. Especially worrisome is that the very foundation of every state-of-the-art Total Quality Management (TQM) system, which is the commitment of leaders and employees to think and act in quality, has been revealed as the weak link in the chain in more than one case. Despite seminal advancements in the field of quality management, more quality-related problems than ever are making the headlines (Flynn & Zhao, 2014). Schneider (2016) comments that the overall number of quality management implementation failures is significant. Studies show that the share of imple-

mentation failures are as high as 80% (Cândido & Santos, 2011; Tata, Prasad & Thorn, 1999; Taylor & Wright, 2003).

Cândido and Santos (2011) designate several reasons for the diverging study results. For instance, the different underlying definitions of quality management failures. Besides, the authors suggest that the results indicate a decreasing trend in implementation failures. However, this decrease could be based on the adaption of the Quality Management (QM) strategies to the prevailing context, but failures will increase again when this contextual environment changes. As we experience unprecedented globalization in the area of customers and markets, as well as on the global supply chain level, we believe that standard quality management system (QMS) implementation no longer fulfils the requirements. Since every single plant in a global supply chain has different capabilities and a different culture, how can we expect that standard implementation of total quality management will be able to deal with the separate and individual realities?

What is needed is the possibility to design a quality system on the plant level, specifically adapted to the individual plant realities. The pre-condition to do this systematically is a quality management model that helps to analyse the relevant levers (enablers) and the respective outcomes to derive the right conclusions for optimization. One of the main outcomes of this book will be the development and data-based validation of such a model.

1.2.2 Quality Discussions in the Pharmaceutical Industry

In the world of pharmaceutical production, it is universally understood that a robust pharmaceutical quality system provides key elements of assurance and oversight for pharmaceutical manufacturing processes. It ensures that patients are provided with medications that are safe, effective, and reliably produced at a high level of quality. However, despite recent advances in the manufacturing sector, quality issues remain a frequent occurrence, and can result in recalls, withdrawals, or harm to patients. Quality issues have also been linked to the rise in critical drug shortages (ISPE, 2013).

Regulatory agencies currently assess the risk profile of manufacturing sites based primarily on their compliance history, as seen in warning letters and field reports, in conjunction with records on product recalls and market-based quality problems. These are not necessarily the most informative measures, and by their nature, provide historical or lagging data. More relevant data relating to the state-of-quality, provided in advance, would better inform the risk factors that might predict quality problems and future drug shortages.

The FDA's approach to quality oversight has evolved in recent years, and the new Office of Pharmaceutical Quality (OPQ) has made it a priority to establish a sounder basis for ensuring that pharmaceutical products meet high quality standards throughout the product lifecycle. Since early 2013, the FDA has been working with the pharmaceutical industry to develop goals and objectives for a quality metrics program. In response, several industry stakeholder groups have worked with the FDA to develop consensus around the goals, as well as to identify potential metric sets, including developing recommendations for their implementation and interpretation. Through a series of extensive engagements between industry and the FDA, there has been an acknowledgement of the complexity of the problem at hand, namely to develop a recommended set of metrics which are objective and meaningful, easy to capture, yet normalized to account for factors such as process differences and technical complexity.

Furthermore, it is required that those elements selected will promote acceptable behaviors and not lead to any unintended consequences or unwanted behaviors. At the end of July 2015, the FDA released its draft guidance entitled *Request for Quality Metrics – Draft Guidance for Industry* which captures the relevant aspects for meaningful quality metrics. The guidance gives the background

and intended purpose of use for the quality metrics. Furthermore, it addresses the legal authority and the use of the metrics, including the effects of non-reporting. In the last section of the guidance, the FDA introduces the reporting of quality data and the logic behind the quality metrics calculation. The following metrics have been proposed in the industry guidance:

1. Lot Acceptance Rate
2. Product Quality Complaint Rate
3. Invalidated Out of Specification Rate
4. Annual Product Review or Product Quality Review on Time Rate

Furthermore, the FDA proposed three optional metrics related to quality culture and process capability. In addition, the FDA issued a request for comment related to the data reporting frequency that needs to be levelled according to a risk based scheme (FDA CDER, 2015). In November 2016 already, the FDA released a revised draft guidance focusing on three metrics only (Lot Acceptance Rate, Product Quality Complaint Rate and Invalidated Out of Specification Rate) (FDA CDER, 2016). We will return to this revised guidance in chapter 11, see page 194.

