Thomas Friedli · Prabir Basu
Daniel Bellm · Jürgen Werani
Editors

Leading Pharmaceutical Operational Excellence

Outstanding Practices and Cases

Springer

Leading Pharmaceutical Operational Excellence

Thomas Friedli • Prabir Basu • Daniel Bellm • Jürgen Werani
Editors

Leading Pharmaceutical Operational Excellence

Outstanding Practices and Cases

Springer

Editors
Thomas Friedli
Daniel Bellm
ITEM-HSG
University of St.Gallen
St.Gallen
Switzerland

Prabir Basu
Pharma Manufacturing and cGMP Consultant
Mt Prospect, Illinois
USA

Jürgen Werani
Schuh & Co
Komplexitätsmanagement AG
St.Gallen
Switzerland

ISBN 978-3-642-35160-0 ISBN 978-3-642-35161-7 (eBook)
DOI 10.1007/978-3-642-35161-7
Springer Heidelberg New York Dordrecht London

Library of Congress Control Number: 2013950271

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

Almost 25 years have gone since we established the expression "lean production" for a set of Japanese techniques which changed the whole competitive landscape of the automotive industry in the 1990s. This in turn led to fundamental changes in how production is managed in industry after industry.

Back in 2006, I wrote the foreword to the book *Operational Excellence in the Pharmaceutical Industry* just as the pharmaceutical industry began its own lean journey, which showed that "lean thinking" knows no industry barriers. I'm glad that the story continued, and if I look at some of the approaches described in the current book, I see an Industry that puts a lot of sophistication and resources in its journey towards Operational Excellence. It has also finally realized that sustainability comes with people and not with tools.

This reminds me of our own lean journey from *The Machine That Changed the World* to *Lean Thinking* and *Lean Solutions* and to establishing the Lean Global Network (www.leanglobal.org). If pharmaceutical companies want to stay ahead of competition, they should have a look at the new evidence presented in this book and draw their conclusions!

Lean Enterprise Academy, UK Prof. Dr. Daniel T. Jones

Contents

Part I
Introduction

Chapter 1
Introduction to Leading Operational Excellence: Making OPEX a Competitive Weapon

Thomas Friedli and Prabir Basu

Do not follow where the path may lead. Go instead where there is no path and leave a trail.

Harold R. McAlindon

Not the cry, but the flight of a wild duck, leads the flock to fly and follow.

Chinese Proverb

Go to the people. Learn from them. Live with them. Start with what they know. Build with what they have. The best of leaders when the job is done, when the task is accomplished, the people will say we have done it ourselves.

Lao Tzu

If your actions inspire others to dream more, learn more, do more and become more, you are a leader.

John Quincy Adams

In our second book on Operational Excellence in the Pharmaceutical Industry titled *The Pathway to Operational Excellence*, published in 2010, we had undertaken an imaginary journey to develop the framework and structure of the book.[1] It gave us the opportunity to describe our experiences from working with dozens of different pharmaceutical manufacturers in the US and Europe. We suggested a sequence starting with preparing for the journey and finishing with the re-definition of the destination leading to the selection of the next destination so that the journey will be an on-going one. Two years later, we have decided to write another book. The main

[1] For inspiration we investigated the similarities between our Journey and one of the Journeys of Captain James Cook undertaken in the eighteenth century. (cf. Friedli et al. (2010), p. 1ff.)

T. Friedli (✉)
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch

P. Basu
Pharma Manufacturing and cGMP Consultant, 1911 E Wood Lane, Mt Prospect IL 60056, USA
e-mail: pbasu001@gmail.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_1,

reason for doing this is the positive feedback we have received on the first two books. The other reason is our conviction that despite the renewed enthusiasm for outsourcing in the industry, manufacturing will remain a critical activity for every major pharmaceutical company, and the continuous improvement of manufacturing will not just be an option, but a necessity.

The concept for this book is somewhat similar to the last book but in some respects, is very different. The similarity is that we again present academic perspectives on OPEX along with industrial perspectives so that the book can facilitate direct insights into practical applications. However, we have structured the book differently this time in order to describe how some of the most advanced travelers in the world overcame the distances and mastered the challenges along their way. This book illustrates some of the best approaches we have seen while researching OPEX and provides a guideline as to how to really improve and close some of the existing gaps in one's own OPEX approaches. Thus, the book is a collection of successful practices in Pharmaceutical OPEX.

The title "Leading Operational Excellence" was chosen deliberately. On the one hand, it gives us the opportunity to look for and to find "leading practice examples". On the other hand, we could dig deeper into the true leadership requirements for a successful and sustainable implementation of Operational Excellence, being fully aware that this is often the most critical part of the whole implementation process.

To set the stage, our book begins with an introductory part where we provide an overview of where the pharmaceutical industry started with OPEX, its current level of operational performance, the biggest gaps in OPEX implementation and the challenges ahead. We also describe the importance of OPEX in today's pharmaceutical environment and how OPEX has become a topic in every major pharmaceutical company in this world. To make it clear early on what we understand by conducting research or talking about Operational Excellence, we provide our definition of Operational Excellence. The main reason for doing this is that in some companies Operational Excellence has unfortunately become synonymous with "cost cutting". But true Operational Excellence is something totally different. Friedli and Bellm start by defining OPEX and describing the importance of it for the Pharmaceutical Industry. Friedli and Werani highlight the major milestones in the short history of Operational Excellence in the pharmaceutical industry. Werani is one of the first pharmaceutical manufacturing plant leaders who introduced "lean", and then became one of the formative designers of the Right First Time Excellence Program at Pfizer. Friedli is one of the first academics conducting research on the various aspects of OPEX in the pharmaceutical industry. They bring together their perspectives to explain the rise of OPEX in the pharmaceutical industry. Friedli, Lembke, Gütter and Schneider (University of St.Gallen) will provide an overview about the current status of OPEX in industry and will compare it to the very beginning when St.Gallen conducted its first Benchmarking exercise based on 2003 data. Additionally, they will also provide a deeper insight into the impact of OPEX tools and practices on performance based on statistical analysis. Calnan will then provide an overview about the advance in regulatory science and the impact this has on OPEX. This is followed by a description of the current pharmaceutical environment by Friedli and Bellm, looking as well on the on-going globalization as

on the changing economic landscape thus framing the context for the OPEX activities. Friedli and Bellm finalize the introductory part with a summary of the identified success factors for a sustainable implementation of Operational Excellence providing a bridge to parts B and C of the book.

Part II "Leading Operational Excellence – Outstanding Practices" brings together successful practices and interesting insights from the whole industry. Friedli and Werani start with an overview and introduction into this part. They are followed by Seller and Davis who describe the development of Pfizer's Operational Excellence activities to one of the most sophisticated OPEX approaches in the industry. Kasper Mejlvang will then explain how Novo Nordisk succeeded in making its program to a brand not only inside of whole Novo Nordisk but also in the industry. cLEAN® became synonymous with succeeding in improving operations and had a direct impact of optimization programs beyond manufacturing. The following chapter belongs to Novartis. Steve Dreamer and Pav Niewiraowski will describe the latest progress Novartis has made in its aspirations to become a lean pharmaceutical manufacturer. Novartis currently leads the field in different innovative approaches to pharmaceutical manufacturing. Starke and Kumor will then give an insight into Abbott's OPEX program. Highlighting how they used the former experiences from Abbott's way to Operational Excellence. They relied on Class A activities as a base to form their very own unique approach to manage Operational Excellence. This is followed by a contribution of Troy Wright from Amgen, explaining how Amgen entered the journey to Operational Excellence and what the main guiding principles of this program are. Werani, Pfahlert, Reimers and Diederich proceed and share their insights in the challenges of an OPEX implementation at hameln pharma overcoming an initial focus on infrastructures to truly embrace people. Sanjit Lamba will then tell the readers the story of his plant in India. Built in record time and winning an award it is one of the leading examples for the potential of the Indian pharmaceutical industry. Morse, South and Walter will contribute their approach to help companies in "succeeding at the harder side of change", drawing heavily from the rich experience of BCG in helping their customers on their way to Operational Excellence. This is followed by Friedli and Lembke who describe considerations about the optimal organizational structures to support excellence. This is followed by an update about the state-of-the-art in integrated product-process development in the industry delivered by Friedli and Ziegler. The idea to introduce already more stable production processes so as to avoid costly counter measures later in production is striking and has been successfully introduced in other industries before. However there are some pharma specifics that are against a fast realization of these benefits. Friedli, Mänder and Bellm will then deliver some guidance how to apply the right tools for specific problems. In a lot of excellence programs there is a focus on training people in specific tools but there is a lack of support in helping them to know when to apply what. This gap will be addressed by this contribution. Seller, Davis, Götzfried and Friedli will then introduce their work about plant complexity, the impact of complexity on performance and what OPEX can do to master complexity. Part II is concluded with some considerations about a structured management of

knowledge in global production networks. This part will be provided by Thomas, Liebetrau and Friedli. Part III is dedicated to leadership. After an overview Friedli and Werani open the part with an introductory chapter about the importance of leadership in change and OPEX. This is followed by Andy Crossman re-telling his experiences from Wyeth and Pfizer/Wyeth about the leadership requirements and how to change leadership behavior in an OPEX supporting way. Hampton from SSA&Company will share his experience about engaging all levels of the company including middle management in Operational Excellence. This is followed by Paul Docherty's account about a Hoshin Kanri approach to do exactly this. Walkhoff will then share her insights into the impact of leadership styles on the success of OPEX programs before McColgan delivers first-hand accounts from his experiences as a global OPEX leader for Nycomed and Takeda/Nycomed especially highlighting the true leadership aspects. Werani will share his rich experience of being responsible for OPEX for a whole geographic region before Sandell, Eriksson & Eriksson; Stigell Warnström and Gjellan from Pfizer share their learnings from leading Pfizer's Strängnäs site.

Part IV will be focused on the future of pharmaceutical production. After an introduction Basu and others will describe the future requirements based on an extended analysis about the reasons for the current status of pharmaceutical manufacturing. This part concludes with the consequences for the optimization of a global network of pharmaceutical plants and provides also some methodological support in optimizing global production networks.

Chapter 2
OPEX: A Definition

Thomas Friedli and Daniel Bellm

There is no clear-cut definition of Operational Excellence (OPEX) in theory or practice. Especially the inflationary use of the term for almost every launched improvement activity rather obscured than clarified its meaning. In some companies it has been used synonymously for cost-cutting, in others similar to Six Sigma or lean production. This chapter explains our understanding of, and our philosophy behind, OPEX. Based on this understanding we discuss the benefits of striving for OPEX in the Pharmaceutical Industry. We start with a short story from a completely different field, the management of a major airline's baggage handling department. This will foster the understanding of hindrances to excellence in today's companies. We proceed with examining existing excellence models, and derive common elements. This sets the stage for the introduction and the explanation of the St.Gallen OPEX Model. We then conclude this chapter with our definition of Operational Excellence.

The Impact of KPIs on Excellence: A Story from Baggage Handling

Some time ago, a major airline asked us for support in the improvement of their daily operations. They planned the roll-out of a global training program as an answer to several problems they had identified at their globally scattered hubs. They thought these problems could be boiled down to failures and shortcomings of the airline's baggage handler crews. The airline blamed the baggage handlers for frequently losing and damaging passengers' bags, or simply causing the bags to be late. The costs for these failures amounted to $5 million a year. Before we got

T. Friedli (✉) • D. Bellm
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; daniel.bellm@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_2, © Springer-Verlag Berlin Heidelberg 2013

involved, efforts were made to find an internal solution to this problem. Soon the airline was sure that poor qualification in baggage handling was the main reason. Several solutions were discussed, from "fire them, and hire better ones", "train them" to "train their supervisors in motivational techniques". In the end, the airline preferred the idea of "sustain and train", and we were engaged to develop a customized training for the airline's baggage handlers.

Before we started, we challenged some of the conclusions made. As we had previously experienced situations in which solutions were derived without really identifying, let alone understanding underlying problems, we suggested taking a closer look first. Simple training staff was not necessarily the answer to the real problem the airline was facing; damaged and delayed bags could be the result of something rather than the actual cause of the problem Thus, we started by trying to get to the bottom of what might be going wrong. Under the disguise of setting up a training program, we conducted several interviews with employees from all hierarchical levels. We gained our first insights from the airline's management. Every morning at 9:00 am (EST) the station managers engaged in a key event – a conference call between all station managers and headquarters. The aim of these conference calls was to discuss basically two topics: yesterday's financials, and on-time departures.[1] Financials were seldom the issue. If managers, however, poorly performed with regards to on-time departures, they were publicly rebuked during the conference call – something everybody tried to avoid. Excluding external factors such as bad weather conditions or heavy air traffic, we identified four groups of potential causes for delayed departures. Firstly, passenger service, i.e. check-in agents and other ground staff responsible for getting people on-board. Secondly, catering; if the crew has to wait for the meals to be boarded this can delay departure. Thirdly, the maintenance crew that is responsible for routine and unplanned maintenance. And, finally, the baggage handlers.

Subsequent interviews with baggage handlers revealed that for them it was essential "to get the plane off on time" but if that was not possible to at least "make sure it was not their department taking the count". We observed a very self-focused behavior of a mere consideration of the baggage handlers' own process steps, referred to as silo mentality. If it became obvious to the baggage handlers that they would fail to meet a slot, they conveniently pushed remaining bags aside, lost them, or put them on another plane, etc. so as not to be the cause of a late departure. Obviously, both customers and airline suffer from such behavior, but at least the baggage handling department looks well. In another incident, a baggage handler took a screwdriver from his pocket and stuck it in the conveyor belt, thereby causing it to halt. The malfunctioning belt became a maintenance issue and the incident thus disappeared from the record of the baggage handling department.

[1] For those who do not know, on-time departure is a big issue in the airline business. Slots for departures are short and scarce, and to miss one means to be delayed for to another one. That is, however, costly.

Again, customer and the airline suffered, but the baggage handling department looked well.

During our interviews, we observed a distinct silo orientation that came from only being worried about the own department and measured by just one metric: on-time departures. There is no doubt that on-time departure is a good metric; why, however, only use one, neglecting other reasonable measures of performance like number of lost, damaged, or late bags? We concluded that the baggage handlers were capable of doing their job right, and it was not a skill or knowledge deficiency that caused problems. Rather, the baggage handlers had to work in an environment in which the only set standard was punctuality of the planes. Until then, nobody had been blamed or penalized for damaging, delaying, or losing bags, as long as the plane took off in time; it was only "on-time departures" that was relevant, and the baggage handlers' behavior was a consequence of this fact.

This case is a very good example of how a performance measurement system works and sometimes might fail. The baggage handlers were behaving very rationally given the environmental system they worked in. Measuring an entire system's performance by solely assessing a single metric (or metrics focusing on a very narrow area), lacking a holistic, balanced perspective of the system, evokes an equally narrow-focused working behavior among employees. Similar stories could be told about companies only focusing on costs.

Shortcomings like these – and their behavioral consequences – have been taken into account in the design of the St.Gallen Model for Operational Excellence. Likewise, existing excellence models and their underlying logic have been a major source of inspiration for our OPEX model. In order to support the understanding of the St.Gallen Model for Operational Excellence selected models that inspired us are introduced in the following.

A Review of Excellence Models: From Toyota to the EFQM Model for Excellence

Over the last decades, a number of excellence models have been established across all industries. When we first started to discuss Operational Excellence (OPEX), our assumptions and understanding were strongly influenced by these models. Yet, they only laid the foundations and set directions for our first research but were not deterministic. We started off with a general understanding of excellence, and while researching it in manufacturing companies in general, and pharmaceutical companies in particular, our own understanding of what constitutes OPEX crystallized little by little. To fully understand the St.Gallen OPEX approach, it is helpful to foster an understanding of the aspects that were major contributors to our research in excellence. In the beginning, one of the central cornerstones of our understanding was the Manufacturing Management Quality Model from Loch and Chick (2006). Their model was very inspiring for us, since it operationalized the

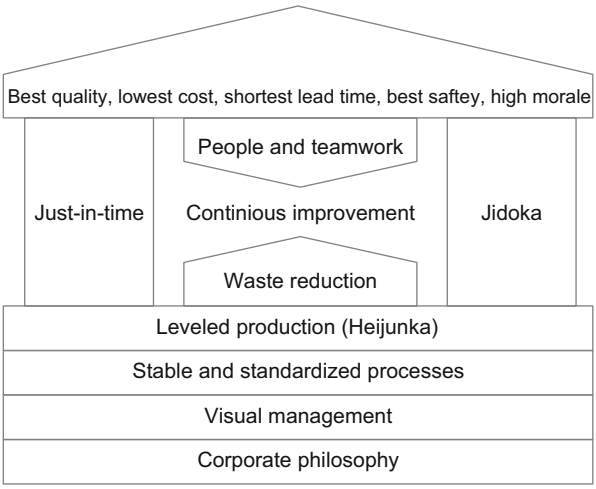


Fig. 2.1 The Toyota Production System (Liker 2004)

hitherto fuzzy term of Management Quality with a strong focus on manufacturing. Since then, several other excellence models and their perception within the industry have influenced our definition and understanding of OPEX. Here, we present a selection of these models, and derive their commonalities.

The Toyota Production System (TPS)

Studying "lean production", one will inevitably come across the Toyota Production System (TPS). This system had evolved over nearly half a century before it was noticed by practitioners and scientists outside Toyota, and it has truly changed the world. Nowadays, it is considered one of the most acknowledged systems in modern manufacturing (Liker 2004), widely spread across all industries and no longer limited to Japanese automotive shop floors (Spear and Bowen 1999).

TPS is frequently and metaphorically described as TPS House Diagram (see Fig. 2.1). The House Diagram comprises various distinctive elements that are depicted in a house-like shape. The house-like structure represents Toyota's philosophy on interrelations between practices – the stability of a house depends on the stability of its architecture. Weak elements or weak links undermine the whole system. Each element of the TPS by itself is decisive and the structure is supported by mutual reinforcement of its elements (Liker 2004).

However, TPS is not a toolkit or just a set of lean tools. It is a sophisticated system in which every single element contributes to the whole. The first element, the roof of the house, represents Toyota's ultimate goals: best quality, lowest cost, and shortest lead time. The roof is held up by three pillars. The outer two pillars are

"just-in-time", the highly publicized and most visible characteristic of TPS, and "Jidoka", the Japanese synonym for stopping the production and never letting a defective part pass into the subsequent process step. The center of the system is constituted of people, as the system banks on their capabilities and continuous improvement. Finally, the foundation comprises various elements that all provide stability to the system: leveled production, stable and reliable processes, visual management, and a commonly shared corporate philosophy (Liker 2004).

Malcolm Baldrige National Quality Award (MBNQA)

The origin of the Malcolm Baldrige National Quality Award (MBNQA) dates back to August 1987, when former U.S. President Ronald Reagan signed a state-subsidized initiative for achievements in quality improvements. Back then, quality of American products and services among other manufacturing capabilities clearly lagged behind global competitors (Wheelwright and Hayes 1985). In order to overcome these shortcomings, a national campaign was initiated that targeted not only quality improvements, but also in an increase in productivity. Similarly to the Japanese *Deming Prize*, arguably the world's most well-known quality prize, the MBNQA promotes the introduction of a Total Quality Management (TQM) model by awarding a prize for achieving superior performance compared to other participating U.S. companies.

The underlying TQM model comprises three sequential layers that progressively become more detailed. The first layer includes seven interrelated categories referred to as Examination Categories (Fig. 2.2, NIST 2009):

While the next two layers further detail each category and make these assessable they build the most important constituents of a modern and effective quality system.

However, the first layer of the framework shown in Fig. 2.2 has from top to bottom three basic elements. Firstly, the *Organizational Profile*. It sets the context for the way any organization operates. A company's environment, working relationships as well as strategic challenges and advantages provide an overarching guide for any organization's performance management system. Secondly, the *System Operations*, composed of the six Baldrige Categories (1-3, 5-7) as shown in the center of Fig. 2.2. The leadership triad is represented by categories 1-3, emphasizing the importance of a leadership focus with regards to both strategy and customers. Categories 5-7 constitute the results triad, highlighting workforce and processes that do the work that yields the performance of a company (NIST 2009).

