

IV

Operational Excellence in the Pharmaceutical Industry: Case Studies from the Field

In this chapter we want to give some guidance for people responsible for implementing Operational Excellence programs. Based on selected case studies we go deeper into some of the topics discussed so far. We start with a case about launching an Operational Excellence program in a global pharmaceutical company: the case of Pfizer. It gives a good overview about several elements of Operational Excellence and how those pieces fit together. Case study two shows how Caspugel, the leading capsule manufacturer, set the floor for its improvement process with regard to Operational Excellence. The third case study highlights the point of maximizing equipment effectiveness by optimizing the whole supply chain: the case of Reckit Benquiser. Case study four is about successfully working with 6-Sigma in a pharmaceutical company. Case study five details the topic of JIT in a pharmaceutical environment. In case study six we leave the pharmaceutical industry and show the importance of management quality in a case study delivered by Christoph H. Loch, who already contributed to the management aspect to our model described in chapter II. We finish with a stage model for achieving Operational Excellence.

IV.1 Case Study: Launching an Operational Excellence Initiative in a Global Pharmaceutical Company – The Case of Pfizer Inc.

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Pfizer: A leading pharmaceutical company

Pfizer is the leading research-based pharmaceutical company of the world. It discovers, develops, manufactures and markets innovative medicines for humans and animals. Founded in 1849 it has grown from a small business into a USD 52.5 billion global enterprise (2004), employing over 120,000 people worldwide. In 2004 it had an annualized net income of USD 11.9 billion.

Pfizer's major business in 2004 included (Warren McFarlan and DeLacey 2004):

1. Prescription Medicines

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- Pfizer's pharmaceutical sales were No. 1 in the world, up from 14th in 1990. Pfizer reported that 11 drugs generated more than a quarter of a billion dollars in the first quarter of 2004 – all aiming to become billion dollar blockbusters. It has a market share in the blockbuster market of 18%.
- 2. Animal Health Products
 - Full year Animal Health sales increase 10% in 2002 to USD 1.1 billion and another 43% in 2003 to nearly USD 1.6 billion.
- 3. Consumer Healthcare Products
 - With a long list of name brand products – Listerine, Benadryl, Actifed, Sudafed, etc. full year sales 2003 increased 20% to more than USD 3.0 billion.

Pfizer is headquartered in New York. It has major research labs in Connecticut, California, Massachusetts, Michigan, England, Japan, and France.

Pfizer: Committed to Manufacturing

"Throughout its history, Pfizer has been unequivocally committed to research and innovation" (Rodengen 1999). Pfizer attributes much of its success to its values-driven culture and behavior, key aspects of which are innovation and strong customer focus. However, Pfizer also has a long history of manufacturing. Responding to an appeal from the US Government to manufacture penicillin to treat soldiers in World War II, Pfizer began production of penicillin and became the world's largest producer of penicillin in 1944. Until the late 1940s Pfizer was a bulk chemical producer and sold its products to other companies that branded them (Pfizer 1999).

As manufacturing has always been seen as a strategic asset, Pfizer is vertically integrated and performs most of its primary and secondary manufacturing in-house. Its manufacturing division is organized as a global function called Pfizer Global Manufacturing (PGM) that provides the three major businesses (Global Pharmaceuticals, Consumer Healthcare, Animal Health) with high quality products. This helps Pfizer to capitalize on its scale and to drive down costs. Costs of goods sold at Pfizer accounts for just 14.4% of its revenue compared to around 30% industry average (Pfizer 2004).

Operational Excellence at Pfizer – Starting with Right First Time

In 2003 PGM rolled out its Right-First-Time (RFT) strategy. RFT aimed to systematically reveal true root causes of unwanted variations in manufacturing processes. By doing so, Pfizer responded to changes caused by a paradigm shift from the Federal Drug Administration (FDA). This shift became evident in three FDA initiatives.

The first one aims to shift manufacturing from an empirical basis to a manufacturing science. The major objective of this initiative was articulated in the second progress report of the cGMP Initiative: *"Pharmaceutical manufacturing is evolving from an art to one that is now science and engineering based. Effectively using this knowledge in regulatory decisions in establishing specifications and evaluating manufacturing processes can substantially improve the efficiency of both manufacturing and regulatory processes. This initiative is designed to do just through an integrated systems approach to product quality regulation founded on sound sciences and engineering principles for assessing and mitigating risks of poor product and process quality in the context of the intended use of pharmaceutical products."* (FDA 2003b).