Quality metrics are widely used throughout the pharmaceutical industry to monitor quality control systems and processes, and many of the components that inform those metrics (e.g., data on process capability output or statistical process control) are already collected and maintained as part of cGMP compliance. Several measures of performance are already common throughout the industry. The challenge is that they are currently defined differently across manufacturers, and even between sites operated by the same manufacturer. The proposed FDA Quality Metrics program is not the first of its kind; rather, it draws from the example of existing private sector quality improvement programs that collect voluntarily reported, standardized quality metrics from a large and varying array of manufacturing sites, which are then used by participating manufacturers to benchmark their performance against industry standards and their peers.

The collection and analysis of standardized quality metrics can serve several functions:

- At a basic level, metrics should provide a quantitative and objective measure of quality at the manufacturing site, and provide a window at a systems level to the effectiveness of the oversight and control of operations at a given site.
- Metrics data collection and analysis should also help mitigate or reduce quality related drug shortages and recalls by allowing for early identification of products at risk of quality failures.
- Metrics provide an opportunity to stratify manufacturing sites according to quality risk and thus prioritize scarce regulatory resources for inspection of plants worldwide.
- Ultimately, these metrics should assist pharmaceutical manufacturers to promote positive behaviours and a corporate culture of responsibility for quality, by providing incentives to improve product and process capability.

Thus, quality metrics may contribute to ongoing broader FDA efforts to reduce risk and improve drug quality.

This book will help to define an approach as to how to deal with and fulfil the requirements of this new regulatory approach, but also to make use of this regulatory push to finally integrate quality and operational excellence into an overall management system. Companies focusing only on the three reportable metrics will not achieve the required shift towards real excellence management. It will also not be sufficient to simply adapt total quality management approaches from other industries. We have shown above that they simply do not match the current challenges. The globalization effect that has made an impact on other industries, such as automotive, electronics, etc., will

also be felt in the same manner in pharma today and tomorrow. Therefore, it would be unwise to simply copy recipes from the past.

1.2.3 Some Conclusions

The challenge for manufacturers across industries to manage quality successfully is tremendous. Well established excellence models based on TQM concepts no longer seem able to deliver the required quality as intended. The pharmaceutical industry is additionally challenged by new regulations. We believe that the main problem does not lie in the basic designs of existing excellence models and quality management systems, but in the way they are organizationally embedded and managed. As there still seems to be a basic belief that there is an inherent trade-off between traditional quality objectives and business related outcomes, quality and excellence are not truly integrated, but in a lot of cases managed as opposite aims. This situation is worsened by consultants translating excellence as cost and pushing industry to cost cutting exercises, eroding the basis for stability and therefore endangering the capability to sustainably deliver the required quality.

1.3 Objectives of this Book

Our book is aimed at providing the industry with a new approach to manage quality. This approach will be based on a true system understanding of manufacturing sites and will help to overcome the divide between quality and operational excellence. To make this approach sound, we will develop a new quality management model and evaluate it based on extensive data analysis. We hope that this data-informed discussion will be more powerful and will result in a faster and deeper impact on the industry rather than having a merely qualitative discussion. At the same time, this approach could also become a role model for other industries, as it will also be a *first* across industries, revealing the data-based interdependencies between quality and excellence. Additionally, this book will inspire companies to seriously embrace the FDA's approach to quality metrics and use it as a chance to increase their competitiveness.

1.4 Structure of the Book

This book is structured in four parts and 18 chapters. In the first introductory part, we lay the foundations for a new approach to manage quality. In the first chapters we describe the paradigm change resulting from moving the industry from compliance-based thinking to excellence based thinking in accordance with the St. Gallen Quality Management Model.




The second part of the book is focused on deepening the understanding of some selected enablers to manage quality in a new way.

The third part highlights different case studies from the field, describing the challenges, as well as the opportunities that come with an integrated management of quality and excellence.

The fourth part summarizes the main findings and provides an outlook to an even broader system-based approach to quality management, based on a research project at the University of St. Gallen funded by the US FDA (Friedli et al., 2017).

Goldsheet, 2002). That is why it is so important for the quality systems and quality processes to work in Pharma. It protects sick patients from defective and ineffective products.

Table 2-1. Pharma manufacturing does not fare well compared with other regulated industries.