Obviously, all actions within *System Operations* point towards results. The central relationship between category 1 (leadership) and category 7 (results) is indicated by the horizontal arrow in the center of the framework. Thereby, also the linkage between the two triads is indicated, which is critical for organizational success.

Thirdly, and finally, the *System Foundation* is illustrated in category 4. The aspects addressed in this category (measurement, analysis, and knowledge management) are considered critical with regards to an effective management of an

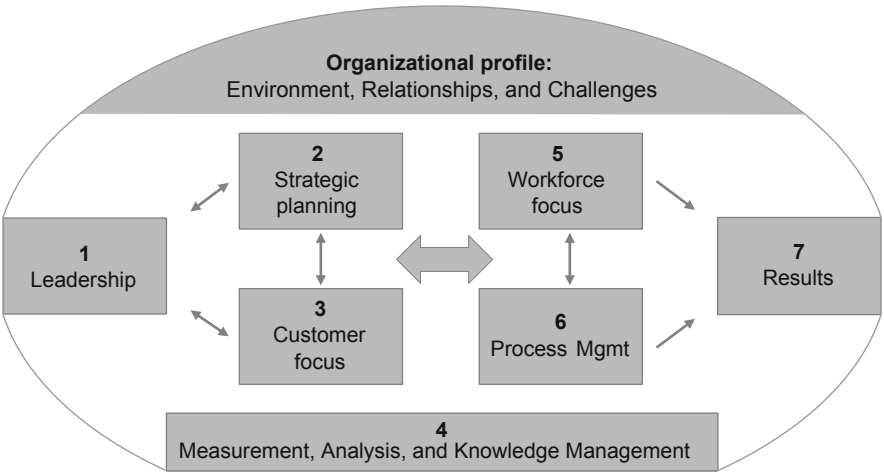


Fig. 2.2 The model of the Malcolm Baldrige National Quality Award (NIST 2009)

organization. Moreover, these aspects support a fact-based and knowledge-driven system for the improvement of an organization's performance and competitiveness (NIST 2009).

European Foundation of Quality Management (EFQM)

In the European business environment, the journey to excellence is mainly led by the excellence model of the European Foundation of Quality Management (EFQM). Introduced in 1991, it comprises all aspects and tasks of a corporate management and thus also serves as a leadership framework at large. It has been revised four times (1999, 2002, 2010, 2013) in order to comply with the latest achievements of management science. However, the general architecture of the model remained untouched (Seghezzi et al. 2013).

The EFQM Excellence model is a framework to facilitate the understanding and management of the complex environment today's organizations are forced to operate in. The underlying philosophy of the model is that sustainable success of any organization relies on strong leadership and a clearly communicated strategic direction. Each organization is responsible for a continuous training of its workforce as well as the development and improvement of partnerships and processes in order to provide its customers with value-adding products and services. Thus, an effective implementation of the right approaches supports the organization in meeting its own and its stakeholders' expectations (EFQM 2012).

Figure 2.3 illustrates the EFQM Excellence. It comprises nine interrelated criteria. Five of these are related to the potential of a company referred to as *Enablers*; the remaining four criteria constitute the *Results* section. The Enabler section subsumes dimensions that are considered as decisive for a sustainable

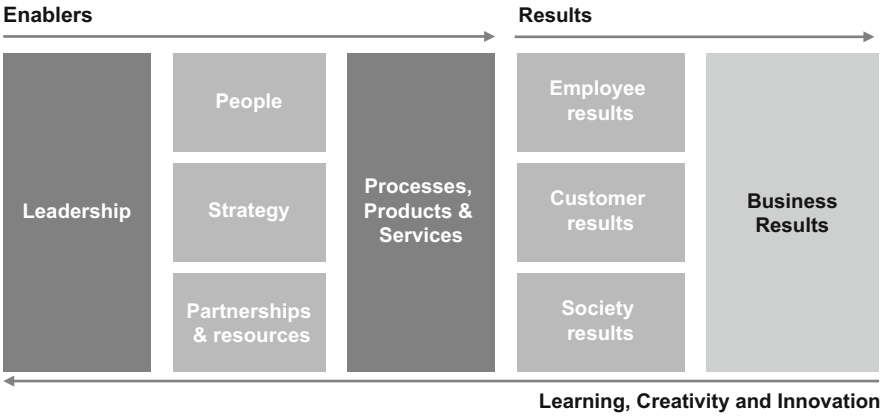


Fig. 2.3 The EFQM model for Excellence (EFQM 2012)

long-term success. Accordingly, the Results section represents that the aspired outcome of all organizational efforts is an improvement of business results (EFQM 2012; Seghezzi et al. 2013).

Like the American Malcolm Baldrige Award, the EFQM model initially evolved from concepts and philosophy of Total Quality Management (TQM). The need for commonly applicable leadership frameworks for corporate management, however, led to a revision of the model in 1999. This entailed a shift of the model's philosophy. As such, the EFQM model nowadays is no longer based on the TQM philosophy but rather incorporates each characteristic of excellence. Along with broadening the model's focus, EFQM defined excellence as superior practices by the management of an organization and by the achievement of its results (Seghezzi et al. 2013).

The criteria of the EFQM model work in a cause-and-effect relationship between Enablers and Results, as indicated by the interconnecting lines. These lines also point to the necessity to clearly align the different parts of an organization to achieve sustainable excellence. Each criterion is subdivided by a varying number of characteristics that describe their meaning. The characteristics themselves, however, are not mandatory and can be adapted to each organization's philosophy. Also, the weight of the nine criteria is optional; for applicants of the EFQM award, EFQM introduced a predefined weight to assure equality for all participants.

The EFQM model serves as a guideline for companies that pursue excellence. An organization's current status of excellence can be determined via self-assessment. The assessment starts with a holistic consideration of all nine criteria, the definition of improvement potentials and how these might be achieved. It is a recurring cycle that is based on the EFQM's RADAR method, a logic procedure to systematically and holistically assess the nine criteria of the EFQM model. The acronym RADAR represents each step of the underlying method, i.e. *R* for the first assessment of the Results, *A* for the Approach chosen to improve the organization, *D* for the Deployment of the approach, *A* for the Assessment, and *R* for the final Review of the achievements (Seghezzi et al. 2013).

Conclusion

The major commonality of all excellence models is their pursuit of superior operational performance. Besides this overarching principle, the three discussed models have several more commonalities that are relevant in the context of operational excellence.

One central aspect of the three models is their strong focus on *leadership* for any kind of organizational improvement. Even though TPS does not explicitly visualize *leadership* in its house diagram,[2] studying the Toyota Way reveals that leadership is an important tenet. Its long-term consistency supports the organizational culture that is necessary to create an environment for a learning organization. It is mandatory for Toyota's leaders to teach their subordinates the corporate way. Thus, they do not only have to understand but also to live the philosophy (Liker 2004; Spear and Bowen 1999). This understanding sets the basis of TPS. As such, Corporate Philosophy is visualized as the foundation of the framework that stabilizes the entire system. The model of the MBNQA ranks leadership first, distinguishing the seniority of leadership and forms of governance and social responsibilities from each other. The EFQM model views leadership as equally important and thus as well starts its assessment with this aspect. The model considers leaders as paragons for the entire organization who develop a company's vision, mission, values and ethical principles (Seghezzi et al. 2013).

All three models consider *people* as an organization's most valuable resource. TPS visualizes the workforce in the center of its house diagram in order to stress their importance for the company. Both MBNQA and EFQM emphasize that it is an organization's workforce that creates value. Thus, it is the organization's responsibility to train and reward employees in order to increase their motivation, well-being and satisfaction.

A focus on the company's *strategy* is explicitly noted by MBNQA and EFQM only. MBNQA examines on the one hand the development of the strategy and on the other hand its deployment in general. EFQM regards strategy as being aligned with the needs and expectations of stakeholders. Furthermore, the strategy is based on a company's performance and capabilities (Seghezzi et al. 2013). That said, it becomes obvious that TPS also considers strategy, as illustrated by the roof of the house diagram.

The EFQM model is the only model to name *resources* as worth considering when striving for excellence. The model provides a framework to assess the sustainable handling of resources, whether they come from suppliers or assets like buildings, financials, and materials. From a technical point of view, TPS also reminds to sustainably manage all organizational resources. According to Ohno (1988) the underlying philosophy of TPS is the absolute elimination of waste.

[2] In this edition we rely on the TPS model as described by Liker (2004). In our first edition "Operational Excellence in the Pharmaceutical Industry" we illustrated two versions of TPS, the "classical version" and the "Genba Kanri" version (Friedli et al. 2006). These two do also not visualize "leadership".

Excessive resource consumption conflicts with this philosophy. Moreover, TPS' just-in-time pillar requires a moderate handling of resources to allow flow production triggered by customers' pull and thus avoiding escalating inventories.

The last communality we would like to describe is the necessity of *process* consideration that is acknowledged by each of the three models. TPS, basically, banks on stable and standardized processes. Stability and standardization build the prerequisite for measuring and improving the processes. Accordingly, EFQM also views processes as an enabler and evaluates how well a company designs and improves its processes to add value for its customers and stakeholders. The framework of the MBNQA additionally distinguishes value creation and support processes for its assessment.

These commonalities have been a major influence for us. We consider their evaluation mandatory in assessing a plant's operational excellence level, i.e. they serve as integral parts in our model. And yet, it is not the communality that makes models special but their subtle differences. Some of these differences, too, served as important influences on our model of OPEX.

In the design phase of our OPEX model we were looking for a strong technical focus. This was supported by TPS. The production system provided us with a multitude of ideas how to organize operations from management to shop floor. Moreover, TPS entailed an abundance of literature examining (discrete) manufacturing operations in various industries. These as well have been considered and if necessary been translated into a pharmaceutical context. However, since our objective was (and still is) the identification of ways to sustainably improve operational performance of pharmaceutical companies in general (Friedli et al. 2006), inspired by the MBNQA, we embedded our OPEX model in a rich set of questions to describe the organizational profile. The consideration of these structural factors allows the comparison of pharmaceutical operations of production plants of all sizes, and from all over the world. An indication of improvement potential and the subsequent derivation of approaches and initiatives to fill those gaps can only be realized properly if there is a certain transparency of "what is done already" and "what is the outcome". Thus, we borrowed the Enabler-Result-logic from the EFQM, implemented it in our own model, and operationalized it with commonly applied lean practices.

The St.Gallen OPEX Model

Our original model from 2006 is shown in Fig. 2.4. It includes several sub-elements, each of which in itself represents an important part that contributes to the overall success.[3] Yet, these distinctive elements reinforce each other. According to this

[3] Cf. for a more detailed description of our model Friedli et al. (2006), p. 47ff and Friedli et al. (2010), p. 18ff.

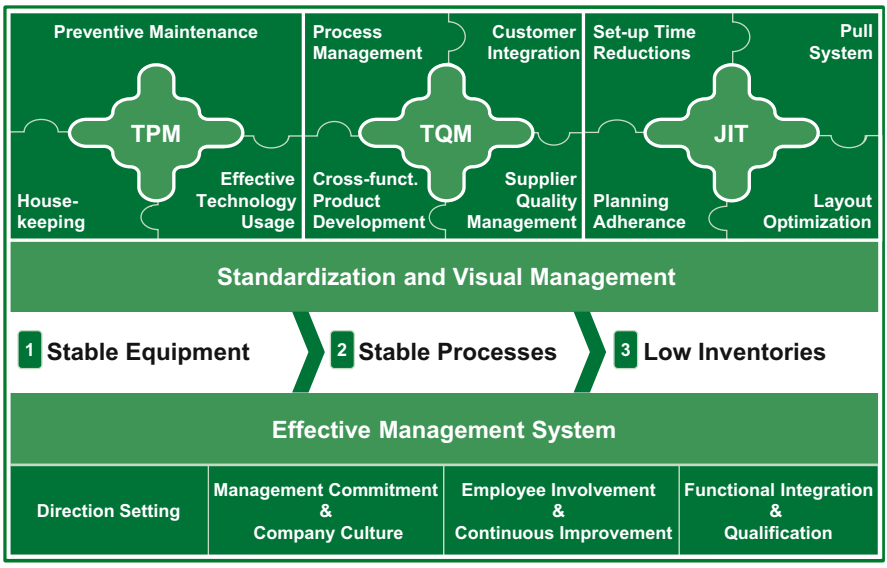


Fig. 2.4 The St.Gallen Model for Operational Excellence

model, manufacturing is viewed as a system in which single elements or interventions have both a direct and indirect impact on other elements.

On the highest level of abstraction, the OPEX reference model can be divided into two larger sub-systems: First, there is a technical sub-system which can be regarded as a tool-kit, comprising practices like Total Productive Maintenance (TPM), Total Quality Management (TQM) and Just-in-Time (JIT), and structuring them in a consistent manner. Second, there is a "social" sub-system which takes up the quest for an operational characterization of management quality and work organization. This second system focuses on supporting and encouraging people to continuously improve processes.

The Technical Sub-system

The objective of the technical sub-system is to analyze the implementation level of "technical" practices, which can be classified as either (core) principles or techniques/tools. Principles usually span a multitude of techniques and tools. For example, JIT is considered a core principle of OPEX as it is rooted in the notion of eliminating waste, and provides a multitude of techniques such as "Single Minute Exchange of Dies" (SMED) to achieve this goal. During our first plant visits in the pharmaceutical industry back in 2004, we realized that most lean tools (e.g., Poka Yoke, Andon etc.) were not known well. Consequently, the model was structured using the high-level principles of operations management without trying to mix them with single tools.

Most of the major widespread operations management principles (TPM, TQM, JIT) usually aim at a certain area of concern (e.g., low equipment availability, low quality, high inventories). Most companies implement them in order to address exactly these concerns. We have chosen the three most widespread "three letter acronyms" as the most important principles for our OPEX model. Analyzing the first data we collected using our model, it became clear that these principles are heavily interconnected. There seemed to be a logical sequence in their implementation, namely:

1. TPM (Total Productive Maintenance)
2. TQM (Total Quality Management), and
3. JIT (Just-in-Time).

We have structured the technical sub-system of our model according to this sequence.

With its focus on achieving the goal of "one-piece flow" and minimal buffer inventory, the JIT concept requires stable and robust processes. With its strong emphasis on variance minimization, the TQM concept can be regarded as a complementary concept to JIT as it should lead to a less variable (i.e. better controlled) and more stable manufacturing process that, in turn, reduces the need for safety stock buffers. In mass production, the break-down of a machine usually does not create a sense of urgency. The maintenance department is scheduled to fix it while inventory keeps operations running. However, in a JIT environment, equipment break-downs will soon lead to production downtimes and thus may bring about a crisis. Hence, the concept of TPM, in which everyone learns how to clean, inspect and maintain equipment, becomes a crucial element of an excellent production environment. Without TPM, the goals of TQM cannot be achieved, as there is no stable process based on unstable equipment. The mastering of TPM and TQM are prerequisites to be able to take out waste without facing the danger that the whole underlying system starts to crash.

For each of the core principles, several sub-elements were introduced.

Total Productive Maintenance (TPM)

We defined the following elements to be the major principles of TPM: "preventive maintenance", "autonomous maintenance", "housekeeping", "cross-functional training" and the "effective technology usage".

TPM is designed to maximize equipment effectiveness, improve overall efficiency by establishing a comprehensive productive maintenance system during the life cycle of the equipment, whilst spanning all equipment-related fields such as planning/buying, use, maintenance etc. Moreover, TPM involves the participation of all employees, from plant management to shop floor workers and thus promotes productive maintenance through motivational management techniques and voluntary small group activities. TPM is usually divided into short-term and long-term

elements. The short-term attention is focused on an autonomous maintenance program for the production department, a planned and preventive maintenance program for the maintenance department, and skill development for operations and maintenance personnel. On the other hand, the long-term elements of TPM focus on the usage of new technology, which should be designed to support people and processes but has to prove its reliability.

Autonomous maintenance can be described by considering the four main goals of a TPM program. First, the program teams up production and maintenance people to stabilize conditions and halt deterioration of equipment. Second, by effectively developing and sharing responsibility for the critical daily maintenance tasks, production and maintenance people are able to improve the overall "health" of equipment. Third, TPM is designed to help operators learn more about how their equipment functions, what common problems can occur, why they occur, and how these problems can be prevented through early detection and treatment of abnormal conditions. This cross-functional training allows operators to maintain equipment and to identify and resolve many basic equipment problems. Fourth, in a TPM program, maintenance technicians are held accountable for completing maintenance tasks within a scheduled timeframe while still meeting production requirements. By using standardized operating procedures such standardization helps to increase schedule compliance which is an important indicator for the health of a TPM system.

Total Quality Management (TQM)

When taking a closer look at the concept of TQM, one will find that TQM is a very rigorous problem-solving approach that is based on facts rather than on gut feeling. Today, the concept of Six Sigma has become much more popular than the term TQM. The difference between these two concepts lies in Six Sigma's even stronger orientation on the statistical measure of sigma (standard deviation). Companies which have truly internalized the principles of TQM or Six Sigma also try to set up operations as experiments to continuously isolate variables that cause deviation, mastering them and, by doing so, being able to continuously improve their processes.

However, TQM goes far beyond statistics. TQM is about management commitment; it is a philosophy of excellence, customer focus, continuous process improvement and people and supplier development. We defined process management, customer integration, supplier quality management and cross-functional product development to be the core elements of a TQM system.

Process management is defined as documenting, measuring, analyzing and improving processes, thus reducing process variances to a minimum level. Process management includes all common tools of quality management aiming to find and control root causes of deviation (e.g., Cause and Effect Diagrams, Pareto Analysis, Design of Experiments, Statistical Process Control etc.). A high level of

documentation and standardization usually goes hand in hand with human and organizational dysfunction (e.g., unmotivated workforce, high absenteeism etc.). In addition, successful process management is more likely to be achieved by peers working in cross-functional teams than by industrial engineers. TQM specialists suggest that companies should choose vendors primarily on the basis of quality rather than solely on the basis of product price. Moreover, supplier quality management aims to integrate suppliers into the internal quality system to ensure high quality levels. To achieve excellent quality, it is essential to know what customers want and to provide products to meet their needs (customer integration). TQM experts point out that cross-functional product development should help to translate customer requirements into high quality products.

Just-in-Time (JIT)

Due to the fact that in most industries the heterogeneity of customer requirements has significantly increased, JIT manufacturing for most companies has become a crucial element to increase flexibility without building up huge inventories. We defined "pull production", "setup time reduction", "layout optimization" and "planning adherence" to be the sub-elements of a JIT production.

Whilst pull production helps to reduce overproduction, inventory and setup time reductions can help to decrease the average lot size. Besides, it can enable a smooth material flow within the manufacturing process. With the need for standardized, stable, reliable processes we regarded the element "planning adherence" as a further element of JIT. Planning adherence, which means smoothly leveling out the production schedule in both volume and variety, should keep the JIT system stable and allow for minimum inventory. Apart from waste caused by overproduction and excess inventory, an integrated JIT program also endeavors to reduce all kind of excessive movements caused by material and handling. Hence, layout optimization based on close arrangements of people and equipment in a processing sequence is an additional principle of JIT implementation.

Basic Elements

After structuring the OPEX model according to the three elements TPM, TQM and JIT, we realized that there are some common practices shared by all three sub-systems, and are not unique to each of the programs. These are, for example, cross-functional training, employee empowerment and teamwork, standardization and visual management. We decided to differentiate between technical practices such as standardization, and the more socially oriented aspects such as employee empowerment or cross-functional training (which we will discuss later).

The following two technically oriented practices cannot be solely related to JIT, TQM or TPM: standardization and visual management. We call them basic elements because they can be regarded as basic prerequisites for successfully implementing TQM, TPM as well as JIT principles. As Imai (1986) explained in his book on continuous improvement, it is impossible to improve any process before it has been standardized, and thus stabilized. Standardization not only refers to processes; it also includes the standardization of technology and equipment. Standardization can be regarded as a common supportive element for TPM, TQM and JIT. A further basic element is visual management. It provides the workforce with updated information on process and performance data which assists the deployment of TPM, TQM and JIT principles (e.g., visual management can provide timely information regarding JIT-related data as, for instance, the actual take time to enhance flow as well as TQM- or TPM-related information such as process variability or equipment reliability to improve problem solving).