The evolution of pharmaceutical manufacturing to a manufacturing science is presented in Figure 27.

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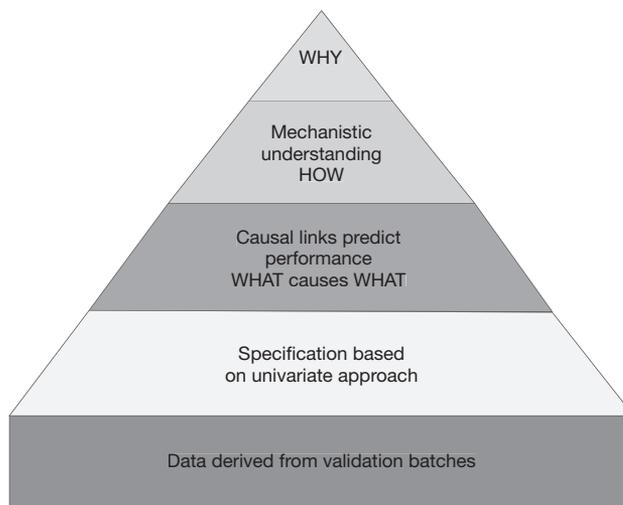


Figure 27: Evolution of pharmaceutical manufacturing (Source: Pfizer Right First Time Team).

The second regulatory guidance is on Process Analytical Technology (PAT), which is supposed to allow and encourage the use of equipment and protocols for continuous monitoring of manufacturing processes. By providing real time information about critical quality attributes or key process parameters as well as physical, chemical and biological characteristics of the raw material, PAT is crucial for developing a better process understanding in pharmaceutical manufacturing. Hence, it will be a main enabler for moving from a former empirical approach to the "desired state" of manufacturing science (see initiative 1).

The third initiative is a more general approach to manufacturing regulations titled risk-based current Good Manufacturing Processes (cGMP). Risk-based cGMP seeks to free the industry from prescriptive rules that are not necessary to ensure quality, and to concentrate the regulatory effort where the largest risk and the best opportunities for quality improvement are. Together, Manufacturing Science, PAT and risk-based cGMP are intended to promote innovation in manufacturing and logistics practices that ensure better, more predictable quality while increasing efficiency (Lockwood 2003). The initiatives aim to shift manufacturing from empirical to science based standards for manufacturing process quality.

The RFT strategy is driven by a global RFT leadership team (RFT LT). The RFT LT was responsible for rolling out the RFT strategy throughout the whole PGM division. This team includes senior PGM leaders each responsible for key geographical areas.

While PGM found themselves as competitive to Pharmaceutical industry standards, the RFT team realized that some other industries were significantly ahead of the pharmaceutical industry with regard to their robustness of their processes and efficiency. Across other industries it was not uncommon to achieve Sigma levels above 5-Sigma; and some "Best-Practice" companies like GE or Motorola had already managed to achieve Sigma levels that were close to 6-Sigma. Before GE started its 6-Sigma initiative, studies revealed that GE's operations were carried out between 3- and 4-Sigma, i.e., about 35,000 defects per million opportunities. According to company estimates, avoidable expenditure of USD 7-10 billion was being incurred in the form of scrap, reworking parts, correction of transactional errors,

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inefficiencies, and lost productivity. Within five years of its implementation of 6-Sigma, GE produced annual benefits of more than USD 2.5 billion for GE worldwide (Sirisha and Mukund 2002). Comparing the initial situation of GE with the current situation of the pharmaceutical industry, the situation in the pharmaceutical industry looks even more challenging. According to G. K. Raju (2003) most pharmaceutical companies today still operate in a range between 2- and 3-Sigma. But, what is the root cause for this? Some explanations offered include:

- Pharmaceutical manufacturing typically focuses on the end product to guarantee the highest quality standards for safety and efficacy with a sigma level exceeding 6-Sigma, but have a limited focus on the process itself.
- Therefore pharmaceutical companies usually have low process capabilities as there was little or no incentive in the past to develop a scientific understanding of their processes. This leads to a high rate of rework and rejects.
- Manufacturing sites usually operate in a fairly isolated way, without integrating process and information flow between suppliers, active pharmaceutical ingredient (API) plants and drug product sites as well as other ingredient sites.
- Pharmaceutical manufacturing processes are often complex and include many non-value adding activities.