			
Regulated Industry	yes	yes	yes
How is Quality Ensured	Quality by Design	Quality by Design	Quality by Inspection
How is Product and Process Designed	detailed model-based design	detailed model-based design	empirical, minimal use of models, multiple scale-ups
Defect Rate	extremely low, >>> Six Sigma	extremely low, >>> Six Sigma	high, Two to Three Sigma
Raw Material Specification	very rigid and controlled	very rigid and controlled	raw materials have variable properties
Status of Technology	well developed technology	well developed technology	technology for product dev and mfg not well developed

We often hear that the reason why pharma manufacturing is lagging behind other industries in sophistication and quality of products manufactured, is because pharma is regulated while other industries are not. Here is a quote by a pharmaceutical manufacturing professional from a Pharmaceutical Forum published in the European Industrial Pharmacy (2010, p. 5), "... I spent sixteen years in the aviation industry, during which time QA and QC took over the whole industry and when incidents through faulty manufacture virtually disappeared. We started to see year on year no incidents attributable to technological faults. As systems were automated the human input was reduced. Clever design made it more and more difficult for the remaining human input to jeopardize safety. However, until all the remaining human input is replaced by technology, muddled thought processes can and will often fail to interact correctly with highly technical systems. Now after sixteen years in the pharmaceutical industry let me say that this industry is nowhere near the standard of compliance that is considered adequate in aviation. Were any auditor from the aviation industry to apply aviation standards during pharmaceutical audits, they would close most, if not all, pharmaceutical plants."

Regulations are not and should not be blamed for relatively poorer quality of manufactured products in pharma compared to industries such as the auto industry, the electronics industry or the aerospace industry. In fact, the true reason for poor quality in pharma is that the tools used to measure and control variability in manufacturing, which have been used by other industries since the middle of the twentieth century, are only being seriously considered by pharma now, after the FDA industry initiative to modernize pharma manufacturing began in the early 21st century. Even then, these tools are currently only being used selectively by a few companies for a few of their products (Ceglarek, 2013).

Derek Ceglarek, University of Warwick, (Ceglarek, 2013) explains the evolution of manufacturing from 1913 with mass production of automobiles by Henry Ford, with the evolution of lean, then flexible manufacturing systems in the 1980s, and now with reconfigurable manufacturing systems

in the 21st century (Koren & Shpitalni, 2011). In the 21st century, companies must design manufacturing systems that not only produce high-quality products at low cost, but also allow for rapid response that can meet changing business goals. Reconfigurable manufacture is novel and facilitates cost effective and rapid responses to market and product changes.

2.1.2 Vision for Pharma Manufacturing

Dr. Janet Woodcock, FDA eloquently defined FDA's vision of 21st century quality as (Iser, 2014) *"A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight."* This vision is in line with what manufacturing is in other industries in the 21st century as illustrated above. Pharmaceutical manufacturing today is not flexible and definitely not agile and efficient. It requires high internal quality oversight and external regulatory oversight. The main reasons behind this is the high variability and unpredictability of manufacturing processes, the lack of ability to take corrective actions before the variation is likely to occur, the lack of continuous improvement and inflexibility of certain regulations such as change-control.

2.1.3 Operational Excellence – a Pathway to Pharma Manufacturing Vision

To meet Dr. Woodcock's vision, there is no doubt that pharma manufacturing needs to embrace operational excellence. Operational excellence (OPEX) is a state in which an organization constantly executes consistently and reliably. Operational excellence is achieved through leadership, teamwork, reducing variability in operations and problem solving resulting in continuous improvement throughout the organization while focusing on the needs of the customer, empowering employees, and optimizing existing activities in the process.