The Social Sub-system: Management System

Based on different sources, we developed a management quality model the objective of which can be summarized as follows: "Motivating and aligning people to work for a common goal". To achieve a common goal, employees need autonomy, they need to feel that they have control over their job and belong to a team (people involvement). Targets have to be clear and consistent, as well as challenging (direction setting) and supported by senior management (management commitment). Feedback on progress needs to be given frequently and in a timely manner, and multiple skills should be developed according to individual potential (functional integration and people development).

Direction Setting

We completely agree with Skinner (1974), Hayes et al. (2005) and Loch et al. (2004) that the implementation of certain practices only makes sense if the management has formulated a strategy that is based on clear and consistent objectives. However, we decided to merge the integration variable and the direction setting variable because they are strongly correlated and conceptually interlinked.

Management Commitment

Evidence from several studies supports that management commitment is a crucial element for facilitating change processes, which is a prerequisite for process

improvement. Especially TQM literature stresses management commitment as one of the key success factors. A quality improvement process must begin with the management's own commitment to quality. However, management commitment is not just vital for rolling out a TQM program; it is equally important for rolling out a JIT and TPM program. The management has to promote a culture which supports people in doing their work.

Employee Involvement and Continuous Improvement

We also included employee involvement into our management quality model. We strongly believe that one major managerial challenge is to get all employees involved into continuously thinking about how to improve the current situation. This is only possible if process improvement is a common task for everybody and not just for few smart industrial engineers.

Functional Integration and People Development

A workforce that is eager to contribute to the goals set by the management but lacks proper know-how in to do so will fail in achieving them. If complex decisions are to be delegated, as it is the case in the concept of autonomous problem solving, this can only succeed if employees are given the chance to acquire new knowledge. Furthermore, the flexibility of the technical system we have introduced (especially the concept of mixed model production) requires a multi-skilled workforce that can perform different tasks. Consequently, functional integration and employee development is a basic pillar for the achievement of goals set by the plant management. We also introduced the aspect of feedback and reward as an enabler for motivation. Organizational scientists argue that rewards go beyond money. The important point is that positive or negative reinforcement ensues as quickly as possible after the action.

OPEX Defined

Modern approaches to Operational Excellence (OPEX) have evolved from the understanding of lean production (Friedli and Schuh 2013) and are generally regarded as part of continuous, corporate improvement concepts. However, OPEX programs cannot be viewed as standalone nor as a new set of methods as they comprise and rely on several already established manufacturing concepts (Gronauer 2012). Since to date no uniform definition of OPEX exists, discussions of such programs are regularly complicated. The subsequent section aims at

overcoming this deficit by clarifying the scientific background before leading over to our definition of Operational Excellence.

The systematic discussion of OPEX can be traced back to Hayes and Wheelwright (1984) publishing their ground breaking book *Restoring our Competitive Edge* and emphasizing the relevance of manufacturing to retain competitiveness of the American industry. They argued that the competitive advantage of Japanese manufacturers stemmed from superior production capabilities, contrary to an erroneously assumed better product design, marketing ingenuity, or substantial financial strength. Whereas American companies lacked a consideration of manufacturing as a key to success, their Japanese competitors had already realized the benefits of streamlined operations as a competitive factor.[4] As such, the World-Class Manufacturing (WCM) project was initiated in order to identify critical success factors of successful manufacturing companies.

Based on the outcome of the WCM project, two dimensions can be distinguished in describing OPEX. The first dimension refers to the effectiveness of a production system, highlighting the role of manufacturing within an organization. The second dimension embraces the effectiveness of applied approaches and practices, and thus considers the utility of selected approaches in terms of their unique combination of different methods.

Discussing the effectiveness of production systems, Hayes and Wheelwright (1984) observed that the most successful companies of their study sample had established more advanced production systems than their competitors. These production systems supported the corporate strategy directly, while at the same time providing organizations with the opportunity to develop unique characteristics. The authors considered different success factors – referred to as competitive priorities – as a central aspect for developing these unique characteristics. These competitive priorities can be understood as distinctive dimensions like quality, cost, and time. By stressing dimensions differently, according to an organization's strategy, companies distinguish themselves from each other, creating their own competitive advantage. Moreover, Hayes and Wheelwright argue that companies should avoid the pursuit of competitive advantages in every dimension since it is "potentially dangerous, for a company to try to compete by offering superior performance along all of these dimensions simultaneously, since it will probably end up second best on each dimension to some other company that devotes more of its resources to developing that competitive advantage" (Hayes and Wheelwright 1984, p. 41). Rather, companies should focus on those dimensions in which they intend to develop their unique capabilities. In literature discussed as the idea of "trade-offs", this has been widely acknowledged by various authors.[5]

Hayes and Wheelwright plead that building competitive strength is dependent on a set of approaches and manufacturing practices assigned to six world class dimensions. If combined in the right way, these practices enable companies to

[4] Hayes and Wheelwright (1984), p. 12.

[5] Cf. Skinner (1974), Porter (1985).

achieve superior performance. These dimensions are categorized as training and qualification of employees at production (workforce skills and capabilities), technical competence of management, the organizational understanding of quality (competing through quality), workforce participation, the degree of proprietary process and machinery development (rebuilding manufacturing engineering), and finally organizational capability to achieve progress by continuous improvement processes (Incremental improvement approaches).

Schonberger (1986) considered 16 manufacturing principles to play a major role in WCM. He enriched the discussion by introducing Total Quality Management (TQM) and Just-in-Time (JIT) which then evolved to the central aspects of WCM. Hall (1987) brought in another set of criteria to describe excellence; most of these match the criteria introduced by Schonberger. Hall defines "Manufacturing Excellence" as a system that comprises JIT production, employee participation, standardized tools and machinery, supplier integration, and design-for-manufacturability.[6]

In the early 1990s, the excellence discussion started to change influenced by one of the most cited approaches in theory and praxis: lean production. First published by Womack et al. (1990), the concept of lean production, describing Toyota's superior production system, took Western manufacturing plants by storm. Numerous empirical studies researching lean production and it constituents (TPM; TQM; JIT) revealed a strong correlation between so-called lean practices and operational performance, and thus contributed substantially to the concept's global dissemination.[7]

A number of other approaches ranking among modern production management contributed to the understanding of OPEX. Yet, these approaches like time-based-manufacturing, agile or dynamic manufacturing have several similarities and overlaps. Looking at the definition of time-based-manufacturing, similarities with lean production become obvious: "Application of time compression techniques into every aspect of manufacturing system design which includes techniques such as pull system, cellular manufacturing, reengineering set-ups, quality improvement, employee involvement and dependable suppliers".[8]

A multitude of studies analyzed the impact of modern manufacturing practices on organizations' operational performance, and showed their effectiveness to be out of question. In fact, it is the context of their application that became the focus of interest.[9] Hayes and Pisano see the central characteristics of excellent manufacturing companies as follows[10]:

[6] The approach "design-for-manufacturability" comprises various methods like QFD, House of Quality, etc. and strives for an engagement of production and other product development related departments at early stages of the development process.

[7] Cf. Sakakibara et al. (1997), Cua et al. (2001), Shah and Ward (2003) etc.

[8] Cf. Stalk and Webber (1993).

[9] Cf. Hayes and Pisano (1994), Pilkington (1998).

[10] Hayes and Pisano (1994), p. 78.

- Excellent manufacturing companies apply modern approaches and manufacturing practices to realize their manufacturing strategy. Their manufacturing strategy is derived from corporate objectives.
- By applying modern approaches and manufacturing practices, excellent manufacturing companies continuously develop new capabilities that provide them with a potential competitive advantage.

Yet, technical aspects summarized in manufacturing practices are only one element of modern OPEX approaches. Social aspects constitute another integral part. They can be considered as a decisive factor for the importance OPEX gained within manufacturing companies in the last years. Although social aspects in the context of manufacturing had been already acknowledged, it was Spear and Bowen (1999) who highlighted managerial and cultural aspects and their impact on the competitiveness of the manufacturing industry in their article *Decoding the DNA of the Toyota Production System*. Loch and Chick (2006) focused on the importance of managerial qualities to explain performance differences in manufacturing plants.

The explanations given above outline that performance of a manufacturing plant or of production in general is multi-facetted, and may only be described and explained by the interaction of different factors. Unfortunately, many approaches that define OPEX, whether they are practical or theoretical, are lacking a multi-facetted and holistic consideration. Moreover, single elements or initiatives are often picked out and treated in isolation, cf. Shah and Ward (2007).

Based on literature and our experience, we see OPEX as the balanced management of cost, quality and time while at the same time focusing on the customer needs. To achieve this end, OPEX comprises structural and behavioral changes thought to optimally support necessary activities. In order to maintain sustainability also in changing or volatile environments, OPEX has to be pushed by top management and has to be designed to engage every single employee (see also Chap. 7, Barriers and Success Factors). Obviously, OPEX is not only concerned with performance. It also encompasses the way leading to that superior performance, and practices that allow an organization to continuously improve itself.

Thus, our definition of Operational Excellence is as follows:

Operational Excellence constitutes the continuous pursuit of improvement of a production plant in all dimensions. Improvement is measured by balanced performance metrics comprising efficiency and effectiveness, thus providing a mutual basis for an improvement evaluation.

Excellence in Pharma Manufacturing

The above section aimed at explaining our OPEX model and our understanding of excellence in general. In the following we will transfer this understanding to excellence in pharmaceutical manufacturing. The performance of a manufacturing plant can be described in several ways. Obviously, high performance in a single

Key Performance Indicator (KPI) can be derived from a mere focus on that respective KPI. However, this is not the case for excellence. Our understanding of an excellent manufacturing site is influenced by the St.Gallen school of systems theory and cybernetics.

Thinking in systems determines the holistic consideration of the system (organization) itself. The systemic approach acknowledges that an organization is embedded in economy and society (Ulrich 1984). The complexity of situations and problems is recognized, and it is sought to consider them in their full context. Isolated consideration of single aspects and inexpedient problem definitions should be avoided (Ulrich and Krieg 1974). As there already is only a limited number of opportunities to monitor and interpret surrounding events and happenings, it is difficult, sometimes even impossible, to reflect interrelations objectively (Bleicher 1995). Thus, it might be misleading to artificially narrow down the horizon. The conscious management of those social systems and therefore an adaption of structures and people's behavior is an approach to mitigate these shortcomings. Moreover, evoking self-organized adaptions from the system itself requires approaches that are based on an evolutionary organizational development in contrast to the steering and directing of just a few managers. As such, also Bleicher (1995) concludes to strive for a holistic consideration in order to satisfy the connectivity of problems and interrelations within the social system.

That said, and referring back to the conclusions of the introductory baggage handler case, we rely on our model's entire technical sub-system in order to distinguish excellent plants from weaker performing ones. Transparent manufacturing operations of an organization are achieved by assigning a distinctive set of KPIs to TPM, TQM, and JIT. This, however, implies that excellent manufacturing sites have high performance on a holistic level instead of high performance on a single KPI only. Analyzing only a single KPI, even average or weak performing sites might excel. But due to the balanced approach of effectiveness and efficiency, overall performance of the manufacturing system is critical to qualify as operationally excellent (see Chap. 4 for detailed insights into KPIs and measured performance).

References

Bleicher K (1995) Das Konzept integriertes management, 3rd edn. Campus, Frankfurt a. M

Cua KO, McKone KE, Schroeder RG (2001) Relationships between implementation of TQM, JIT, and TPM and manufacturing performance. J Operations Manag 19(6):675–694

EFQM (2012) An overview of the EFQM excellence model. www.efqm.org. 4 February 2013

Friedli T, Schuh G (2013) Wettbewerbsfähigkeit der Produktion an Hochlohnstandorten, Wettbewerbsfähigkeit der Produktion an Hochlohnstandorten. Springer, Heidelberg

Friedli T, Kickuth M, Stieneker F, Thaler P, Werani J (eds) (2006) Operational excellence in the pharmaceutical industry. ECV – Ed.-Cantor-Verl, Aulendorf

Friedli T, Werani J, Basu PK, Gronauer T (eds) (2010) The pathway to operational excellence in the pharmaceutical industry: overcoming the internal inertia. Editio Cantor, Aulendorf

Gronauer T (2012) Einfluss von internen Kontext- und Prozesselementen auf die Etablierung eines Operational Excellence Programms. Eine vergleichende Fallstudienanalyse aus der pharmazeutischen Industrie. Ph.D. thesis, institute of technology management, University of St.Gallen, St.Gallen, 2012

Hall RW (1987) Attaining manufacturing excellence: Just-in-time, total quality, total people involvement. Dow Jones-Irwin, Homewood

Hayes RH, Pisano GP (1994) Beyond world-class: the new manufacturing strategy. Harv Bus Rev 72:77–86

Hayes RH, Wheelwright SC (1984) Restoring our competitive edge: competing through manufacturing. Wiley, New York

Hayes RH, Pisano GP, Upton DM, Wheelwright SC (2005) Operations, strategy, and technology: pursuing the competitive edge. Wiley, Hoboken

Imai M (1986) Kaizen: the key to Japanese competitive success. Random House, New York

Liker JK (2004) The Toyota way: 14 management principles from the world's greatest manufacturer. McGraw-Hill, New York

Loch CH, Chick SE (2006) Management quality and factory performance and the role of management quality in the context of operational excellence. In: Friedli T, Kickuth M, Stieneker F, Thaler P, Werani J (eds) Operational excellence in the pharmaceutical industry. Editio Cantor, Aulendorf

Loch CH, Demeester L, Eichler K (2004) Organic production systems: what the biological cell can teach us about manufacturing. Manuf Serv Oper Manag 6(2):115–132

NIST (2009) Criteria for performance excellence. www.nist.gov. 4 February 2013

Ohno T (1988) Toyota production system: beyond large-scale production. Productivity Press, Portland

Pilkington A (1998) Manufacturing strategy regained: evidence for the demise of best-practice. Calif Manage Rev 41(1):31–42

Porter ME (1985) Competitive advantage – creating and sustaining superior performance. Collier Macmillan, New York

Sakakibara S, Flynn BB, Schroeder RG, Morris W (1997) The impact of Just-in-time manufacturing and its infrastructure on manufacturing performance. Manag Sci 43 (9):1246–1257

Seghezzi D, Fahrni F, Friedli T (2013) Integriertes Qualitätsmanagement: Der St. Galler Ansatz. Carl Hanser, München

Schonberger R (1986) World class manufacturing: the lessons of simplicity applied. Free Press/ Collier Macmillan, New York/London

Shah R, Ward PT (2003) Lean manufacturing: context, practice bundles, and performance. J Oper Manag 21(2):129–149

Shah R, Ward PT (2007) Defining and developing measures of lean production. J Oper Manag 25 (4):785–805

Skinner W (1974) The focused factory. Harv Bus Rev 52:113–121, Harvard Business School Publication Corp

Spear S, Bowen HK (1999) Decoding the DNA of the Toyota production system. Harv Bus Rev 97–106. (September-October 1999)

Stalk G Jr, Webber AM (1993) Japan's dark side of time. Harv Bus Rev 71(4):93–102

Ulrich H (1984) Die Betriebswirtschaftslehre als anwendungsorientierte Sozialwissenschaft. In: Dyllick T, Probst G (eds) Management. P. Haupt, Bern, pp 168–199

Ulrich H, Krieg W (1974) St. Galler management-model, 3. verb. Aufl. Haupt, Bern

Wheelwright SC, Hayes RH (1985) Competing through manufacturing. Harv Bus Rev Jan–Feb:99–109

Womack JP, Jones DT, Roos D (1990) The machine that changed the world. Maxwell Macmillan International, New York

Chapter 3
The History of OPEX in the Pharmaceutical Industry

Thomas Friedli and Jürgen Werani

The History of Operational Excellence in the Pharmaceutical Industry is still short. Serious initiatives were only launched around 10 years ago. This chapter provides some background on how and why OPEX became a topic of serious interest in this industry.

> As pharmaceutical manufacturing evolves from an art to a science and engineering based activity, application of this enhanced science and engineering knowledge in regulatory decision-making, establishment of specifications, and evaluation of manufacturing processes should improve the efficiency and effectiveness of both manufacturing and regulatory decision-making.[1]
>
> ..., industry's hesitancy to broadly embrace innovation in pharmaceutical manufacturing is undesirable from a public health perspective. Efficient pharmaceutical manufacturing is a critical part of an effective U.S. health care system. The health of our citizens (and animals in their care) depends on the availability of safe, effective, and affordable medicines.[2]

Compared to other industries, the pharmaceutical industry was rather slow to adopt programs to increase Operational Excellence and strive for Continuous Improvement. By the late 1990s, only a few actions with rather limited scope had been taken. In the first decade of the 2000s, OPEX then gained momentum. Since then, OPEX has become a priority not only for the top management and workforce of almost every major pharmaceutical manufacturer, but also for small and

[1] FDA, Final Report "Pharmaceutical CGMPs for the 21st Century – A Risk-Based Approach", September 2004.

[2] Guidance for Industry PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance, FDA, September 2004, Page 3.

T. Friedli (✉)
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch

J. Werani
Schuh & Co, Komplexitätsmanagement AG, Langgasse 13, 9008, St.Gallen, Switzerland
e-mail: juergen.werani@schuh-group.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_3, © Springer-Verlag Berlin Heidelberg 2013

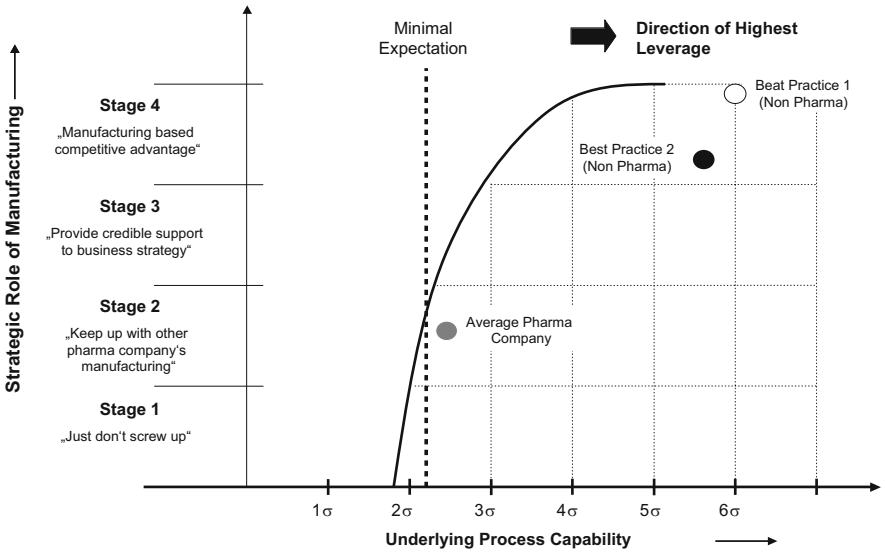


Fig. 3.1 Current status of the pharmaceutical industry (Source: Raju (2003) cited by Kickuth and Friedli 2006)

medium-sized contract manufacturers. Even so, the industry still has a lot to do to catch up with excellence levels of other industries that have been working towards continuous improvement for decades. According to G. K. Raju, in 2003 the sigma level of the pharmaceutical industry was around 2–3 sigma (see Fig. 3.1).

U.S. Food and Drug Administration (FDA) first encouraged serious Operational Excellence efforts in a meeting of the scientific advisory board at the end of 2001. At that time, one of the difficulties the agency faced was the increasing number of post-approval manufacturing amendments (see Fig. 3.2)

This high number of post-approval changes made it difficult for the FDA to fulfill their inspection obligations. It also demonstrated that the industry lacked in the scientific mastering and understanding of its production processes. It was generally agreed that GMP manufacturing worked rather empirically than science-based and that the industry as well as the regulators were risk-averse.[3]

At the same meeting, Doug Dean and Francis Brutton from PricewaterhouseCoopers (PwC) presented a rather bleak analysis of the status quo of pharmaceutical manufacturing. In one of their slides they came to the following conclusions[4]:

- The status quo is untenable
- Pharmaceutical manufacturing – lots of room for improvement
- Traditional metrics hide poor performance
- Compliance infrastructures are not economic

[3] Janet Woodcock (2011).