The RFT team realized that an increase in overall manufacturing performance can only be achieved by increasing process capability first. While the elimination of waste is crucial for achieving sustainable performance improvements, the RFT strategy was not launched as a "cost-cutting exercise". The major objective of the strategy was to improve quality first by getting a thorough understanding of the sources of variation in the process and then to reduce variation to a minimum level. G. K. Raju's model of Operational Excellence in the pharmaceutical industry describes this as four levels of Excellence in plant capabilities, with each level requiring mastery of the levels below it (Figure 28).

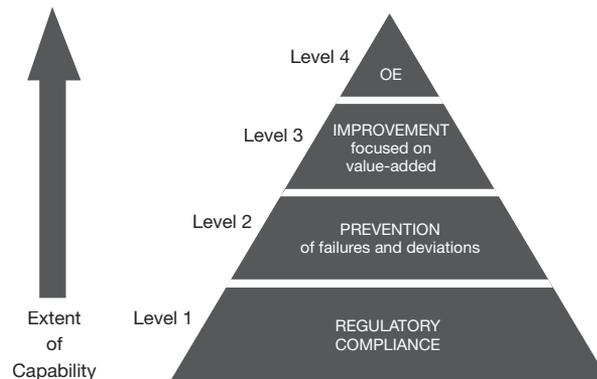


Figure 28: Levels of Operational Excellence (adapted from Raju 2003).

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Level 1

– The main objective is to meet regulatory requirements by performing excessive quality control. Most pharmaceutical companies in 2003 tended to be a “Level 1” company. This was the situation that was also characteristic for most of PGM’s operations in 2003. However, Pfizer was already on the move to climb level 2.

Level 2

– A company develops capabilities that help to get a scientific understanding about the process and root causes of deviations to move to a predictive performance rather than a reactive compliance. PGM has started at the end of 2004 to systematically perform capability assessments on their major products which will continue over the next years.

Level 3

– A company develops capabilities to understand value from the viewpoint of the customer and to eliminate waste – especially inventory, which reduces responsiveness and masks process problems. Once the capability assessments have been successfully completed and improvement projects initiated it will be the time for a company to combine 6-Sigma with projects focusing on value added, taking advantage of robust and highly reliable processes.

Level 4

– A company has eliminated all significant root causes for deviations (the company has reduced variability to a 6-Sigma level) and has simultaneously managed to eliminate all sources of waste throughout its operations (the company has become “agile”). At this stage a company has managed to tackle the two goals “Effectiveness” and “Efficiency” simultaneously becoming a leader in Operational Excellence.

Based on the four levels of Operational Excellence (Figure 28), the RFT strategy aimed to reduce variation to enhance process capability. It was mainly based on the 6-Sigma methodology.

While the 6-Sigma concept is strong in reducing variability of individual processes by providing a structure for addressing problems, it does not provide a means to analyze and optimise the operation in its entirety. For this reason a company also has to look to the concept of Agile Manufacturing. With its focus on the entire value stream, and on value-added activities, Agile Manufacturing helps to prevent the sub-optimizing and improvement of non-value-added steps that can happen when 6-Sigma is done alone. There is an obvious case for a harmonious marriage between 6-Sigma, which fixes individual processes, and Agility, which fixes the connections between processes (Liker and Choi 2004) (see Figures 29 and 30).

The deployment of the RFT strategy

For the deployment of the RFT strategy, Pfizer decided to adopt the 6-Sigma DMAIC (Define, Measure, Analyze, Improve, Control) mechanism throughout all levels of the organization. Each of the phases was designed in a way to ensure that the program is implemented in a methodical and disciplined way.

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While the Define phase was already quite advanced as there was a clear objective what to achieve (see Levels of Operational Excellence), the question was *how* to Measure and Analyze the main areas of improvement. On a business level Pfizer defined the main issues of concern and linked those to several key performance indicators that should allow tracking the improvement process (see Figure 31).