Operational excellence in manufacturing is directly related to agility, flexibility and efficiency of manufacturing operations. Quality is the outcome of manufacturing and operational excellence, and this quality does not come at any added cost, but it is associated with significant cost savings. It is well recognized that the elements which are essential in an efficient and agile operation are also responsible for improving quality of products, manufactured by that operation. Operationally excellent organizations develop specific competences – related to cost management, quality management and process excellence – that allow them to offer the better service to their customers. A common element shared by all involved with pharma manufacturing is that to improve pharma manufacturing to the 21st century standards and to attain Dr. Woodcock's vision, variability in manufacturing should be reduced. According to Orloff (2014), reducing variation to improve quality would lead to minimized costs and maximized profits while reducing risk to the patient. Orloff also contends that the *"key to a 'maximally efficient, agile, and flexible industry' could be a single meaningful metric to focus attention on process variation and separate regulatory oversight into distinct departments for compliance and performance. This metric is the out-of-specification (OOS) rate."* When products and processes are designed with little process understanding, performance is left to chance and is the root cause of high variability in manufacturing. The ability to predict product performance also reflects a high degree of process understanding. That is exactly the goal of all OPEX programs. Manufacturing plants that have implemented 21st century OPEX programs do not complain about regulations. They know that quality is an obvious outcome of their OPEX programs. It would be highly logical if the FDA would consider giving more flexibility to making changes to equipment and processes where the plant has high quality OPEX programs in place. That would be an added incentive for such companies who are already motivated to excel.

This therefore is the ultimate challenge, re-coding the cultural DNA of the pharmaceutical industry to recognize that excellence in quality is not the obsessive management of one attribute within the organization in isolation from the rest; but a competitive business strategy that requires the passionate determination of everyone to never compromise the patient with the *second rate* as mentioned by Tuchman above.

4.8 Cultural Excellence

We cannot solve our problems with the same thinking we used when we created them.
Albert Einstein

To expand further on this theory, the author proposes the following hypothesis, that the traditional *Culture of Compliance* is a fatal flaw engrained within the DNA of the pharmaceutical industry.

To continue the analogy, a breakthrough therapy for the industry is now required to genetically re-engineer the cultural DNA of the pharmaceutical industry to one of a *Culture of Quality*. The evolution towards a *Culture of Quality* will require re-ordering of the sequence to build a double helix, strengthened from a combination of *patient focus* and *excellence*. This concept is depicted in fig. 4-2, as follows:



Fig. 4-2. The cultural DNA of quality for the pharmaceutical industry.

In *Scaling Up Excellence*, the authors recount how organizations that spread and sustain excellence are infused with a relentless restlessness that is driven by the *“nagging feeling that things are never quite good enough”* (Sutton & Rao, 2014). The authors describe the process of building and uncovering pockets of exemplary performance and then spreading those *“constructive beliefs and behaviors from the few to the many”* [ibid.], noting that it is more important when scaling excellence to bring one thousand people forward one foot at a time rather than one person forward by a thousand feet.

Borrowing from Tuchman's *Quality as Excellence* definition referenced earlier, this never-ending pursuit of perfection will require an *“investment of the best skill and effort possible to produce the finest and most admirable results possible”*, coupled with a determination to never settle for second best. This is the type of transformation that is necessary to re-code the cultural DNA of the phar-

maceutical industry. This theory is also supported by one of Deming's statement from his fourteen points for transformation; *"Improve constantly and forever the system of production and service"* noting that *"transformation is everyone's job"* (Deming, 2000). In the case of pharmaceutical products this includes both the regulators and the industry.

4.9 Why a Patient Focus?

Patients and consumers are key stakeholders in the Agency's work and have specific knowledge and expertise to offer. EMA⁴

The question of why a patient focus is necessary may seem so obvious that even to pose it may be considered absurd. There are many obvious reasons why a strategy for excellence in the pharmaceutical industry should maintain a focus on the patient, but first among them is because the patient assumes all the risks of *harm* attendant in the development, manufacture and delivery of the medicine; where harm is defined as *"damage to health, including the damage that can occur from loss of product quality or availability"* (Glossary, ICH Q9).

However, as discussed earlier, due to the complexity of the many stakeholders involved across the lifecycle of a pharmaceutical product, the patient is often not first among equals. Moreover, in the heat of the trenches of day-to-day operations where the decisions are taken, it can often be difficult to maintain a line of sight to the patient. Short-term objectives trump long-term vision. Yet, Rick Friedman (FDA) reminds us that, *"every decision made in drug companies every day can have such tremendous repercussions"* (Calnan, 2015).

Despite the obvious reason for patient focus, there is another compelling reason to maintain a line of sight to the patient at all times, which is linked to a key success factor for achieving sustainable excellence: it demands consideration of the end-to-end supply chain.