[4] Bruttin and Dean (2004).

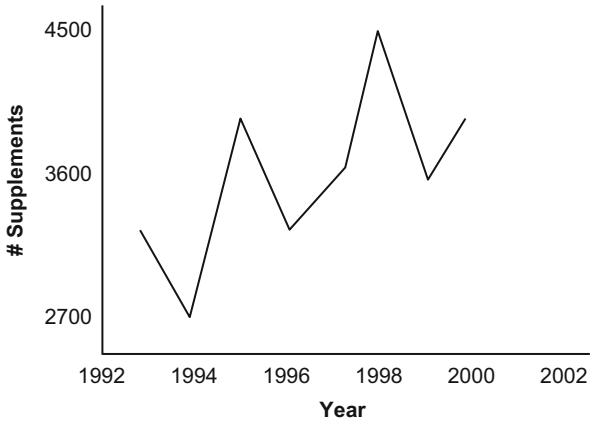


Fig. 3.2 Post approval manufacturing supplements (Woodcock 2011)

- Technologies are critical enablers – but not in isolation
- Huge potential for industry & regulators to create a win-win

They identified some of the reasons for this situation: the transfer of processes that were neither fully understood nor feasible at commercial scales; lengthy and elaborate new product introduction exercises that generated data but failed to provide critical information; 50 % of production costs being locked before the start of Phase III; "institutionalized" process inefficiencies and lacking a scientific basis for the trade-off of investing time and gaining deeper process understanding.

Both the industry and the FDA were well aware of the deficiencies in pharmaceutical manufacturing. To move forward, they jointly encouraged organizations the use of innovative technologies to enhance process understanding and to establish science- and risk-based approaches to quality and regulatory processes. FDA selected Process Analytical Technology (PAT) as a pilot to evaluate how they could further promote the approach of a science-based process management. The PAT team and the manufacturing science work group stated in the executive summary of a report[5]:

> Pharmaceutical manufacturing operations are inefficient and costly. The cost of low efficiency is generally not understood or appreciated (e.g., manufacturing costs far exceed those for research and development operations). Low efficiency is predominantly due to "self-imposed" constraints in the system (e.g., static manufacturing processes, focus on testing as opposed to quality by design, approach to specifications based on discrete or the so called "zero tolerance" criteria, a less than optimal understanding of variability, etc.). These constraints keep the system in a corrective action mode. Continuous improvement is an essential element in a modern quality system and it aims at improving efficiency by optimizing a process and eliminating wasted efforts in production. In the current system continuous improvement is difficult, if not impossible.

[5] Cf. Report of the PAT Team and Manufacturing Science Working Group 2004, Page 1.

In response to these findings, the FDA changed its position: instead of measuring quality by focusing on product purity and potency, more time should be spent on trying to address issues dealing with actual physical manufacturing processes. For example, what effects, if any, do small changes in the reactor vessel, blending, drying, compressing, coating or other manufacturing steps have on the final dosage form?[6] The main objective was to gain a more thorough understanding of pharmaceutical manufacturing processes and thereby more predictable and efficient manufacturing. Although process analytics are potentially the vital tools, the PAT initiative is essentially about process understanding, predictability and efficiency. PAT should be thought of as a system for designing and controlling manufacturing through timely measurements of critical quality and performance attributes, and of raw and in-process materials and processes, with the goal of ensuring superior product quality. Associated with the greater understanding of processes, additional benefits can be achieved, such as faster development of new products; shorter manufacturing cycle times; higher yields; reduced waste materials; and fewer product recalls.[7] The PAT initiative preceded the broader cGMP initiative by about a year. In August 2002, the Food and Drug Administration announced this significant new initiative to enhance and modernize the regulation of pharmaceutical manufacturing and product quality. The main objectives of this initiative were: *(1) to encourage the early adoption of new technological advances by the pharmaceutical industry, (2) to base regulatory review and inspection policies on state-of-the-art pharmaceutical science, (3) to facilitate industry application of modern quality management systems*, *(4) to use risk-based approaches that focus both industry and agency attention on critical areas*; and *(5) to incorporate enhanced quality system approaches into the agency's business processes*.[8]

The initiative also stated a so-called desired state for pharmaceutical manufacturing:

- Product quality and performance achieved and assured by design of effective and efficient manufacturing processes
- Product specifications based on mechanistic understanding of how formulation and process factors impact performance
- Continuous improvement approaches, with innovative use of new technology as desired
- Continuous "real time" assurance of quality

The PAT activities became part of cGMP. Importantly, cGMP was impacted by economic considerations, leading to a new paradigm: Quality and Productivity came on the agency's agenda, opening new opportunities to the industry.

[6] Cf. Clark (2004): FDA's PAT initiative, in: Pharmaceutical Technology Europe.

[7] Clark (2004).

[8] Cf. Report of the PAT Team and Manufacturing Science Working Group 2004.

> Quality and productivity improvement share a common element – reduction in variability through process understanding (e.g., application of knowledge throughout the product lifecycle). Reducing variability provides a win-win opportunity from both public health and industry perspectives. And, since manufacturing technologies and practices are generally similar between both innovator and generic companies, facilitating efficiency improvements provide opportunities for both sectors of the pharmaceutical industry.[9]

With this, Lean Thinking (Operational Excellence) became part of the game.

Later FDA activities were all based on the same underlying idea: to modernize the scientific base of pharmaceutical manufacturing and pharmaceutical quality management. This can be observed in the documents about the "Critical Path Initiative" as well as in the work along of ICH Q8–Q10, in the more recent QbD initiative and the new process validation guideline released in 2011. The regulatory basics will be discussed more detailed later in Chapter 5. Though the idea of "continuous improvement" has become more widespread in manufacturing, adjusting to a new paradigm and overcoming decades of a "no change culture" continues to be difficult and takes both time and effort:

> Continuous improvement is an essential element in a modern quality system. Its aim is to improve efficiency by optimizing a process and eliminating wasted efforts in production. Improvement efforts are carried out in a structured manner with appropriate predefined protocol and oversight. These efforts are primarily directed towards reducing variability in a process and product quality characteristics and are not for changing the fundamental design of a manufacturing process. Generally the term continuous improvement is broadly used for all improvement efforts including those that result from corrective actions. In the regulatory setting a distinction between corrective action and continuous improvement is essential. Need for corrective actions occur when product quality characteristics are in question (e.g., out of specification). Such a situation can require urgent risk assessment and sound quality decisions to prevent any adverse impact on patients. In the current state corrective actions are the dominant mode for improvement and continuous improvement is difficult.[10]

The Critical Path Initiative from 2003 had its own industrialization perspective (cf. Figs. 3.3 and 3.4) and QbD was the logical next step: making sure that introduced processes were better understood from the launch.

In summary, the industry aspirations to reduce (production) costs rooted in the increasingly difficult environment the industry faced. The end of formerly successful business models, increased competition and cost pressure from health care organizations, combined with support from the regulatory agencies opened the way to a new thinking. Operational Excellence became not only an urgent and demanding economic necessity but also was expected to be welcomed by the FDA.

The introduction happened in three major stages described in more detail in Gronauer et al. (2010) (Fig. 3.5).

The first phase was the "pre-OPEX" phase, which lasted until the late 1990s, followed by a "Best-Practice Transfer" phase, which gave way to today's "Transformation" phase. Looking ahead, we have added a fourth phase, an "Integrated

[9] FDA 2004b.

[10] FDA 2004b.

Dimension	Definition	Examples of Activities
Assessing Safety	Show that product is adequately safe for each stage of development	• Preclinical: show that product is safe enough for early human testing Eliminate products with safety problems early • Clinical: show that product is safe enough for commercial distribution
Demonstrating Medical Utility	Show that the product benefits people	• Preclinical: Select appropriate design (devices) or candidate (drugs) with high probability of effectiveness • Clinical: Show effectiveness in people
Industrialization	Go from lab concept or prototype to a manufacturable product	• Design a high-quality product - Physical design - Characterization - Specifications • Develop mass production capacity - Manufacturing scale-up - Quality control

Fig. 3.3 The three dimensions of the critical path FDA (2004a)

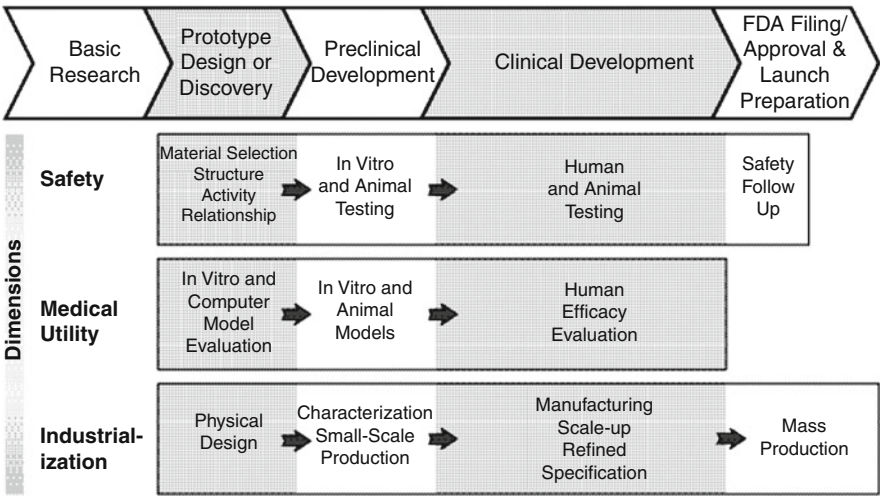


Fig. 3.4 The industrialization perspective along the product lifecycle FDA (2004a)

Operations Systems" phase, which we expect to be the future dominating pattern in the industry. In our opinion, some of today's pharmaceutical companies are already on the threshold of entering this fourth phase. The pathway to OPEX in the pharmaceutical industry and its four phases are illustrated in Fig. 3.5.

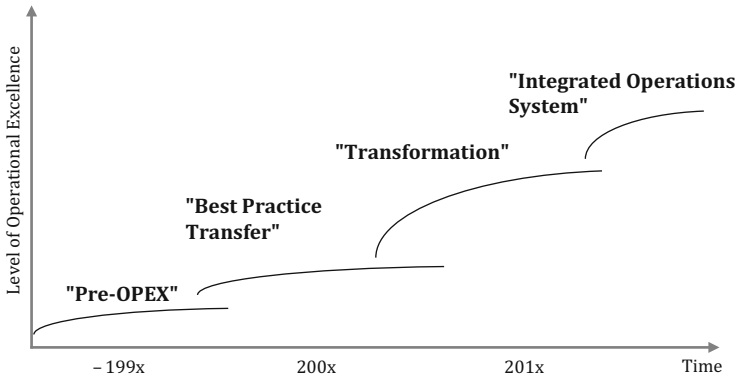


Fig. 3.5 The pathway to operational excellence (Gronauer et al. 2010)

Even today's most advanced OPEX programs, i.e. the ones on the threshold to the "Integrated Operations Systems" phase, have not evolved over night. They, too, went through all the other phases.

The pre-OPEX phase is characterized by isolated manufacturing improvements that were not the result of a structured and carefully designed approach. Changes were only introduced reluctantly; the underlying culture was one of "no-change". The rising cost pressure and new FDA directions (as outlined above) made a new approach necessary. Pharmaceutical production managers visited plants from BMW, Audi, Toyota etc. The main intention was to copy successful lean thinking practices and apply them to the pharmaceutical production floor. After some initial successes, however, it became clear that simply copying methods and tools and transferring training programs did not suffices to get a buy-in from employees.

The next phase therefore focused on people, and was designed as a huge change management approach. Most of the more advanced companies still are at this transformation stage. We foresee, however, more integrated approaches in the near future that will, on the one hand, bring together preventive and reactive OPEX (e.g., QbD and OPEX combined) and, on the other hand, align all improvement initiatives on the top management level. This is a necessity to ensure employees understand the great potential and benefits that OPEX offers a company.

Conclusions

A combination of reasons led to the rise of OPEX in the industry: The increased pressure on drug prices, the often cited productivity crisis in pharmaceutical R&D, but also regulatory agencies' increased focus on bringing science to pharmaceutical manufacturing processes. The industry has overcome initial beliefs that success could be achieved by copying training plans, methods and tools from other

industries, and has adapted new, unique approaches dealing with people in the organization. Most of the examples in parts II and III of this book evidence these developments.

References

Bruttin F, Dean D (2004) Managing the cost of compliance in pharmaceutical operations. http://www.efcg.cefic.org/fdxdownload_13.iK23abe1ee02e8be1e/publication_file/managing-the-cost-of-compliance-in-pharmaceutical-operations.pdf. Retrieved 22 January 2013

Clark G (2004) FDA's PAT initiative, in: pharmaceutical technology Europe. http://www.pharmtech.com/pharmtech/Analytical/article/detail/129539. Retrieved 20 January 2013

FDA (2004a) Challenge and opportunity on the critical path to new medical products. www.fda.gov. Retrieved January 2010

FDA (2004b) Final report "pharmaceutical CGMPs for the 21st century – a risk-based approach", September 2004. www.fda.gov. Retrieved January 2010

Gronauer T, Friedli T, Götzfried M (2010) The roadmap to operational excellence – pattern and elements of OPEX programs. In: Friedli et al. (2010) The pathway to operational excellence – overcoming the internal inertia. Editio Cantor Verlag, Aulendorf

Kickuth M, Friedli T (2006) The pharmaceutical plant of the future. In: Friedli T, Kickuth M, Stieneker F, Thaler P, Werani J (eds) Operational excellence in the pharmaceutical industry. ECV – Ed.-Cantor-Verl, Aulendorf

Report of the PAT Team and Manufacturing Science Working Group (2004) Innovation and continuous improvement in pharmaceutical manufacturing – pharmaceutical CGMPs for the 21st century. www.fda.gov. Retrieved January 2010

Woodcock J (2011) Presentation, meeting of the FDA science board, November 16th, FDA, Regulation of drug quality: new challenges. www.fda.gov. Retrieved 20 January 2013

Chapter 4
The Current State of Operational Excellence Implementation: 10 Years of Benchmarking

Thomas Friedli, Nikolaus Lembke, Uli Schneider, and Saskia Gütter

More and more pharmaceutical companies report success stories about their way to Operational Excellence (OPEX). First implemented only 10 years ago, the history of OPEX in the pharmaceutical industry is relatively short (cf. Chap. 3); Toyota, for example, looks back on 70 years of experience. Pharma's way to OPEX methods and tools was paved by rising cost pressure, the end of the traditional blockbuster business model and the productivity crisis in pharmaceutical R&D (cf. Chap. 6), in combination with a push from regulatory authorities (cf. Chap. 5). The pharmaceutical industry has invested a lot of time and resources in building up some of the most sophisticated OPEX management frameworks across industries (cf. especially part B of this book). It seems a good point in time to reflect on achievements made over the last 10 years – is it possible to measure the impact of made efforts?

Since 2004, the University of St.Gallen has been conducting an international benchmarking project that deals with the implementation of OPEX in the pharmaceutical industry. As of May 2013, the St.Gallen OPEX database includes data of 248 pharmaceutical manufacturing sites (API, Formulation & Packaging, and Biotech) from more than 90 different companies that range from small and medium-sized companies to Big Pharma. The following chapter presents results from the analysis of 10 years of benchmarking data (2003–2012). This comparison is presented in reference to the two sub-systems of the St.Gallen OPEX model: (1) the technical sub-system, consisting of the building blocks Total Productive Maintenance (TPM), Total Quality Management (TQM), Just-in-Time (JIT), and (2) the social sub-system, represented by the Effective Management System (EMS) (see Chap. 2). The level of OPEX implementation is determined by two indices: First, the median of enablers (Defined as "methods and tools leading to better performance") and second, by the corresponding performance, which is assessed

T. Friedli (✉) • N. Lembke • U. Schneider • S. Gütter
Institute of Technology Management, Chair of Production Management, University of St. Gallen, Dufourstrasse 40a, St.Gallen, St.Gallen 9000, Switzerland
e-mail: thomas.friedli@unisg.ch; nikolaus.lembke@unisg.ch; uli.schneider@unisg.ch; saskia.guetter@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_4, © Springer-Verlag Berlin Heidelberg 2013

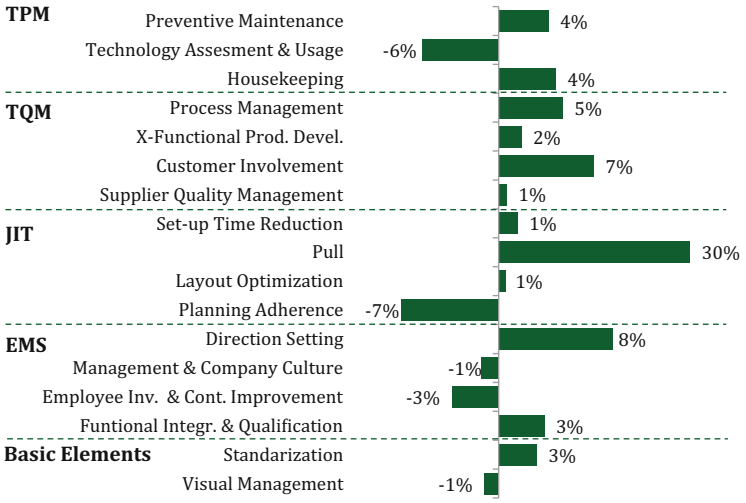


Fig. 4.1 Average growth rate of enablers over the last 10 years (Comparison of median implementation level in 2003 and 2012)

by calculating the median of Key Performance Indicators (KPIs) ("metrics for tracking progress and comparing with other companies"). The enablers and KPIs can be found in the latest version of the 2013 OPEX questionnaire in the appendix of this book (the enabler definitions are provided in the appendix of this chapter). The final section of this chapter, "enabler implementation – taking a closer look", then reviews recent scientific findings.

The Development of Enabler Implementation

Since 2003, the St.Gallen OPEX data base has been continuously enlarged by adding more and more participants providing information on general company data, KPIs and so-called enabler implementation evaluations, indicating the undertaken efforts for implementing OPEX. This data allows us to examine advancements in the pharmaceutical industry over the last 10 years, improving our understanding of the industry's activities in pursuing OPEX. Based on self-reports, implementation of enablers are assessed on a Likert scale from 1-*not at all* to 5-*completely*. Figure 4.1 shows the averages of the median growth rates of the different enabler categories between 2003 and 2012.

Overall, aggregated categories show only minor changes in the level of implementation. Therefore, the following section will analyze corresponding sub-categories.

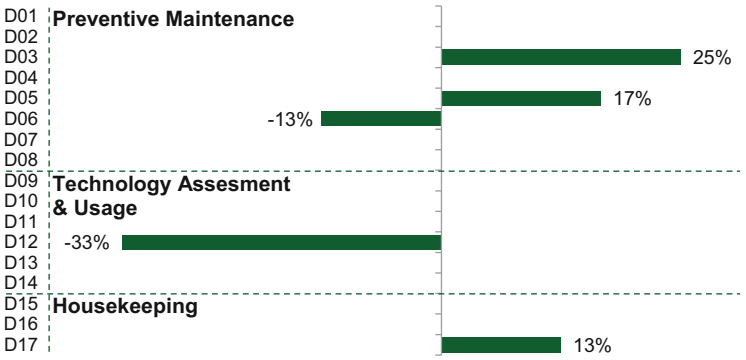


Fig. 4.2 Growth rate of TPM enablers between 2003 and 2012 (Comparison of medians)

Total Productive Maintenance

The first element of the technical sub-system – TPM – has been described in Chap. 2. The major principles considered in the St.Gallen OPEX model are Preventive Maintenance, Technology Assessment & Usage, and Housekeeping.

A first look at the enabler implementation on the level of these aggregated categories might lead to the conclusion that only little efforts have been made to improve TPM. However, a closer look at single enabler level reveals that the focus on single actions has changed. While some actions and tools received more attention, others decreased in importance. Figure 4.2 gives an overview of the changes in the medians implementation levels of different TPM enablers. Only enablers that show striking changes in their implementation level will be discussed. A complete list and detailed description of the enablers can be found in the appendix of this chapter.