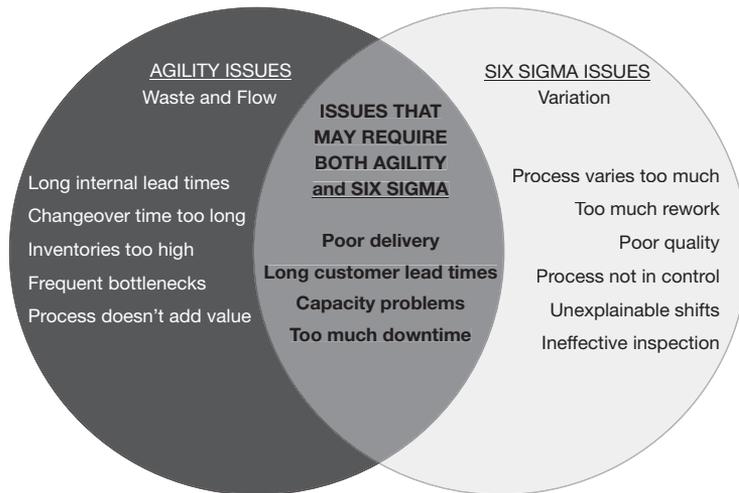


Figure 29: Issue of doing 6-Sigma or Agility projects (Source: Rath & Strong).

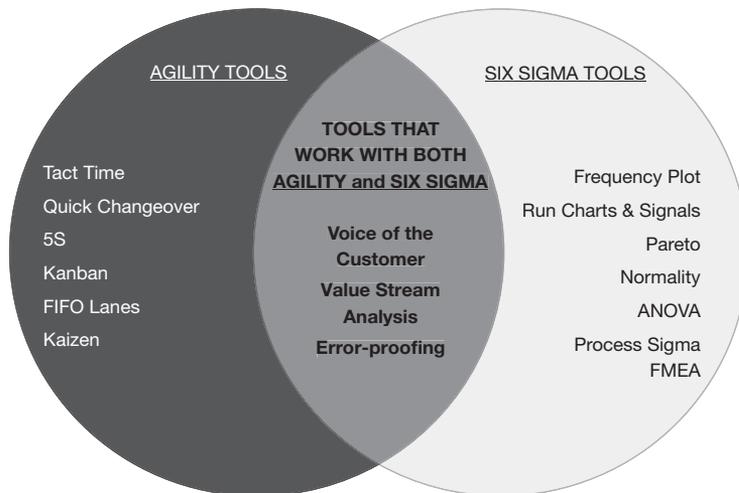


Figure 30: Combining 6-Sigma with Agility projects (Source: Rath & Strong).

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$y = f(x)$									
x	y								
Issue of concern		Yield	Cost of Quality	Capacity Utilization	Cycle Time	Overhead Ratio	Inventory Level	Service Level	
Quality problems		Impact high						Impact medium	Impact medium
Reliability problems					Impact high	Impact medium			
Process variability		Impact high	Impact high	Impact high	Impact high	Impact high	Impact high	Impact high	Impact high
Product complexity				Impact high	Impact high	Impact high			
People performance		Impact high	Impact high	Impact high	Impact high	Impact high	Impact high	Impact high	Impact high

Figure 31: Key performance figures indicating the issues of concern (Source: Right First Time Leadership Team).

This analysis revealed that there were two issues of concern that affected all key performance indicators that were tracked by the RFT team. The number one issue of concern was process variability. Hence, the RFT team realized that its approach to first concentrate on a reduction in process variability had proved to be the right strategy. However, the analysis revealed that PGM had to pay attention to a further question that was expected to have a high impact on the success of the overall RFT strategy: How should PGM develop its employees and managers in a way that supports the RFT strategy to address the second main concern of how to enhance people performance?

For most industries the expectation is that process variability will be reduced through process improvement programs. However due to the high risks of doing things that do not comply with regulatory requirements there was little motivation to take the initiative to improve pharmaceutical processes. The new regulatory polices described in the 21st century cGMPs promises to change this situation. As a consequence, one of the major pillars of the RFT strategy was to create a culture of entrepreneurial action and leader behavior among all employees in the Pfizer group. Figure 32 clarifies the linkage between the PGM mission and the ambitious goal to increase effectiveness and efficiency of its processes, which was dependent on a cultural change within the PGM group.

After analyzing the main areas of improvement, the RFT team started to deploy the strategy throughout the organization. When Pfizer officially launched the initiative in 2003, two hundred top executives of PGM were invited to Florida, USA to understand the objectives as well as the importance of the RFT strategy. In the following months the global objectives of the RFT strategy were linked with the objectives of each plant by developing a "RFT site master plan". The RFT site master plan included "hard facts" that provided improvement potential based on RFT-related KPIs addressing manufacturing, laboratory and documentation deficiencies for the next five years, as well as a guideline concerning the number of RFT projects