Viewing the supply chain through the lens of risk to the patient promotes an *Appreciation for a System* approach envisaged by Deming in his system of profound knowledge (Deming, 1994). This application of systems thinking offers opportunities to overcome the silo based thinking that has beset the industry and enables management within the pharmaceutical industry to *"view its organization in terms of the many internal and external interrelated connections and interactions"* [ibid.]. This is particularly critical within the context faced by the pharmaceutical industry today recently characterized as *stressed, complex and fragmented* (Woodcock, 2014). Never has this need for a systems thinking approach been more relevant for the industry and the patient. Viewing the organization as a system facilitates examining the network as a series of interdependent components that work together to accomplish the overall aims of the system. Deming's systems thinking theory states that *"recognition of the distinction between a stable system and an unstable one is vital for management"*, adding that *"a stable system is one whose performance is predictable"* (Deming, 1986).

Predictability may at first glance seem a lower ambition - but it is a key attribute for an excellence journey toward the desired state. Predictability confers the necessity for *robustness* in the pharmaceutical quality system to achieve the *high quality* requirement and *resilience* in the supply chain to achieve the desired *availability* requirement. Notably, Deming identifies a further benefit that a systems view can bring, in addition to improving the quality of its products and services, which he

⁴ European Medicines Agency, 2014

7 The St. Gallen Quality Benchmarking: Developing a Quality System Analysis

Christian Mänder, Thomas Friedli, and Nuala Calnan

7.1 Introduction

This chapter presents a newly developed quality management system model for the pharmaceutical industry that follows Ulrich's understanding of systems thinking in management (Ulrich, 1984). Furthermore, the authors will analyze the relationship between quality and Operational Excellence (OPEX) performance to bridge a gap that has been created by the industry through the pursuit of both goals as separate from each other. The authors are convinced that this model can support pharmaceutical production companies trying to implement a holistic quality management system that helps to overcome the still widespread divide between quality and excellence in the industry. The underlying thinking has directly influenced our work with the US FDA along with its quality metrics initiative. We will return to this in later chapters of the book.

7.2 The St. Gallen Quality Benchmarking Model¹

7.2.1 Quality Management System Model

As a general foundation, the quality system model draws from the OPEX understanding of the University of St. Gallen that is based on the OPEX reference model, detailed in chapter 6, see page 117 (Friedli et al., 2013; Friedli et al., 2006; Friedli et al., 2010).

Embedded in the overall OPEX model, our quality management system model contains the following categories: quality enabler, management system performance, quality effectiveness and quality efficiency. Quality enabler and management system performance reflect company and employee engagement in areas with a direct impact on the resulting quality outcomes. Quality effectiveness and efficiency deal with resource consumption and goal attainment related to quality. To derive the Quality effectiveness measures, we analysed the TPM, TQM and JIT KPIs from the original St. Gallen OPEX model and chose the ones directly related to quality outcomes from an overall system perspective (meaning taking into consideration the whole value-adding chain from supplier to the customer). Quality efficiency addresses the financial and headcount structures of the more dedicated quality-related organizational units, namely maintenance (because of its impact on equipment stability) and QC/QA. To some degree this is an over-simplification, as in a Total Quality Management environment everybody is involved in quality. However, it gives us the possibility to

¹ Chapter 17, see page 276.

directly derive conclusions for the Quality Organization. This integrated systems approach to quality and excellence allows one to analyze the impact of quality on the overall OPEX performance of a pharmaceutical production site. The quality management system model is structured like a pyramid, with quality enabler and management system performance as prerequisites and related quality effectiveness and efficiency as outcomes (Maender, 2016). Cultural aspects are essential for a successful and sustainable quality implementation (Batten, 1992; Black and Porter, 1996; Bowen, 1996; Donk, Dirk Pieter van and Sanders, 1993; Mehra and Ranganathan, 2008; Sinclair and Collins, 1994; Trerise, 2010). The quality effectiveness and quality efficiency components in the upper part of the model reflect the measurable resulting outcomes of applied practices and engagement. The quality management system model itself is embedded in the OPEX system following the approach of the University of St. Gallen. The entire system integrates OPEX and quality to use synergies of both approaches (Maender, 2016). Figure 7-1 shows the integrated St. Gallen quality system model.