Preventive Maintenance programs help the industry to ensure that processes run continuously and stably. The implementation of this enabler category has grown by 4 % over the last decade. In detail, the industry put more emphasis on the relationship between better maintenance and better quality (D03: +25 %), and the continuous improvement and optimization of existing maintenance programs (D05: +17 %) in 2012 compared to 2003. In contrast, assistance of machine operators from the maintenance department to execute preventive maintenance activities declined (D06: −13 %).

The implementation level of TPM's second pillar – Technology Assessment and Usage – slightly decreased since 2003 (−6 %). Although pharmaceutical companies use new technologies and state of the art machines, they neither expanded their focus on proprietary process technologies, nor did the number of patents on established processes increase. The major change in this category is that pharmaceutical companies increasingly rely on vendors for all of their equipment instead of developing their own solutions (D12: −33 %).

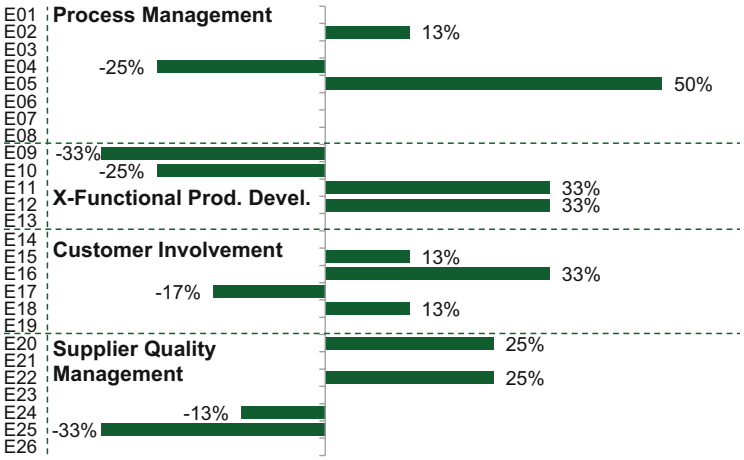


Fig. 4.3 Growth rate of median TQM enablers between 2003 and 2012

The implementation of Housekeeping activities has been high ever since benchmarking started in 2003; in 2012, it amounted to a median implementation degree of 82 %. Although overall activities have not changed too much, a closer look reveals that compared to 2003, efforts with regards to methodology were higher in 2012 and more checklists used than before (D17: +13 %).

Total Quality Management

In our OPEX model, the major Total Quality Management principles considered are Process Management, Cross Functional Product Development, Customer Involvement, and Supplier Quality Management (Fig. 4.3).

Process Management deals with the continuous improvement of processes by means of measuring, documenting, and analyzing. Although the overall Process Management shows no changes, the continuous measuring of activities within the production processes (E02) increased by 13 % in the observed period. An even more impressive change can be seen in the application of Statistical Process Control (E05), which increased by 50 % between 2003 and 2012. Yet, the industry still seems to struggle in defining responsibilities for planning management and improvement of their processes (E04: −25 %). After all, Process Management is well implemented. This is likely due to GMP requirements. Another important component of TQM is Cross Functional Product Development, to guarantee that the processes are designed for Quality (manufacturability). Over the last 10 years, communication and exchange between R&D and manufacturing engineering specialists has been reduced (E09: −33 %, E10: −25 %), despite the Quality by Design (QbD) initiatives that have been intensively discussed throughout the

pharmaceutical industry (we still believe that we will see a positive outcome of QbD in the near future, cf. Chap. 16). Yet, compared to 2003, participants in 2012 pushed for faster product launches (scale ups) (E11: +33 %) and less delays in product launches (E12: +33 %). There is a certain trade-off between this "time to market" focus and the resources and time needed to develop a stable, cross-functional production process.

One of our TQM principles deals with Customer Involvement. In 2012, participants appreciated the key role of customer involvement more than 10 years ago, as indicated by more regular customer requirements surveys (E16: +33 %), more frequent customer feedback on quality and delivery performance (E15:+13 %) and an increasing pursuit of an on-time delivery philosophy (E18: +13 %). Yet, the industry reduced satisfaction survey activities (E17: −17 %). Overall, the implementation level of the Customer Involvement enabler was already high in 2003, at a level of 72 %, and has slightly increased since then by 7 %.

Another influential and critical business practice impacting the quality of output is Supplier Quality Management. Since quality aspects can be very costly and time-consuming, it is vital to establish a strong relationship with suppliers. Even though the observed increase of 1 % in the implementation of the respective overall enabler seems insignificant, efforts have been made in this field. For instance, the focus on quality in supplier selection rose by 25 % (E20). Additionally, the industry now relies much more on suppliers that have been validated (E22: +25 %). In turn, opposing trends to the positive effects in the Supplier Quality Management are the more rigorous control of the whole shipment (E25: −33 %) or inspections of incoming materials are usually not performed in proportion to the past quality performance or type of supplier (E24: −13 %). A reason for this could be the impact of reported issues with supplier quality and a strong focus of regulatory agencies on the legal responsibility of drug application owners with regards to the quality of products.

Just-In-Time

In the St.Gallen model, Just-in-Time (JIT) consists of Set-up Time Reduction, Pull System, Layout Optimization and Planning Adherence (see Chap. 2) (Fig. 4.4).

Increasing emphasis on set-up time reductions results from companies' higher JIT awareness: The benchmark reveals an increase of 33 % in activities in continuous Set-up Time Reduction (F01), and an increase of 17 % in the optimization of Set-up scheduling (F05). However, activities for set-up training (F03: −17 %) and lower batch sizes have been reduced (F04: −25 %) since 2003.

The pull system (F08), in which customer demand triggers production, shows the biggest increase within the JIT category. In the last 10 years, the implementation level of this enabler increased by remarkable 200 %. This development is in line with the increased implementation of on-time delivery by suppliers (F12:+17) and demand-orientated JIT delivery (F13: +50). However, participants' production

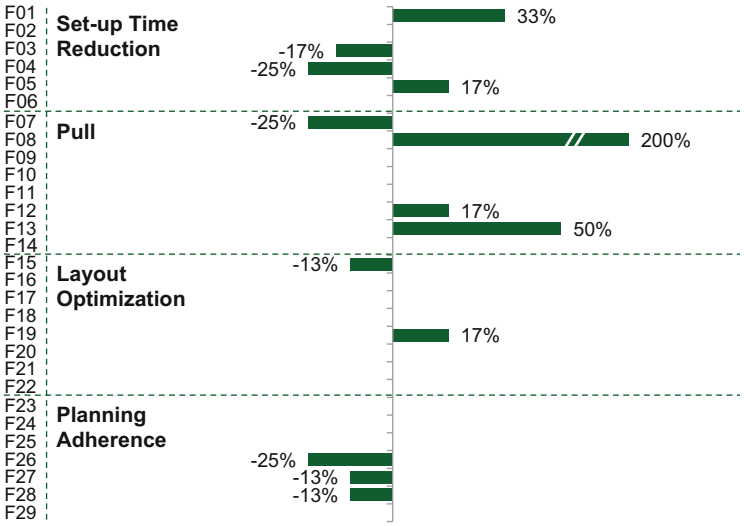


Fig. 4.4 Growth rate of median JIT enablers between 2003 and 2012

schedules do not allow capacity for backlogs due to interruptions in the productions (F07: −25 %). In terms of layout optimization, trends are contradictory: while processes for products with the same requirements were collocated (F19: +17 %), focus on the reduction of material handling activities and storage by better layouts dwindled (F15: −13 %). For enabler implementation in the Planning Adherence category negative trends can be observed. Compared to 2003, in 2012 data was to a smaller extent shared with customers (F26: −25 %), production capacities were not leveled out (F27: −13 %), and shift flexibility lost importance in production (F28: −13 %).

Effective Management System

The Effective Management System (EMS) is another key component of the St. Gallen OPEX model. It is regarded as essential to establish a sustainable OPEX system in a manufacturing site. EMS is determined by Direction Setting, Management Commitment & Company Culture, Employee Involvement & Continuous Improvement as well as Functional Integration & Qualification (Fig. 4.5).

Compared to 2003, alignment of the site vision with OPEX as well as the communication of both the vision and its relationship to OPEX was intensified in 2012 (G01: +25 %). We can see the same for management focus on, and prioritization of, crucial success factors for production (like low cost, delivery, or quality) (G06: +25 %).

Since an aligned corporate culture is an important prerequisite for a sustainable OPEX implementation, particular importance is given to the employees. However,

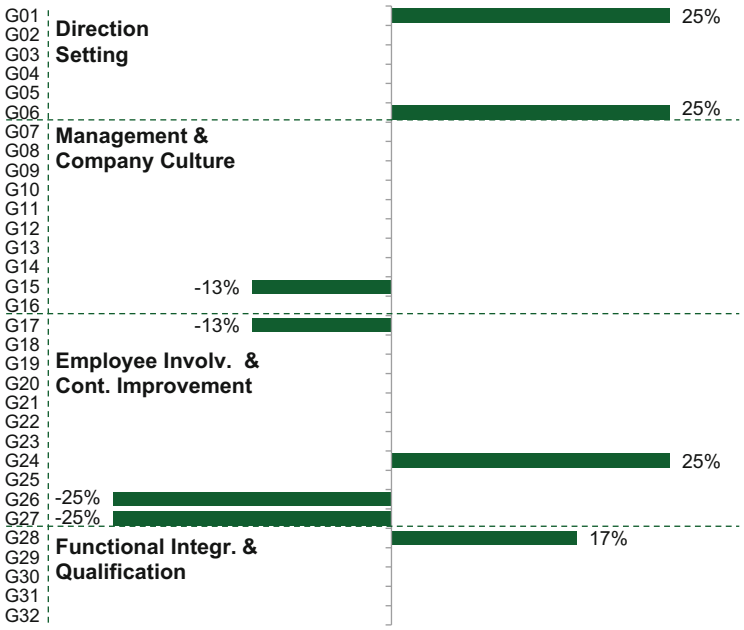


Fig. 4.5 Growth rate of median EMS enablers between 2003 and 2012

we observed reduced encouragement of employees' striving for continuous improvement (G15: −13 %). This shows how difficult it can be to establish a sustainable corporate identity in the context of operational excellence.

This development is paralleled in the category of employee involvement and continuous improvement: In 2012, less methods and tools were used to realize a Continuous Improvement Process (G17: −13 %). Though cross-functional teams became more frequent (G24: +25 %), teamwork and its organizational integration was cut back (G26/G27: −25 %). The increased use of cross-functional teams was also reflected in the increased implementation of its prerequisite, i.e., additional Cross-skilled Training of staff (G29: +17 %).

Basic Elements

Basic Elements are crucial components of the holistic model – they cannot be uniquely assigned to one of the building blocks, but support all of them. Sub-categories of the Basic Elements are Standardization and Visual Management (Fig. 4.6).

Compared to 2003, participating sites in 2012 extended their use of documented operating procedures to standardize their processes (H02: +25 %), and in the case of best-practice processes, processes were increasingly rolled-out throughout the

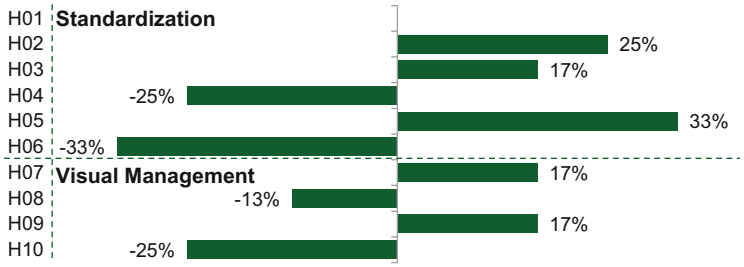


Fig. 4.6 Growth rate of median Basic Element enablers between 2003 and 2012

whole site (H03: +17 %). However, consistent functional descriptions of processes were limited, as they did not meet expectations regarding the reduction of the vocal training time for new employees (H04: −25 %). Yet, Standardization in the industry goes beyond processes and practices, and therefore sites increasingly relied on standardized machines and equipment in order to achieve high up-times in 2012 (H05: +33 %). But the development of enabler H06 shows that standardization is not cost driven (−33 %).

Visual Management is a tool to create transparency which, in turn, motivates employees. In 2012, annual targets (H07: +17 %) and current performance charts (H09: +17 %) were displayed and accessible to all shop floor employees. Nevertheless, it seems that full transparency through showing current schedule compliances is not intended (H10: −25 %). Another declining trend in this category concerns the easy access to, and the visibility of, technical information, which was found to be reduced in 2012 compared to 2003 (H08: −13 %).

Interim Conclusion

A closer look on the different categories of TPM, TQM, JIT, and EMS in the preceding section has revealed that notable developments and improvements have been attained in the last 10 years. From a TPM perspective, one of the major advancements is the acknowledgment of the positive relationship between maintenance and quality.

One of the most important steps that has been taken in the previous years is an expansion of measuring activities and the use of tools like Statistical Process Control. Knowledge derived from precise measuring is essential in quality terms and fosters a science-driven approach to pharmaceutical manufacturing. JIT production in 2012 seems to be predominantly driven by aligning processes to the customer and by implementing pull production. Thereby, scrap is decreased whilst processes can be better coordinated. On a cultural level, the major change is the promotion of OPEX with all its aspects. In contrast, reduced efforts to implement OPEX in employee structures (i.e., in the form of team work) has led to a decreased acceptance of OPEX amongst employees.

The observed developments of enablers correspond to changes in the performance of manufacturing sites, which will be discussed in detail in the next section of this chapter.

The Development of Performance

The St.Gallen OPEX Benchmarking assesses a set of production-specific KPIs that are closely linked to the technical sub-system (comprising TPM, TQM and JIT), as well as KPIs that are related to the EMS. The benchmark shows an improvement in performance over the last 10 years in the pharmaceutical industry in terms of both effectiveness and efficiency.

Total Productive Maintenance Performance

The core idea of TPM is to maximize effectiveness of equipment used in production (see Chap. 2) at moderate costs. Therefore, the main focus of TPM optimization does not lie on a short-term reduction of costs of equipment and maintenance; rather, TPM is concerned with the optimal support of production processes based on stable and reliable equipment. Thereby, TPM provides the basis for improvements in efficiency. TPM does not only focus on technical aspects such as equipment reliability, but also involves engaging all employees in maintenance-related activities.

Looking at the technical aspect, it is clear that equipment breakdowns and losses[1] in the manufacturing process result in different kinds of waste and thus create no value but costs. The overall equipment effectiveness (OEE) is an appropriate KPI to reveal hidden costs and to identify losses (Nakajima 1988; Jonsson and Lesshammar 1999). Nakajima (1988) introduced OEE as a measure of TPM to analyze the interrelated effects of plant availability, performance and quality. Within this context, OEE is considered as an operational measure of internal efficiency. We use OEE to ensure a valid and distinct measurement of equipment usage and stability. The OEE also indicates efforts in continuous improvement of equipment. In the St.Gallen OPEX Benchmarking, the OEE is calculated as a product of (OEE-) Availability, (OEE-) Performance, and (OEE-) Quality (see also Nakajima 1988). Between 2003 and 2012 the OEE score increased by 53 %. In 2012, the median score of the pharmaceutical industry in production and

[1] Robinson and Ginder (1995) define the following losses: (1) downtime due to machine breakdown; (2) time required for set-up and adjustments; (3) time or cycles lost to inefficient start-up; (4) time or cycles lost to tooling; (5) time or cycles lost to minor stoppages; (6) operating at less than ideal speed; and (7) producing defective or off-spec product that is rejected, requires rework or repair, or is sold at a lower price.

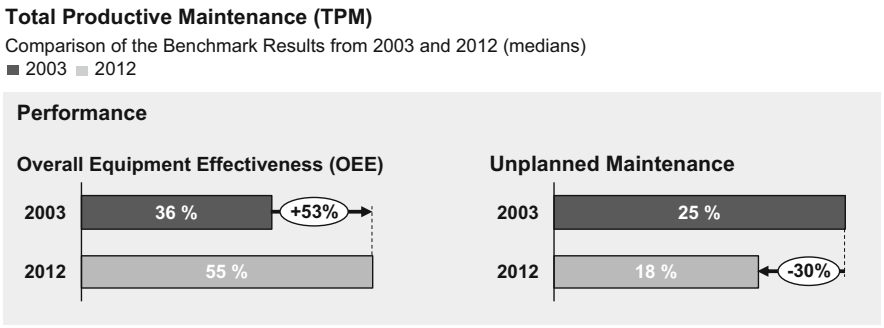


Fig. 4.7 Growth rate of median TPM performance between 2003 and 2012

packaging was 55 %. A closer look at the OEE, however, reveals that while (OEE-) Performance and (OEE-) Quality are on a rather high level, Availability shows room for improvement. The OEE increase goes hand in hand with a decrease in Unplanned Maintenance of nearly 30 % between 2003 and 2012 (see Fig. 4.7). While the Unplanned Maintenance score was 25 % in 2003, a decrease to 18 % could be observed in 2012. Nevertheless, most pharmaceutical companies still need a more comprehensive maintenance program to further reduce Unplanned Maintenance. This would be beneficial as the reduction in Unplanned Maintenance as a percentage of the overall time spent for maintenance work has a positive impact on the overall availability of the machines. In addition, we can observe a positive influence on the quality of products and the workplace safety.

As described in the enabler section, the overall score for TPM did not significantly change between 2003 and 2012. However, key components like Preventive Maintenance and Housekeeping did show improved levels of implementation in 2012, which can explain the improvements pharmaceutical companies have achieved in the field of TPM over the last 10 years. Stably running machines do have a positive impact on other sub-systems such as TQM (e.g., Rejected Batches) and JIT (e.g., Service Level). Positive effects of TPM on subsequent building blocks of the technical sub-system are discussed in the following section.

Total Quality Management Performance

TQM is a holistic quality philosophy. It is based on the assumption that costs for correcting quality activities and complaints management exceed costs for preventive quality activities like continuous improvement and the involvement of suppliers (Hackman and Wageman 1995).

As shown in the enabler section, efforts with regards to Process Management, the application of Statistical Process Control, and a better understanding of customer requirements have been increased over the last 10 years. This reflects in a

positive development of the Complaint Rate Customer.[2] It has decreased from 1 % in 2003 to 0.57 % in 2012. The Rejected Batches score (given as percentage of all batches produced) stayed at 0.75 % from 2003 to 2012. To achieve a higher score, further activities need to be considered; a higher availability level with less breakdowns could be one of these. However, process quality itself must be improved. Further increasing the rate of equipment on the shop floor that is under Statistical Process Control could prove beneficial for process quality. Yet, it is not only technical aspects that are important; notoriously underestimated levers are people's knowledge and leadership that empowers employees in their daily work. Training employees and delegating responsibility for planning, managing and improving processes to them could be beneficial. Quality should be the joint responsibility of employees from different departments and hierarchical levels, and not an isolated task of the quality department.

Quality is also affected by suppliers. A better integration of suppliers into the company could have a significant impact on quality. The Complaint Rate Supplier[3] shows an increase from 1 % in 2003 to 2 % in 2012. This increase may have been caused by more rigorous controls of whole shipments (see respective enabler, p. 39 of this book) due to reported issues as well as by the influence of regulatory administration. The fact that pharmaceutical manufacturer require higher quality to get closer to a zero-failure quality can lead to a higher Complaint Rate Supplier, too. The increased focus on quality in supplier selection, and the fact that more pharmaceutical manufacturer rely on suppliers which have been validated (see enablers, p. 39 of this book), is positive and shows that the pharmaceutical industry is on a good way in terms of long-term supplier management. And this is getting more and more important. Given that the average number of active suppliers in 2012 amounted to 180, a well-managed supplier base is the prerequisite for improvements in quality and productivity (Fig. 4.8).

Just-In-Time

A guiding principle of JIT is the continuous reduction of overproduction, unnecessary inventory and inconsistencies by creating a pull production with reduced set-up times and an optimized layout. As inventories decrease in an OPEX environment, the number of turns over a certain period of time should increase. We take these inventory turnovers as main measures of JIT performance and also take a look at the Service Level. This allows us to observe how OPEX enablers affect performance.

[2] We define Complaint Rate Customer as "Number of justified complaints as a percentage of all customer orders delivered."