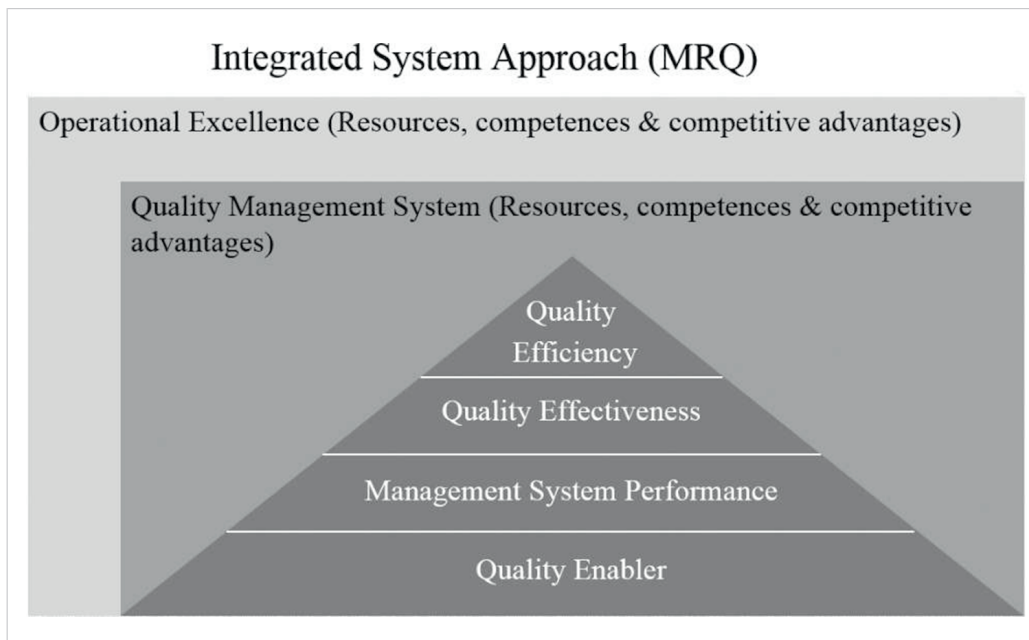


Fig. 7-1. The integrated St. Gallen quality system model for the pharmaceutical industry.

7.2.2 The St. Gallen Quality Metric

Seghezzi et al. (2013) state that any metrics system utilized by management needs to reflect information in a comprehensive format (Seghezzi et al., 2013).

The following chapter examines the literature on measuring performance, with a special focus on quality-related resources, and introduces the St. Gallen quality metric, based on the elements of the St. Gallen quality system model mentioned above.

In today's customer-orientated and quality-focused production environment, especially in the pharmaceutical industry, it is not sufficient to only consider financial measurement and accounting models. Indeed, recent studies conclude that traditional performance measurement is useless (Silvi, Bartolini, Raffoni, Visani, 2015).

9 Fostering a Healthy Culture of Quality: Achieving Cultural Excellence

Nuala Calnan and Thomas Friedli

Culture as a concept is an abstraction, but its behavioral and attitudinal consequences are very concrete indeed. Edgar H. Schein

This chapter explores the critical role that quality cultural plays in protecting the patient and examines cultural excellence as a means of realizing the ICH Q10 *desired state* for pharmaceutical quality. *"ICH Q10 demonstrates industry and regulatory authorities' support of an effective pharmaceutical quality system to enhance the quality and availability of medicines around the world in the interest of public health"* (ICH, 2008).

Understanding the impact that culture can have on the performance of an organization requires a fresh perspective of the role that *people*, involved right across the fragmented pharmaceutical supply chain, have in delivering *high quality, available* medicines. This requires going beyond viewing the *people* resources of an organization as a qualified and trained workforce that operates compliantly within the regulatory boundaries of approved standard operating procedures (SOPs). Organizations that recognize the value of leveraging the tacit knowledge and experience of their workforce in their everyday activities do so by creating environments that facilitate and sponsor the importance of honest dialog at the heart of their work practices. This requires building the capabilities of a learning organization where work is conducted through product and process based learning teams.

Charan, in a renowned HBR article from 2001 on *Conquering a Culture of Indecision*, proposes that *dialog* is the basic unit of work in an organization. He cites dialog as the single most important factor underlying the productivity and growth of the *knowledge worker*, and notes that *"dialog shapes people's behaviors and beliefs – that is, the 'corporate culture' – faster and more permanently than any reward system, structural change, or vision statement I've seen"* (Charan, 2001). Linking culture to dialog draws the loop back to the need to manage the conversations in the organizations. For Charan, *managing the conversations* requires that there is intellectual honesty in the connections between people and therefore meetings and other social interactions must have honest dialog at their core. To achieve this behavior of honest dialog, leaders must ensure that consistent feedback mechanisms are used to reward achievers, coach those who are struggling and discourage those whose behaviors are blocking the organization's progress towards its goal. Senge confirms the importance of dialog, referring to how the *"discipline of team learning starts with dialog, [including] the capacity of members of a team to suspend assumptions and enter into a genuine 'thinking together'"* (Senge, 1990). Helpfully, he also provides a definition of dialog, from the original Greek, as: *"Dialogueos: A free-flowing of meaning through a group, allowing the group to discover insights not attainable individually."*

The concept of *flow* emerges as important, in this case in relation to meaning and insights. The clarification provided by Senge that dialog differs from *discussion* is noteworthy, discussion has its roots “with ‘percussion’ and ‘concussion’, literally a heaving of ideas back and forth in a winner-takes-all competition” [ibid., p. 12]. This distinction between discussion and dialog provides the essence of understanding the defining characteristics of the culture the pharmaceutical industry must aspire towards. The ultimate challenge for the leadership in the pharmaceutical industry (Pharma) lies in the ability to perceive the limitations of the traditional prevailing compliance-led culture and determine the need to evolve towards a new *enabling* culture, adaptively. To fulfil this challenge, *Pharma* leaders must first overcome another hurdle: that of understanding the *dynamics* of culture. The cultural change required within the *Pharma* industry hinges on transforming from the static (maintaining the status quo) to the dynamic (embracing a continual improvement journey).

In summary, this chapter will outline the body of inquiry that identifies the key characteristics of the new enabling culture and the links between culture, attitudes, behaviors and ultimately performance (for a data-backed analysis also see chapter 18, see page 279).

9.1 What Do We Talk about When We Talk About Culture?

The way we do things around here. Marvin Bower

The concept of *culture* has been the subject of much debate over the past 35 years and Bower’s well-used phrase quoted above, so simple in construction and sentiment, belies the complexities of comprehension. Schein rightly identifies that culture is an *abstract* concept, difficult to describe and comprehend; yet the forces that derive from culture are powerful and he cautions that “if we don’t understand the operation of these forces, we become victims to them” (Schein, 2004). Schein also provides a simple, more internally focused, definition for culture as “how we perceive, think about, and feel about things” [ibid., p. 19] and formally links behavior to culture by indicating that behavior is a *derivative* of culture.

It is this link to behavior that provides a *concrete* means to understand and interpret the “operation of the powerful forces” he warns of. Schein’s work lends from a DNA analogy and proposes that the prevailing cultural paradigm of an organization can be thought of as “critical ‘genes’ in the cultural DNA” [ibid., p. 21]. To map the links between culture and behavior, he extends the analogy to note that if the total set of shared basic assumptions of a given organization’s culture can be thought of as its DNA, then individual genes can be examined in terms of their potency in forcing growth in *certain kinds of behaviors* while other genes *inhibit or prevent specific behaviors*. This work by Schein has influenced our thinking in this area and led to the proposal of the need for a transformation of the cultural DNA for the pharmaceutical industry from a compliance-led culture to an excellence-led culture of quality (Calnan, 2016a).

This DNA analogy provides an opportunity to examine the *genetic building blocks* necessary to facilitate the identification and selection of the *desired* behaviors in order for them to be “hard-wired into new habits so that employees can become assets to, and champions of, the transformation effort” (Morse, South & Gideon, 2013). Critical to this are *enabled leaders* who build a case for change and whose own behaviors accelerate adoption of the new way at all stages of the transformation through an *engaged workforce* that is motivated and mobilized in the change effort.

Viewing the relationship between culture and behaviors as an *abstract-concrete* continuum is helpful, particularly when designing behavior-led culture change strategies. However, Schein cautions

against evaluating cultures in an absolute or superficial way, as good versus bad or strong versus weak. This is sound advice that *Pharma* should heed in order to avoid falling into the trap of paying lip service to developing the *right kind of culture* or even a *culture of quality*. Culture as a concept is most useful when it facilitates a better understanding of the hidden and complex aspects of organizations and groups; and least helpful when conveyed as merely a slogan or management rhetoric.