[3] We define Complaint Rate Supplier as "Number of complaints as a percentage of all deliveries received (from your supplier)."

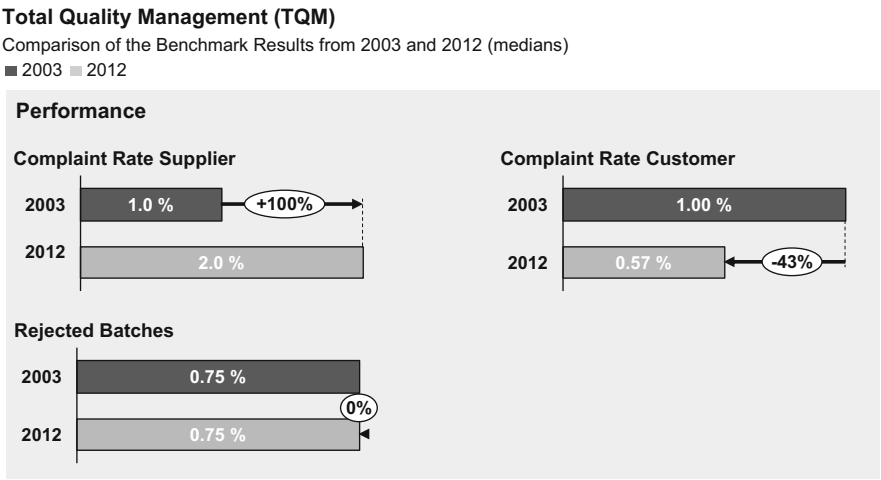


Fig. 4.8 Growth rate of median TQM performance between 2003 and 2012

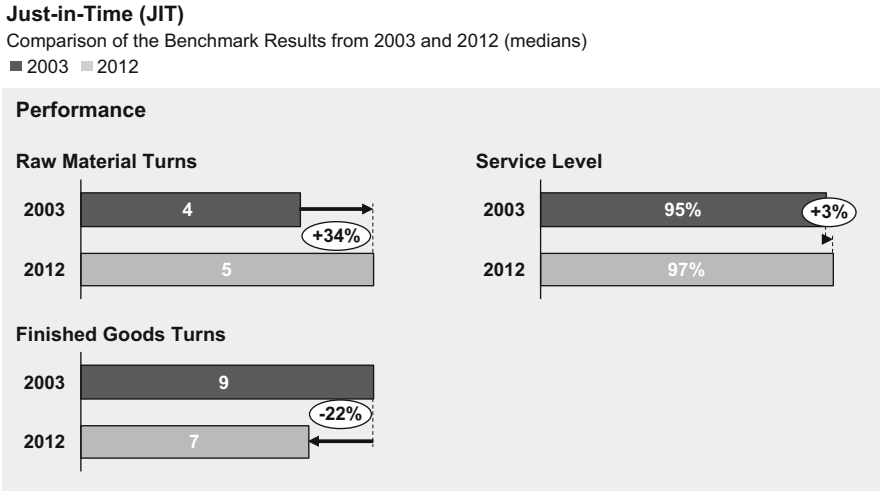


Fig. 4.9 Growth rate of median JIT performance between 2003 and 2012

Looking at the median score of performance of the overall sample, a change in Raw Material Turns[4] from 4 turns per year in 2003 to 5.35 turns per year in 2012 can be seen (see Fig. 4.9). In the same period, Finished Good Turns[5] decreased from

[4] We define Raw Material Turns as "Annual cost of raw materials purchased divided by the average raw material inventory."

[5] We define Finished Good Turns as "Annual cost of goods sold divided by the average finished goods inventory."

9 to 7 turns per year. Taking a look at the performance of high performing[6] production sites only, we can observe a much higher 2012 performance with a median of 7.1 Raw Material, and even 16.1 Finished Good Turns per year. This parallels the higher implementation level of JIT in high performing sites (10 % higher than the median sample level).

Within the pharmaceutical industry the most important increase is the stronger use of a Pull system (Kanban squares, containers or signals) for production control, in which customer demand triggers production. Within the last 10 years, the Pull enabler increased by 200 %. A JIT system aims to reduce the amount of pre-process and post-process inventories as well as the in-process inventory. Kanbans especially are used to control work-in-progress (WIP), production, and inventory flow (Ohno 1988). We can observe that high performing sites have WIP of 12.40 turns per year while the median is only 8 turns per year. A higher level of turn goes hand in hand with less inventories in the process, which leads to a reduced danger for products to be damaged during handling and storage. However, as evidenced by the median calculation, there is room for improvement on the performance side. Companies more and more try to deliver their customers with a demand-oriented JIT instead of a stock-oriented approach (see rise of enabler F13); this effort can be seen in the improvement of the Service Level.[7] The median Service Level score increased from 95 % in 2003 to 97 % in 2012. This higher score in perfect order fulfillment (i.e., order fulfilled in the right quantity and quality) parallels a lower score in Complaint Rate Customer, reflecting the increased quality level companies delivered to their customers 2012.

In the enabler section, the St.Gallen OPEX Benchmark revealed an increase of 33 % in Continuous Set-up Time Reduction and 17 % in the optimization of the Set-up Scheduling between 2003 and 2012. As we can observe the trend to a smaller batch size and a greater number of batches (increase of 67 % in the number of batches in packaging (median calculation) from 2009 to 2012) and a corresponding higher number of changeovers, this increased effort in Set-up Reduction and optimization in Set-up Scheduling is indeed needed. JIT is also concerned with the cooperation between supplier and customer (Ohno 1988). As we can observe from the TQM, Supplier Integration needs be extended.

JIT with the demand-orientated pull of products and Kanban as a method for the realization of JIT as well as the organization of work help to reduce overproduction and inventory (see Chap. 2). However, other industries have shown that activities are only beneficial if reductions derive from sustainable process improvements instead of being achieved by simply driving down inventories without stabilizing the processes. This requires highly controlled processes in an organized, well-maintained and clean work environment. Therefore, a sophisticated TPM and

[6] Definition of high performers see Chap. 2.

[7] We define Service Level as "Perfect order fulfillment (percentage of orders shipped in time from your site (+/− 1 days of the agreed shipment day) and in the right quantity (+/− 3 % of the agreed quantity) and right quality) to your customer."

TQM system is needed from the technical perspective, but the right management has to be in place, too. Thus, the subsequent section takes a look at the developments of the Effective Management System.

Effective Management System

The St.Gallen OPEX questionnaire's EMS performance assesses the performance of companies' management systems on their way to OPEX. As the use of rating scales has been criticized for being based on subjective perception only, our model uses KPIs to operationalize EMS performance.

In general, most participating sites organize production employees into production area teams. For each team, one dedicated team member is responsible for supervisory tasks. Employee involvement and active delegation of authority are crucial aspects to improve OPEX. This is reflected by the recent development towards flatter organizations with fewer layers and higher span of control. Reducing layers and empowering employees on all levels are often sought to achieve in conjunction. At the same time, pharmaceutical companies tried to work more in cross-functional teams in 2012 (see enabler G24: +25 % since 2003). This leads to a higher level of cross-trained employees, which better understand the entire process and are more responsive to changing needs and demands of customers. Training employees is critical in this context, and this is evidenced by an increase in Training Days. Training Days have more than doubled over the last 10 years: While in 2003 employees were trained for 3 days a year, in 2012 employees received 7.7 days of training a year. This also leads also to a lower Level of Unskilled Employees: In 2012, only 4 % of employees had no work-related qualification, while in 2003 the score had been 10 %. A high level of qualification is important to achieve a continuous improvement culture and to obtain a certain degree of flexibility. Each production worker is expected to be a multi-skilled operator, who has the ability to run multiple machines, to do his own quality control, to solve quality problems, and to fulfill a variety of jobs involving a variety of skills and talents.

Continuous improvement is only possible with the contribution of employees. Thus, workers need to feel appreciated and valued. We use Absenteeism and Fluctuation as measures of employee satisfaction. Absenteeism, measured as the percentage of the total working time an employee is absent, decreased from 4 % in 2003 to 3.3 % in 2012. Fluctuation,[8] however, increased by about 50 % from 5 % in 2003 to 7.5 % in 2012. If we disrecard economic aspects, we can assume that a higher level of employee involvement and continuous improvement would be beneficial for OPEX. As we can see from the enabler sections, especially the increased existence of a site vision and increased alignment with corporate vision

[8] We define fluctuation as "Employees leaving per year your site due to terminations, expired work contracts, retirements etc. as a percentage of all employees."

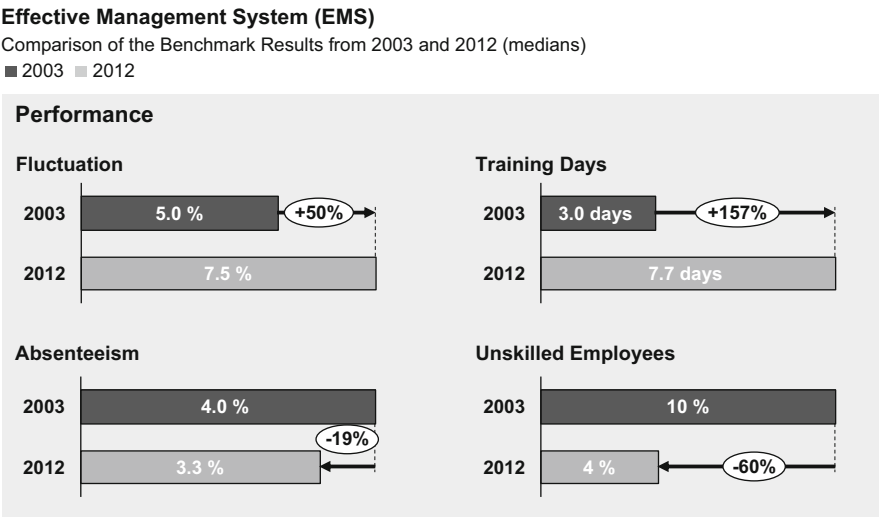


Fig. 4.10 Growth rate of median EMS performance between 2003 and 2012

and strategy (G01: +25 %), and an increased management's focus on identifying crucial success factors of production (G06: +25 %) seemed to have had a positive impact on the EMS. The pharmaceutical industry is on a good way to provide the right framework for OPEX (Fig. 4.10).

So far, we have taken a look at the development of the level of OPEX implementation in the pharmaceutical industry over the last 10 years, and related effects on technical and management performance. We proceed with presenting new scientific findings on enablers in the following section.

Enabler Implementation: Taking a Closer Look

Decisions on which enabler to implement or to focus on are often rather based on gut feelings than led by facts. We tried to determine if there are visible patterns of enabler implementation by taking a closer look at the manufacturing strategy of the single plants. As a result, we could identify four distinct strategic groups. For each of these groups the implementation level of single enablers and their correlations are analyzed in depth and results are compared.

The first group emphasizes all four investigated strategic priorities (Flexibility, Quality, Service Level and Costs), leading us to name it *"do all"*. Implementation levels for the *do all* group range between 56 % for Layout Optimization and 90 % for Management Commitment and Company Culture. For the *do all* group, the five enablers with the highest level of implementation are: Management Commitment and Company Culture, Housekeeping, Process Management, Customer Involvement,

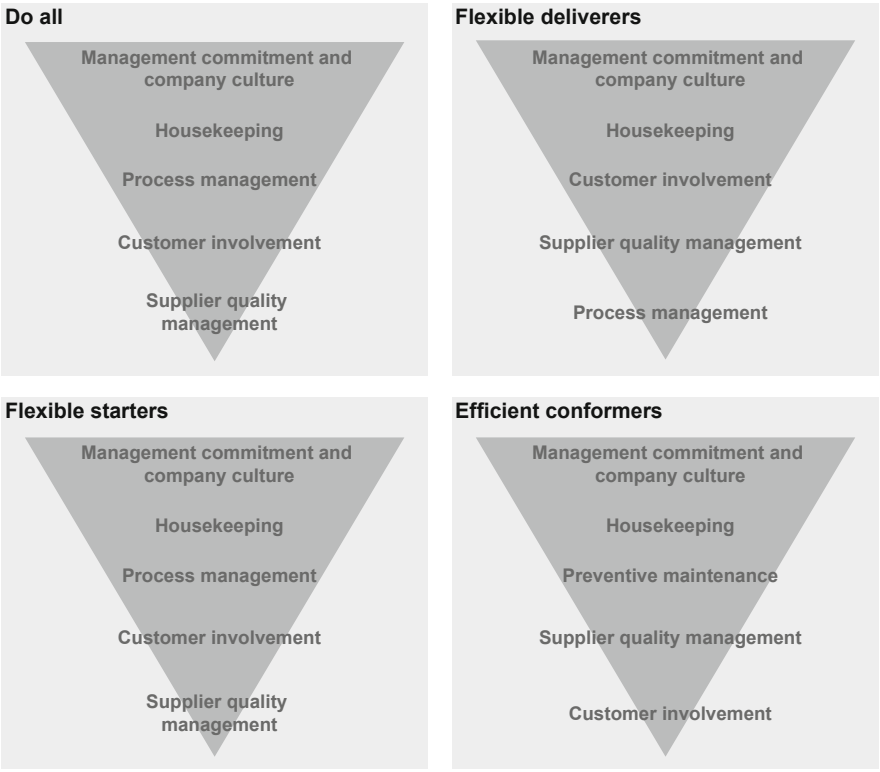


Fig. 4.11 Implementation of the five highest enablers in the four strategic groups

and Supplier Quality Management. The second group focuses on delivery and flexibility and is therefore named *"flexible deliverers"*. Implementation levels range between 54 % for Set-up Time Reduction and 82 % for Management Commitment and Company Culture. The group *flexible deliverers* prioritizes the following enablers: Management Commitment and Company Culture, Housekeeping, Customer Involvement, Supplier Quality Management, and Process Management (Fig. 4.11).

The third group, *"flexible starters"*, has a low emphasis on the development of competitive priorities, with the highest value for Flexibility. Implementation levels range between 42 % for Layout Optimization and 79 % for Management Commitment and Company Culture. The *flexible starters* have the highest implementation levels for: Management Commitment and Company Culture, Housekeeping, Process Management, Customer Involvement, and Supplier Quality Management. The fourth group, *"efficient conformers"*, has high emphasis on cost and also on quality. Implementation levels range between 45 % for Layout Optimization and 80 % for Management Commitment and Company Culture. For the group *efficient conformers* the implementation of the following five enablers is rated highest: Management Commitment and Company Culture, Housekeeping, Preventive Maintenance, Supplier Quality Management, and Customer Involvement.

For all four groups the best-implemented enabler is Management Commitment and Company Culture, followed by Housekeeping. Supplier Quality Management, Process Management, and Customer Involvement are among the enablers with the highest implementation levels for each but the fourth group, *efficient conformers*. For *efficient conformers* the enabler Process Management is replaced by Preventive Maintenance. A similar picture can be seen for the five enablers that show the lowest implementation in each group. Except for *flexible deliverers,* the enabler Layout Optimization is the least implemented. The second lowest implementation level (respectively the lowest for *flexible deliverers)* can be found with the enabler Set-up Time Reduction. The enablers Employee Involvement and Continuous Improvement, Technology Assessment and Usage, as well as Cross-functional Product Development show low levels of implementation, too.

This shows that independent of the strategic group, the same enablers are regarded as important, though they vary in their extent of implementation. The basis for a successful OPEX implementation seems to be the same for all pharmaceutical production strategies. The same holds true for the correlations between enablers; some correlations can be observed in each of the four groups.

One is the association of Layout Optimization and Pull Production, which are strongly and positively correlated in all four groups, and especially so for *do all*s. Nevertheless, the implementation level of Pull Production has changed faster than has that of Layout Optimization.

Though in general positively correlated, effect sizes for the association of Set-up Time Reduction and Process Management vary greatly between the single groups. The correlation coefficient in the *efficient conformers* group is rather high, for the *do all* group it is still moderate whereas the values for the *flexible deliverers* and the *flexible starters* are already weak. Obviously, *efficient conformers,* with their emphasis on high quality and low costs, benefit more from the positive impact of Set-up Time Reduction than the other groups do.

Correlation coefficients for Management Commitment and Company Culture and Functional Integration and Qualification vary, too. In general it can be stated that an engaged management and a common culture slightly foster the integration and qualification of employees in a plant, independent of the competitive objective. For Management Commitment and Company Culture and Preventive Maintenance the correlation coefficients are rather low. Nevertheless, a weak correlation exists between a committed management and the implementation of preventive maintenance. Obviously, the implantation of a preventive approach to maintenance is at least somewhat affected by the commitment and mind-set of management and employees.

Contrasting an enabler's implementation level (and thus the importance it has in a company) with the influence it has according to the correlations allows for further insights. Management Commitment and Company Culture, which has a high implementation level, could positively influence the implementation of two other enablers in all four groups. Consequently, a committed management that promotes a common company culture is not only a prerequisite for the implementation of other enablers, but also supports the process of implementation.

The other correlations shared by all four groups mainly involve enablers with low levels of implementation. The least implemented enablers do not seem to be regarded as important when starting with the OPEX implementation. But their correlations with other enablers show that they can have positive impacts during an advanced stage of OPEX implementation. Therefore, it is necessary to put more effort into the implementation of those enablers after the first successes with other enablers. They can then unfold their positive impact and be a promoter for a successful OPEX implementation.

Summary and Outlook

The illustrated results are an excerpt of the on-going St.Gallen Operational Excellence Benchmark and provide an overview of the development in the industry. The results we presented in our 2010 book "The pathway to Operational Excellence" indicated that the pharmaceutical industry was on the right path. Back then, we had not observed any grand-scale developments, but continuous improvement steps across the practices TPM, TQM, JIT and EMS. In particular, the effectiveness blocks TPM and TQM had seemed to be in the focus of most pharmaceutical companies while they now more work on efficiency (JIT).

As the pharmaceutical industry is facing increasing challenges, like a rising complexity the time has come to realize the potential of sustainably implementing OPEX. Because of the complex and inter-connected nature of integrated production systems, adjustments of one sub-system affect all of the other sub-systems. In conclusion, there is more potential in TPM and TQM performance that could and should be activated, while keeping mind interdependencies between sub-systems and in their impact on performance. We have shown that over the past 10 years, notable improvements have been attained within the different categories of TPM, TQM, JIT, EMS. From a Total Productive Maintenance perspective, one the major advancements is the increased awareness of the relationship between good maintenance and good quality. But as evidenced by the (OEE-) Availability in the OEE calculation, there is still room for improvement regarding breakdowns (unplanned downtimes) and set-up downtime availability. One of the most important steps which has been taken in the previous years is an expansion of measuring activities and the use of tools such as Statistical Process Control. The knowledge which can be derived from precise measuring is essential in terms of quality terms and fosters a science of manufacturing.

The majority of OPEX implementations has focused on improving manufacturing operations, without an accompanying focus on the rest of the supply chain, such as procurement. Without focusing on the entire supply chain, however, benefits will be limited; long lead times and high inventories within external logistics pipelines can cancel out OPEX successes in operations. JIT production so far has been predominantly driven by aligning the processes to the customer and by implementing pull production.

The major driver on a cultural level is the promotion of OPEX with all its aspects and the increasing effort in training. In contrast, the implementation of team work has decreased which led to decreasing acceptance amongst the employees. Taking a closer look at the enablers, data shows for all four described groups that the implementation of the enabler Management Commitment and Company Culture is highest followed by Housekeeping.

For the future there are several aspects of performance improvements. First, the set of KPIs should cover those aspects that indicate potential future improvements. Second, instead of functioning as passive control only, the measure itself should identify and generate continuous improvements. This is especially true for operational measures focusing on non-value adding activities, such as OEE. According to Ishikawa (1982), data should not be collected to provide the basis for nice figures, but to create a basis for action and the development of processes. Collecting the right data and using it as an objective performance indicator in a continuous improvement process will prove to be highly beneficial to pharmaceutical companies.