9.2 Culture of Quality – More than a Slogan

The recent regulatory, industry and even media focus on developing the *right* culture of quality runs the risk of denigrating the idea of culture change to little more than a slogan (Calnan, 2016a). While the attention has undoubtedly generated lots of discussion, until recently very little substantive content has been available on exactly what constitutes a *Culture of Quality* for the pharmaceutical industry.

The 2014 CEB *Creating A Culture of Quality* survey proposed that organizations must find a new approach to quality, “one that moves beyond the traditional ‘total quality management’ tools of the past quarter century” (Srinivasan & Kurey, 2014) and even proposes that a company with a highly developed *culture of quality* on average spends \$350 million less per year fixing mistakes than a company with a poorly developed one. In their research across 60 multinational organizations, they examined several tools commonly used to encourage employees to care about quality, including training, best-practice sharing, and monetary incentives. They concluded that only four attributes are actually predictive of a culture of quality, see table 9-1:

Table 9-1. CEB Culture of Quality Survey 2014 – The Fours Essentials of Quality.

Leadership Emphasis	Managers are told that quality is a leadership priority. Managers <i>walk the talk</i> on quality. When evaluating employees, bosses emphasize the importance of quality.
Message Credibility	Messages are delivered by respected sources. Workers find that communications appeal to them personally. Messages are consistent and easy to understand.
Peer Involvement	Most employees have a strong network of peers for guidance. Peers routinely raise quality as a topic for team discussion. Like members of a sports team, peers hold one another accountable.
Employee Ownership	Workers clearly understand how quality fits with the job. Workers are empowered to make quality decisions. Workers are comfortable raising concerns about quality violations and challenging directives that detract from quality.

In line with points raised regarding the need for change from a *culture of compliance* to a *culture of quality*, the CEB Survey notes that although the specific actions needed to shift from a rules-based quality environment to a true culture of quality will differ from company to company, the first step in the process will always be the same: “Managers must decide that a *culture of quality* is worth pursuing”. The survey concludes that employees must become passionate about eliminating mistakes by learning to apply skills and make decisions in complex situations while reflecting more deeply about the risks and consequences of their actions.

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Thomas Friedli is a Professor for Production Management at University of St. Gallen in Switzerland. His main research interests are in the fields of managing operational excellence, global production management and management of industrial services. He is a lecturer in the (E)MBA programs in St. Gallen, Fribourg and Salzburg. He spent several weeks as Adjunct Associate Professor at the Purdue University in West Lafayette, USA. He is responsible for the St. Gallen OPEX Benchmarking in the Pharmaceutical Industry, the largest independent Benchmarking in this field. Prof. Friedli leads a team of 14 researchers who develop new management solutions for manufacturing companies in today's business landscape. He also is the editor, author or co-author of 13 books and various articles. Among his books are *Leading Operational Excellence in the Pharmaceutical Industry*, published in 2013, *The Pathway to Operational Excellence in the Pharmaceutical Industry*, published in 2010 as well as *Operational Excellence in the Pharmaceutical Industry*, published in 2006.

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Basu worked in the pharmaceutical industry (Pfizer, Pharmacia, and Searle) for over 20 years in various capacities in research, development and manufacturing. During 1992–2004, Basu had broad-ranging global senior management responsibilities for product development, manufacturing and outsourcing.

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Nuala Calnan, has over 20 years' experience in the pharmaceutical industry and is currently an Adjunct Research Fellow with the Pharmaceutical Regulatory Science Team at DIT, Ireland, where she leads a number of patient focused regulatory science research projects at Masters and PhD level.

Nuala's focus is on the integration of *Knowledge Excellence, Operational Excellence & Cultural Excellence* in delivering enhanced quality outcomes for the patient and has led a recent Irish Industry research study in this field examining the *Product Recall and Quality Defect* data at the Irish medicines regulator, HPRA. She is currently a member of the St. Gallen University led team who were awarded a two-year research grant by FDA examining the role of Quality Metrics in determining risk-based inspection planning. Nuala also works closely with industry in the areas of delivering quality excellence, designing metrics that matter, data integrity and behaviors and implementing quality cultural excellence programs.

Nuala co-leads the ISPE Quality Culture Team that published the recent "ISPE Cultural Excellence Report" and the ISPE/ PQLI Task Team on Knowledge Management. She was also lead editor on a new knowledge management book entitled "A Lifecycle Approach to Knowledge Excellence in the Biopharmaceutical Industry" (CRC Press 2017).

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