Appendix

Total Productive Maintenance

Preventive maintenance	
D01	We have a formal program for maintaining our machines and equipment
D02	Maintenance plans and checklists are posted closely to our machines and maintenance jobs are documented
D03	We emphasize good maintenance as a strategy for increasing quality and planning for compliance
D04	All potential bottleneck machines are identified and supplied with additional spare parts
D05	We continuously optimize our maintenance program based on a dedicated failure analysis
D06	Our maintenance department focuses on assisting machine operators perform their own preventive maintenance
D07	Our machine operators are actively involved into the decision making process when we decide to buy new machines
D08	Our machines are mainly maintained internally. We try to avoid external maintenance service as far as possible

Technology assessment and usage	
D09	Our plant is situated at the leading edge of new technology in our industry
D10	We are constantly screening the market for new production technology and assess new technology concerning its technical and financial benefit
D11	We are using new technology very effectively
D12	We rely on vendors for all of our equipment
D13	Part of our equipment is protected by the firm's patents

(continued)

Technology assessment and usage	
D14	Proprietary process technology and equipment helps us gain a competitive advantage
Housekeeping	
D15	Our employees strive to keep our plant neat and clean
D16	Our plant procedures emphasize putting all tools and fixtures in their place
D17	We have a housekeeping checklist to continuously monitor the condition and cleanness of our machines and equipment

Total Quality Management

Process management	
E01	In our company direct and indirect processes are well documented
E02	We continuously measure the quality of our processes by using process measures (e.-g. On-time-in-full delivery rate)
E03	Our process measures are directly linked to our plant objectives
E04	In our company there are dedicated process owners who are responsible for planning, management and improvement of their processes
E05	A large percentage of equipment on the shop floor is currently under statistical process control (SPC)
E06	We make use of statistical process control to reduce variances in processes
E07	For root cause analysis we have standardized tools to get a deeper understanding of the influencing factors (e.g. DMAIC)
E08	We operate with a high level of PAT implementation for real time process monitoring and controlling
Cross-functional product development	
E09	Manufacturing engineers (e.g. Industrial engineers) are involved to a great extent in the development of a new drug formulation and the development of the necessary production processes
E10	In our company product and process development are closely linked to each other
E11	Due to close collaboration between the R&D and the manufacturing department, we could significantly shorten our time for product launches ("scale-ups") in our plant
E12	For the last couple of years we have not had any delays in product launches at our plant
E13	For product and process transfers between different units or sites standardized procedures exist, which ensure a fast, stable and complied knowledge transfer
Customer involvement	
E14	We are frequently in close contact with our customers
E15	Our customers frequently give us feedback on quality and delivery performance
E16	We regularly survey our customer's requirements
E17	We regularly conduct customer satisfaction surveys
E18	On time delivery is our philosophy
E19	We jointly have improvement programs with our customers to increase our performance
Supplier quality management	
E20	Quality is our number one criterion in selecting suppliers
E21	We rank our suppliers; therefore we conduct supplier qualification and audits

(continued)

Supplier quality management	
E22	We use mostly suppliers that we have validated
E23	For a large percentage of suppliers we do not perform any inspections of the incoming parts/materials
E24	Inspections of incoming materials are usually performed in proportion to the past quality performance or type of supplier
E25	Basically, we inspect 100 % of our incoming shipments
E26	We jointly have improvement programs with our suppliers to increase our performance

Just-In-Time

Set-up time reduction	
F01	We are continuously working to lower set-up and cleaning times in our plant
F02	We have low set-up times for equipment in our plant
F03	Our crews practice set-ups regularly to reduce the time required
F04	To increase the flexibility, we put high priority on reducing batch sizes in our plant
F05	We have managed to schedule a big portion of our set-ups so that the regular up-time of our machines is usually not effected
F06	Optimized set-up and cleaning procedures are documented as best-practice process and rolled-out throughout the whole plant

Pull production	
F07	Our production schedule is designed to allow for catching up, due to production stoppings because of problems (e.g. quality problems)
F08	We use a pull system (kanban squares, containers or signals) for production control
F09	We mainly produce according to forecasts
F10	Suppliers are integrated and vendors fill our kanban containers, rather than filling our purchasing orders
F11	We value long-term associations with suppliers more than frequent changes in suppliers
F12	We depend on on-time delivery from our suppliers
F13	We deliver to our customers in a demand-oriented JIT way instead of a stock-oriented approach
F14	We mainly produce one unit when the customer orders one. We normally do not produce to stock

Layout optimization	
F15	Our processes are located close together so that material handling and part storage are minimized
F16	Products are classified into groups with similar processing requirements to reduce set-up times
F17	Products are classified into groups with similar routing requirements to reduce transportation time
F18	The layout of the shop floor facilitates low inventories and fast throughput
F19	As we have classified our products based on their specific requirements our shop floor lay-out can be characterized as separated into “mini-plants”
F20	Currently our manufacturing processes are highly synchronized over all steps by one take

(continued)

Layout optimization	
F21	Currently our manufacturing processes from raw material to finished goods involve almost no interruptions and can be described as a full continuous flow
F22	At the moment we are strongly working to reach the status of a full continuous flow with no interruption between raw material to finished goods
F23	We use "Value Stream Mapping" as a methodology to visualize and optimize processes
Planning adherence	
F24	We usually meet our production plans every day
F25	We know the root causes of variance in our production schedule and are continuously trying to eliminate them
F26	To increase our planning adherence we share data with customers and suppliers based on a rolling production plan
F27	We have smoothly leveled our production capacity throughout the whole production process
F28	Our plant has flexible working shift models so that we can easily adjust our production capacity according to current demand changes
F29	A smoothly leveled production schedule is preferred to a high level of capacity utilization

Effective Management System

Direction setting	
G01	Our production site has an exposed site vision and strategy that is closely related to our corporate mission statement
G02	Our vision, mission and strategy is broadly communicated and lived by our employees
G03	Goals and objectives of the manufacturing unit are closely linked and consistent with corporate objectives. The production site has a clear focus
G04	The overall objectives of the production site are closely linked to the team or personal objectives of our shop-floor teams and employees
G05	Our manufacturing managers (Head of manufacturing, Site-leader etc.) have a good understanding of how the corporate/divisional strategy is formed
G06	Our manufacturing managers know exactly what the most important criteria for manufacturing jobs are (i.e. low costs, delivery, quality etc.)
Management commitment and company culture	
G07	Plant management empowers employees to continuously improve the processes and to reduce failure and scrap rates
G08	Plant management is personally involved in improvement projects
G09	There is too much competition and too little cooperation between the departments
G10	The communication is made via official channels
G11	The company has an open communication culture. There is a good flow of information between the departments and the different management levels
G12	About innovations we are informed early enough
G13	Problems (e.g. reclamations etc.) are always traced back to their origin to identify root causes and to prevent doing the same mistakes twice
G14	The achievement of high quality standards is primarily the task of our QA/QC departments

(continued)

Management commitment and company culture	
G15	Our employees continuously strive to reduce any kind of waste in every process (e.g. waste of time, waste of production space etc.)
G16	Command and control is seen as the most effective leadership style rather than open culture
Employee involvement and continuous improvement	
G17	We have implemented tools and methods to deploy a continuous improvement process
G18	Our employees are involved in writing policies and procedures (concerning site vision down to standard operating procedures)
G19	Shop-floor employees actively drive suggestion programs
G20	Our work teams cannot take significant actions without supervisors or middle managers approval
G21	Our employees have the authority to correct problems when they occur
G22	Occurring problems should be solved by supervisors
G23	Supervisors include their employees in solving problems
G24	Our plant forms cross-functional project teams to solve problems
G25	The company takes care of the employees
G26	We have organized production employees into teams in production areas. For each team there is one dedicated team member that is responsible for supervisory tasks
G27	We have organized production employees into teams in production areas. For team leadership we have an additional supervisory level in our organization
Functional integration and qualification	
G28	Each of our employees within our work teams (in case workers are organized as teams) is cross-trained so that they can fill-in for others when necessary
G29	At our plant we have implemented a formal program to increase the flexibility of our production workers. Employees rotate to maintain their qualification
G30	In our company there are monthly open feedback meetings
G31	The information of these official feedback meetings is used systematically in further training
G32	We continuously invest in training and qualification of our workers. We have a dedicated development and qualification program for our production workers

Basic Elements

Standardization and simplification	
H01	We emphasize standardization as a strategy for continuously improving our processes, machines and products
H02	We use our documented operating procedures to standardize our processes (e.g. set-ups)
H03	Optimized operating procedures (e.g. shortened set-ups) are documented as best-practice processes and rolled-out throughout the whole plant
H04	Standardized functional descriptions have reduced the period of vocational training for new employees

(continued)

Standardization and simplification	
H05	We use standardized machines and equipment (e.g. standardized machine design, standardized spare parts etc.) to achieve a high up time of our machines
H06	By using standardized machines and fixtures we could significantly lower our material costs for spare parts

Functional integration and qualification	
H07	Performance charts at each of our production processes (e.g. packaging) indicate the annual performance objectives
H08	Technical documents (e.g. maintenance documents) and workplace information (e.-g. standardized inspection procedures, team structures) are posted on the shop floor and are easily accessible and visible for all workers
H09	Charts showing the current performance status (e.g. current scrap-rates, current up-times etc.) are posted on the shop-floor and visible for everyone
H10	Charts showing current take times and schedule compliance (e.g. Andonboards) are posted on the shop-floor and visible for everyone

References

Hackman JR, Wageman R (1995) Total quality management: empirical, conceptual, and practical issues. Adm Sci Q 40:309–342

Ishikawa K (1982) Guide to quality control. Asian Productivity Organization, Tokyo

Jonsson P, Lesshammar M (1999) Evaluation and improvement of manufacturing performance measurement systems – the role of OEE. Int J Oper Prod Manag 19(1):55–78

Nakajima S (1988) Introduction to Total Productive Maintenance (TPM). Productivity Press, Cambridge, Herter

Ohno T (1988) Toyota production system. Productivity Press, Portland

Robinson CJ, Ginder AP (1995) The North American way. Productivity Press, Cambridge

Chapter 5
Leading the Advance in Regulatory Science

Nuala Calnan

. . .transformation is everybody's job (Deming 2000)
[Deming: Principles for Transformation]

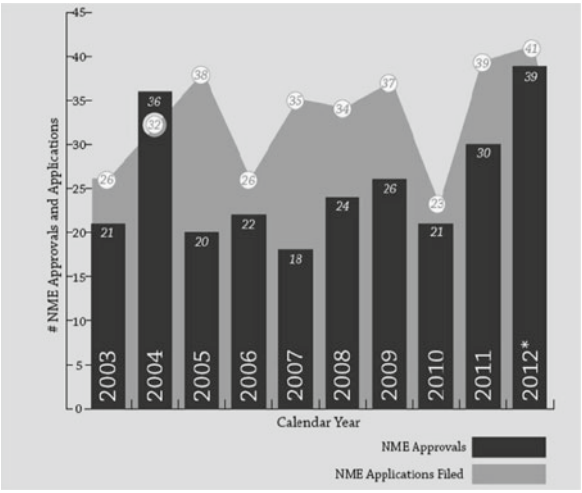
Global Industry Drivers for Change

That the pharmaceutical industry is undergoing a period of great transformation can be in little doubt, with so many industry reports highlighting the magnitude of the impact of the patent cliff on *big pharma* revenues and share prices. Pharmaceutical researcher EvaluatePharma has reported that in 2013 alone, patents will expire on drugs that currently have sales of $29 billion annually (FiercePharma 2013). Despite the recent good news regarding the record number of approvals of novel new medicines or New Molecular Entities (NME's) at the Food and Drug Administration (FDA) in 2012 reaching a decade high of 39 (Buckman-Garner 2013), the imperative for change is not going away for traditional *Big Pharma* (Fig. 5.1). Indeed, the FDA itself cautions that the trend in actual NME applications filed remains relatively static while current industry estimates include that $290 billion (FiercePharma 2013) of sales remain at risk from patent expirations between 2013 and 2018.

Couple these effects with the on-going price and drug reimbursement pressures being exerted by governments, payers and insurers worldwide which further erode threatened margins and you have, what some have called, the perfect storm for big pharma. The pressure is on in every big pharma boardroom to address the fall in profits and to contain costs. At the June 2013 ISPE 'Creating, Implementing and Sustaining a Culture of Quality', cGMP Conference, Andrew D Skibo, RVP Biologics at AstraZeneca/MedImmune (Skibo 2013) asked what is the impact of

N. Calnan (✉)
Dublin Institute of Technology (DIT), Dublin, Ireland
e-mail: nuala.calnan@gmail.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_5, © Springer-Verlag Berlin Heidelberg 2013



*The final number of NME Applications filed in 2012 is projected, pending final validation of the data and dependant on the outcome of applications submitted in later 2012.

Fig. 5.1 New molecular entity approvals at FDA – 10 year historical comparison

the continuing pressure to lower costs in the pharmaceutical industry? He questions if the executive teams operating at board level in many pharma companies understand the risk-reward model adequately when seeking to retain threatened profit margins by simply driving down costs. The result of these cost focussed strategies may account for the increases in product quality issues we see today and a lowering of customer service levels across the industry.

On the other hand, could this fiscal crisis finally drive the industry to embrace *operational excellence,* not as a means to cut costs, but as a pathway to improve efficiencies and enhance quality by tackling sources of waste (variation) across the entire lifecycle of the drug products they produce? For those that understand the impacts of getting the risk-reward model wrong, *operational excellence* (OPEX) presents a potential win-win situation of reducing both patient and business risk at the same time.

Of course, one man's loss is another man's gain and EvaluatePharma predicts that more than 70 % of the revenue losses attributed to patent expiration will be won by the ever expanding 'lean' generics sector. This concurs with other recent analysis (Center 2013) into the widening growth gap between IMS Health's global drug market forecast (4 % CAGR) and industry analysts' estimates of falling sales for big pharma. The analysis points to the growth in opportunities which have been presented to the next tier of companies in the industry, namely – specialty pharma (which includes generics firms) and big biotech firms. A more optimistic outlook is taken by Deloitte in their Global Life Science outlook for 2013 (Deloitte 2013), in which they refer to the current challenges as "a new normal" for the industry and summarise several long-term trends which remain favourable for the biopharmaceutical industry as a whole;

- Aging Population
- Rising incidence of chronic diseases
- Opportunities in emerging markets
- Technological advancements and product innovation
- Health care reform provisions, specifically the extension of health insurance to more than 30 million uninsured U.S. citizens under the Patient Protection and Affordable Care Act (PPACA or ACA) in 2014

With the rising impact of China, India and other emerging nations on global pharmaceutical production, the geographic location and sector of the industry that is servicing the market demand is experiencing rapid change. Nevertheless the facts remain; there are more people, in more markets, with more diseases driving demand for top quality medicines which are available to meet the health needs of the public globally.

Global Regulatory Drivers for Change

The pressures of globalisation, growth in emerging economies and increasing complexity associated with both the rate of product innovation and the diversity in the supply chain are not just felt by the industry alone. The global regulatory community is also attempting transformational change in order to respond to these drivers. FDA Commissioner Margaret A. Hamburg (2013a), in quoting the figures on the percentages of drugs used in the US today which are manufactured overseas noted that 40 % of finished pharmaceuticals and a staggering 80 % of the active ingredients used in the drugs consumed in the US come from abroad. She states that: "Today we recognize that to successfully protect U.S. public health, we must think, act, and engage globally. Our interests must be broader than simply those within our own borders." These percentages are understood to also reflect a similar scenario for pharmaceutical imports into the EU, and underpin the current trends in development of global regulatory coalitions through organisations such as the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) and the International Conference on Harmonisation (ICH). These programs of harmonisation of technical standards, which have brought us the ICH suite of Q8(R2) (ICH 2009a), Q9 (ICH 2009b), Q10 (ICH 2008) and Q11 (ICH 2012) guidance documents, give clear insights into the expectations of the global regulatory community regarding the use of science and risk based approaches to drive innovation and continuous improvement in process performance and product quality. The access to the PIC/S system of information sharing between regional regulatory authorities, regarding the outcomes of pharmaceutical facility inspections, strengthens the regulators hand in regard to transparency of recalls, GMP deficiencies and assessment of risks to public health. Yet amid this maelstrom of transformation, despite widespread acknowledgement of the challenges by industry and regulators alike, we continue to see a proliferation of

fundamental product quality issues posing on-going unacceptable risks to public safety. Which raises the question of how an industry rich in intellectual, technological and financial resources continues to fail to get to the root cause of product quality defects?

Unresolved Quality Problems

This is the same question raised by Dr. Janet Woodcock (Director of CDER at FDA) in her article entitled 'Reliable Drug Quality: An Unresolved Problem' in the May/June 2012 edition of the PDA Journal (Woodcock 2012), when she wrote;

> Clearly the responsibility for maintaining quality rests squarely with the manufacturers themselves.... The widespread and successful adoption of six sigma and related quality management techniques in other manufacturing sectors would imply that reliable, high quality manufacturing is also attainable in the pharmaceutical sector. We must ask ourselves, in an area where the stakes are so high, why is this not being achieved?

Woodcock goes on to query whether 'In response to this on-going cluster of [manufacturing quality] problems, it may be time to step back and try to uncover the root causes of this seemingly intractable issue'. This focus on quality as a priority was reiterated by Commissioner Hamburg during her recent (February 2013) (Margaret and Hamburg 2013b) address to the Annual Meeting of the Generic Pharmaceutical Manufacturers Association, where she stated that FDA has chosen to make quality one of their highest priorities this year and appealed to the industry to follow suit. In saying,

> I want to take this opportunity to really focus on how we can assure that the American people will get the products they need, in a timely way and of the highest quality possible.
>
> Year in and year out we say much about safety and efficacy. But without product quality, none of us can feel confident that the product will be either safe or effective. These concepts go hand and hand. And unfortunately, we've seen far too many quality lapses throughout the pharmaceutical industry over the past few years. . . ., they are warning signals that we can and must do more.
>
> That's why we've chosen to make quality one of our highest priorities this year and we'd like you to do the same.

This focus on product quality as a means to assure the safety and efficacy of drugs can come as no surprise to anyone watching the global regulatory community's response to *Drug Shortages* in recent years. In their investigation into the risks posed to public health as a result of product supply shortages, the findings have pointed directly at the on-going issues with unresolved product quality defects as the primary root cause of failure causing supply shortages. In November 2012, the European Medicines Agency (EMA) issued a "Reflection paper on medicinal product supply shortages caused by manufacturing/Good Manufacturing Practice Compliance problems" (EMA 2012) and they note that other international partners including FDA, Health Canada (HC) and the Therapeutic Goods Administration (TGA) in Australia have confirmed their interest in the

area of security of product supply and expressed their willingness to participate in collaborative efforts to share information about product supply issues.

Indeed, FDA had issued an earlier report on *Medicinal Product Shortages* in October of 2011 (FDA 2011a) stating that in the period 2005–2011 the number of drug shortages in the US had tripled from 61 cases in 2005 to 178 cases in 2011. Notably, of a subset of 127 cases studied from 2010 to 2011, 80 % were *sterile injectable products* and in 43 % of these cases the primary reason leading to the shortage was given as *manufacturing quality deficiencies*. Hindsight provides 20/20 vision of course, but could this study have been an early warning alert for the need to overcome the political impasse regarding regulatory responsibility and ensure adequate oversight of the many compounding facilities engaged in producing *sterile injectable products* (often to plug a drug shortage gap (Grady Denise and Tavernise 2012)) a year before the New England Compounding Company (NECC) (McLaughlin 2012) tragedy unfolded. As of March 10, 2013, 48 people have died of fungal meningitis attributed to the contaminated products supplied by NECC and over 720 are being treated for persistent fungal infections (News 2013).

The EMA reflection paper is interesting, as it focuses specifically on the public health crises that arise due to unforeseen disruptions within the manufacturing process, caused by manufacturing/GMP compliance problems. One conclusion drawn, highlights that the industry's approach to risk management tends to be "very reactive rather than proactive" and they indicate that "sustained pressure" will be needed in order to bring about a change in the manufacturer's approach to quality risk management and supply chain security. This 'sustained pressure' has led directly to a major revision of Chap. 8 of the EU GMP Guide on "Complaints and Product Recall" which is currently being drafted and is expected for final publication in the coming year. The main changes are outlined as the application of Quality Risk Management (QRM) principles associated with defect/complaint investigations, a strengthening of requirements regarding Corrective and Preventive Actions (CAPA) programs and the reporting requirements to the supervisory regulatory authorities. This is a clear example of the EU regulatory authority updating the actual regional GMP's to reflect guidance formally issued in international guidance documents (ICH Q9 and ICH Q10) as early as 8 years earlier because of their dissatisfaction with the industry's adoption of the principles outlined.

On this point in the US, we need look no further than the FDA's Process Validation Guidance (FDA 2011b) (published January 2011) for evidence of alignment on the lifecycle approach, establishing and maintaining the state of control and the expectations for on-going monitoring and trending. The reality is that the regulator's expectations for modern pharmaceutical development, manufacture and distribution comprehensively outlined and issued in the ICH guidance documents of Q8(R2), Q9, Q10, Q11 have far-reaching consequences, which are already impacting the way in which regional regulations are enforced, and are increasingly being reinforced through on-going updates to the regional GMP's. This was confirmed during the *International Regulator Forum* at the ISPE Annual Meeting held in San Francisco during November 2012, when US, EU and PIC/S

representatives outlined an extensive list of local regional regulations and guidelines that are currently undergoing routine updating, including incorporating the ICH principles.

One might say that the time has come for the industry to revisit these important guidance documents and review how their current practices measure up. Certainly, what remains unclear is whether the industry's response to the imperatives for change and the regulators demands for improved (in fact, continuously improving) product quality will result in a science-led industry which is positioned to "... enhance the quality and availability of medicines around the world in the interest of public health." *[Introduction to ICH Q10 Pharmaceutical Quality Systems.]*

Regulatory Guidance Leading the Way to Excellence

A simple reading of the ICH Q10 *Pharmaceutical Quality System* guidance will show just how many points of resonance there are between the recommendations outlined within ICH Q10 and the key philosophies embodied in the international *operational excellence* literature. Not least in regard to the emphasis placed on;

- Continual improvement
- Innovation
- Enhancing process capability
- Eliminating sources of variation.

Implementing the ICH Q10 guidance provides one concrete means for the pharmaceutical industry to address this renewed regulatory focus on product quality whilst delivering not only compliance benefits but hard business benefits as well. For those that are embarking on reviewing their current *Quality Management System* with a view to implementing an ICH Q10-based *Pharmaceutical Quality System*, embedding the *Operational Excellence* principles which have paid dividends for other non-pharm industries is a good place to start. Particularly, when planning *Quality Process Performance Monitoring* programmes which focus on eliminating sources of variation while delivering innovation and continual improvement.

However, as ICH Q10 has been with us since June 2008, we might ask why the transformation of the traditional quality management systems in use within the pharmaceutical industry, remains an aspiration for all but a few forward thinking organisations. No one could be under any illusion about the reality of the 'paradigm shift' (Group and I. Q. I. W 2012) currently underway or the compelling public health and business imperatives to getting pharmaceutical quality *right first time*. However, despite intensive investment by the industry throughout the past decade on sophisticated enterprise wide quality management systems and highly skilled resources, we continue to experience increases in the number of product recalls, globally.

Year	2004	2005	2006	2007	2008	2009	2010	2011
Critical	50	66	84	173	127	105	173	231
Major	167	199	238	216	300	345	332	364
Others	93	62	49	84	128	164	246	322
Total	310	327	371	473	555	614	751	917
Recalls	82	74	58	97	141	98	168	253

Fig. 5.2 Irish medicines board (IMB) quality defect and product recall statistics, 2004–2011

In Ireland alone, based on recent statistics issued by the Irish Medicines Board (IMB) (O''Donnell and Irish Medicines Board (IMB) 2012) for the period 2004–2011, there has been a 309 % increase in product recalls, i.e. recalls of pharmaceutical products – with quality defects – which have found their way into the market place. Unfortunately for all of us 'patients' who take these medicines, these poor quality trends hold true internationally too (Fig. 5.2).

Indeed, in those drug shortage figures released by FDA (referred to earlier), 54 % of all medicinal product supply shortages in the US in 2010 were cited to be as a result of either product recalls or quality defects. Most seriously as witnessed recently in the NECC case, quality defects put patient lives at risk, and the protection of public health is the fundamental purpose for the regulators. However, quality defects also place companies themselves at risk with remediation costs, loss of revenue and in some cases, legal charges/fines associated with product recalls running from several hundreds of thousands of euros/dollars to hundreds of millions of euros/dollars depending on the severity of the event.

Operational Excellence as a Route to Enhancing Quality

For those interested in quantifying the potential business benefits which may accrue to organisations who undertake a path towards operational excellence, it is useful to look at some of the recent results from the St.Gallen University *OPEX Benchmarking* (Transfer Center for Technology Management 2012) project of the pharmaceutical industry (cf. also Chap. XY).

The results are compelling and were presented at the *Global Pharma Manufacturing Summit* in June 2012 (Friedli 2012) (based on 2010 data compiled from 181 biopharmaceutical sites of 91 different participating companies), across four benchmarking modules of;

1. Total Productive Maintenance (TPM)
2. Total Quality Management (TQM)
3. Just-in-Time (JIT)
4. Effective Management Systems (EMS)

The results presented conclude that the 'Top Performers' amongst those who have commenced *Operational Excellence* programs have higher overall performance scores, specifically in the categories *Quality* and *Productivity* and also achieve better performance results in regard to the measurement of *Effectiveness* and *Efficiency*. What does all this mean in real terms for product quality? The results demonstrate how the top performers enjoy;

- Higher **overall equipment effectiveness** (OEE)
- Lower percentages of **unplanned maintenance**
- Release their **finished products faster**
- Have a **lower customer complaint rate**

The results also show how these top performing companies enjoy;

- *Significantly* lower overall costs for maintenance and for those costs associated with poor quality

Based on this research, the business case is clear on the tangible benefits which may accrue from applying excellence philosophies across your operations. The St. Gallen OPEX team do sound an important note of caution in terms of the long-term sustainability of these results if the OPEX programs are simply rolled out on a project by project basis. This philosophy concurs directly with the ICH Q10 message which clearly states that long-term sustainable development of the *Pharmaceutical Quality System* will require the direction and leadership of the corporate and senior management teams with a relentless commitment to continuous improvement and to delivering top quality medicines, each batch, each day.

Ensuring that future *Pharmaceutical Quality Systems* are designed with excellence in mind, are knowledge led and based on sound scientific principles will facilitate better decision making. It will also go a long way to address the challenges faced in *demonstrating* your ability to establish and maintain the 'State of Control' for the products you produce. ICH Q10 outlines a pathway to embrace innovation and continuous improvement as a means to overcome the unsatisfactory *Status Quo* approach which has gripped the industry for too long. Perhaps most significantly, in the much neglected Annex 1 of ICH Q10, it offers the potential of future regulatory flexibility for those organisations who truly transform their operations across the product lifecycle using practices appropriate for the twenty-first century.

Effective Validation: A Route to Assuring Drug Quality

The latest FDA *Guidance for Industry on Process Validation* (FDA 2011b) (PV) states up front that effective process validation contributes significantly to assuring drug quality and any prospective program to enhance product quality in the

industry will need to take the recent changes in regulatory expectations in relation to process validation seriously. The FDA has led the charge by publishing its final guidance in January 2011, while the EU issued their draft *Guideline on Process Validation* EMA (2012) in March 2012 and the update to EU GMP Guide Annex 15 on *Qualification and Validation* has already commenced.

One important point of distinction between the PV guides is that they are written to address different purposes;

- The FDA PV guide outlines the principles and approaches that manufacturers can use to validate manufacturing processes for drug products.
- The EU draft PV guideline outlines the information relating to process validation that should to be considered as part of the dossier submission, when applying for a *Marketing Authorisation* and as such is mainly aimed at the pharmaceutical assessors.
- The proposed update to Annex 15 of the EU GMP Guide: Qualification and Validation will contain the details associated with the actual qualification and validation studies undertaken at commercial scale prior to release of product into the marketplace.

Nevertheless, the EU Draft PV guide does take a full lifecycle approach in regard to how a company can gather and justify their validation data and acknowledges that the information presented in the submission dossier may also be useful for (and used by) the inspectors who are charged with conducting subsequent GMP facility/product inspections. Final publications of both of these EU documents are expected in the coming 12–18 months.

Therefore, while the purpose of the US and EU guides may differ, the lifecycle based approaches bear many similarities and both emphasize that they draw upon the concepts outlined in ICH Q8, 9 and 10. In essence, they agree that a lifecycle approach should be applied which links;

1. Product and process development
2. Validation(EU)/Qualification (US) of the commercial manufacturing process
3. Maintenance of the process in a ‘state of control’ during routine commercial production

Both guides stress that the ability to design an *efficient process*, which operates an *effective process control approach*, to the manufacture of *products which consistently meet their quality attributes*, is dependent on the level of process knowledge and understanding gained. Both guidelines also note that the success of the validation program will hinge upon the quality and depth of the product and process understanding gained, largely during the development phases of the lifecycle. The importance of utilising the knowledge gained through the *application of scientific approaches* (ICH Q8) and *quality risk management* (ICH Q9) to the development of a product and its manufacturing process is emphasized. The FDA guide gives specific recommendations on using this knowledge to:

- Understand the sources of variation within the process
- Detect the presence and degree of variation
- Understand the impact that variation has on the process and ultimately on the product attributes

Finally, the FDA guide points to the importance of being able to demonstrate *control of the variation* in a manner *commensurate with the risk* it represents to the process and product.

On the matter of control, both the EU and US guidelines agree that successful process validation programs must now focus on the *Control Strategy* employed at each phase of the lifecycle and both emphasise that product quality can no longer be deemed to be adequately assured merely by conducting in-process and finished-product inspection or testing alone. The EU guide clearly states that "Process validation should not be viewed as a one-off event" and ". . .should focus on the control strategy which primarily includes critical process parameters".

Understanding the Nuances

At time of writing it must be acknowledged that the EU PV guidance remains a draft and we may see some significant changes before final publication. It is, as mentioned, primarily a guide relating to the process validation approach to be included in a dossier submission and does not currently focus on the very structured (and useful) three Stage approach as outlined in the FDA PV guide;

- Stage 1 – Process Design
- Stage 2 – Process Qualification
- Stage 3 – Continued Process Verification

What the draft EU guide does expand on are the three possible PV approaches a company may consider when planning a PV program.

- A Traditional Process Validation Approach
- A Continuous Process Verification (CPV) Approach
- A Hybrid Approach

The EU recommendations indicate that a traditional PV approach must now be lifecycle based and take process knowledge and understanding into account to focus on the control strategy as a means to assure product quality.

In regard to employing a new 'alternative' CPV approach this will require a rigorous application of the ICH Q8, 9 and 10 principles to design ". . . a process that operates within the predefined specified parameters consistently produces material which meets all its Critical Quality Attributes (CQAs) and control strategy requirements". In this case, the manufacturing process performance is continuously monitored and evaluated through extensive in-line/at-line controls which will monitor both process performance and product quality in a timely manner. This

CPV approach is likely to be most suited to applications where a *Quality by Design* (QbD) approach to process and product development has been used, that includes the deployment of Process Analytical Technologies (PAT) for real time control and monitoring.

The Hybrid Approach presents a possibility of using a blended combination of traditional PV and 'alternative' CPV approaches for various individual process steps as a valid way forward.

Much Ado About Nothing

There has been much discussion in industry forums over the past couple of years about the elimination of the 'three golden batches' requirement from the FDA PV Guidance. This unseemly fixation on the 'how much is enough' debate may be feeding the implementation uncertainty which has emerged and drawn attention away from the key point made by both EU and US guidelines that; the means to justifying the approach selected (including determining the amount of studies/batches necessary) will be founded on knowledge. The success of the validation program will hinge on the quality of the knowledge gained, developed and enhanced.

- Knowledge *gained* in the product and process development stage
- Knowledge *developed* during the validation studies
- Knowledge *enhance* throughout the on-going routine manufacture and distribution

Knowledge is the key to unlocking effective process validation programs which in turn are the route to assuring and enhancing product quality. ICH Q8 (R2) captures this message succinctly when it acknowledges that it is "…the level of knowledge gained, and not the volume of data, provides the basis for science-based submissions and their regulatory evaluation."

Begin with the End in Mind

As process validation is not a one off event and we have seen that a 'three batches and done' strategy will be increasingly difficult to justify, the change with the biggest likely impact within both the EU and US guidelines are the implications of what is described as *Continu**ed** Process Verification*.

This is defined simply in the FDA PV guide as "Assuring that during routine production the process remains in a state of control" while the EU guide goes on to say that "This will provide assurance of the continued capability of the process and controls to produce product that meets the desired quality and to identify changes that may improve product quality or performance."

This will require that those charged with designing the PV program understand at the outset which aspects of product data are critical and relate directly to the product quality and which aspects of process data are statistically important and related to process capability. They will need to ensure that the system(s) necessary

to collect and analyse this data are incorporated in the process design from the beginning and that these systems are flexible enough to respond, as either new knowledge emerges or changes/improvements arise.

The FDA advises that the data collected should include the relevant process trends and quality of incoming materials or components, in-process material, and finished products. Furthermore, they expect that this data will be statistically trended and reviewed by personnel trained in statistical process control (SPC) techniques and that a data collection plan is prepared describing the statistical methods and procedures used in measuring and evaluating process stability and process capability. Unsurprisingly, this aligns directly with the ICH Q10 PQS recommendations that monitoring programs should include both *internal factors* such as deviations, CAPA and change management processes, risk assessments, trending, and audits and *external factors* such as complaints, customer audits and regulatory inspections and findings.

Be assured, this expectation goes far beyond merely conducting an annual product review of the batch records and associated complaints/changes. It expects a regular and systematic review by trained personnel of all sources of critical and/or influential data about a product *and* an ability to demonstrate the outcomes and actions taken arising from these reviews.

Knowledge: A Path Towards Excellence

> . . .continuous innovation and the knowledge that enables such innovation have become important sources of sustainable competitive advantage (Nonaka et al. 2000) [Ikujiro Nonaka]

This expectation for enhanced monitoring and analysis presented in both the ICH suite of guidance documents and the recent PV guidance documents alike will present a significant challenge to many organisations to deliver on. Particularly, when using existing *records based* quality management systems which have an unhealthy obsession with locking down and securing the quality related data and records, often creating expensive but impenetrable data mountains. The new *Product Quality and Process Performance Monitoring* programs will need to be designed with the ability to unlock the knowledge which exists within each organisation by translating these valuable libraries of quality data and records into actionable process improvements. In an industry which has concentrated more on document management than on knowledge management and which has traditionally valued *explicit knowledge* (that which is written down e.g. SOP's) above *tacit knowledge* (that which is known e.g. insights and intuition), the change required in institutional behaviour should not be underestimated.

Beware of the current fashion for 'Big Data' or data analytics platforms which claim to be solution to all your data management and analysis problems. No doubt they will have a role to play, but this is about moving an industry heretofore

Fig. 5.3 Knowledge continuum – from quality data to process wisdom (Note: Adapted by the author from Ackoff, R. L., "From Data to Wisdom", Journal of Applies Systems Analysis, Volume 16, 1989)

focussed on data and records management along the knowledge continuum towards process wisdom (Fig. 5.3).

Nonaka(2999) define knowledge as a 'dynamic human process. . .' and state that what "knowledge management" should achieve is not a static management of information or existing knowledge, but a dynamic management of the process of creating knowledge out of knowledge. The authors point to the fact that this will require a new kind of leadership, a message that also rings loud and clear from section two of ICH Q10 where a range of enhanced responsibilities are laid at the door of senior management.

There is much consensus in the international literature on knowledge creation on the importance of *inter-organisational* cooperation in the emergence, diffusion and transfer of new knowledge. Other industries that engage in successful six-sigma or operational excellence programs, such as the automotive, aeronautics or nuclear power industries, regularly engage in knowledge creation projects which involve suppliers, customers, regulatory authorities and even direct competitors. Traditionally, the pharmaceutical industry has focused its collaborations in the development phase of the lifecycle and typically came by new knowledge in the commercial manufacturing phase as a result of mergers or acquisitions with other organisations. In many of these cases, the focus was more on integrating the systems or 'right sizing' the operations than on seeking to create new knowledge which would lead to enhanced manufacturing performance.

This author believes this is changing and the realisation of the value of transparency and the competitive advantage benefits to be gained from collaborative arrangements rather than simple contractual arrangements is slowly beginning to dawn on the regulators and industry alike. From a pharmaceutical product quality perspective, a good place to start would be for the Europeans Medicines Agency (EMA) to come clean and finally meet their commitment (2001) Parliament E Article 111(6) of directive 2001) to provide a transparent online database which actually *includes* details of compliance/quality defects identified (and notified) by the European national competent authorities. Instead of the entirely meaningless *EudraGMP* database ((2013)) they currently publish online which only allows public access to view listings of manufacturing or importation authorisations and

copies of the successful GMP certificates issued. The claim on their website that "Almost all information uploaded into the database is available to the general public" is a blatant untruth. Furthermore, the thin excuse that "National Competent Authorities are able to exclude some information from public view. This includes information of a commercially sensitive or personal nature. . ." does not hold water in a world of global manufacturers where international inspections undertaken by FDA of the same facilities, which result in a warning letter being issued, will have that letter published via the FDA website. If FDA has figured out how to redact information of a commercially sensitive nature why cannot the EMA and European NCA's? It should be noted that even though FDA does at least make their warning letters freely available to the public, access to their 483 reports are often only accessible through one of several commercial organisations at a steep cost. Worse still, the current method of capture and reporting of the deficiencies, make comparative review practically impossible.

Transparency of data relating to medicinal product quality can only lead to greater understanding of the risks presented to public health and enhance people's ability to choose (or influence) the provenance of the medications they take. Academic research on the common causes of failure could only help in discovering and assigning root causes of failures. Systematic reviews of GMP deficiencies could be able to trend influences of regional, corporate or product related deficiencies and lead to open debate and/or collaboration on the provision of possible solutions. Indeed market forces might elicit a more robust response from industry in addressing these 'unresolved quality issues' than 100 years of behind-closed-doors regulation has achieved.

Advancing Regulatory Science

This brings us full circle right from the opening title of this chapter. Both the FDA and the EMA have released documents in the past number of years outlining their commitment to engage in advancing the role of regulatory science in the protection of public health. The FDA's report entitled *Advancing Regulatory Science at FDA* (FDA 2011c) defines regulatory science as;

> The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products.

In this report FDA outline their Strategic Plan for Regulatory Science which is designed to allow the Agency to meet both today's public and animal health needs and to be fully prepared for the challenges and opportunities of tomorrow. In the introduction, the report acknowledges that the challenges of modern product development and globalization underscore the critical importance of modernizing and advancing *regulatory science* ***to match*** advances in *basic and applied science and technology*. FDA says it will accomplish this by applying its knowledge base, laboratories, scientific computing capabilities, and expertise, leveraging resources

and collaborating with domestic and international partners in government and academia. If this application of knowledge, leveraging of resources and collaboration is undertaken in an environment of transparency and openness perhaps they will achieve their vision; to advance regulatory science to speed innovation, improve regulatory decision-making, and get safe and effective products to people in need.

From a European perspective the European Medicines Agency (EMA) has prepared a report called 'Roadmap to 2015' where they outline their mission as;

> To foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.

The EMA has defined Regulatory Science as;

> A range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products and that inform regulatory decision making throughout the lifecycle of a medicine.

They too speak of their increased collaboration with industry, academia and patient/consumer groups as a means to enrich regulatory decisions by complementing them with the views of those directly affected by regulatory decisions. Interestingly, they have undertaken in their report to strengthened efforts to make up-to-date medicinal product information readily available. The report however acknowledges that providing greater transparency will entail specific challenges for the agency, such as finding the right balance between making more information and documents available more quickly and protecting *commercially confidential information*, while also complying with personal-data legislation.

They say that more openness of operation and increased transparency should go hand in hand with efficient and targeted communication. Let's watch this space and see what emerges – perhaps it will be new knowledge that contributes to enhancing product quality and reducing risks to public health.

In Conclusion: Are You Ready to Deliver Excellence in Pharmaceutical Quality?

Perhaps you might take a moment now to consider the current quality management strategies in place within your organisation today;

1. Would you consider the practices in place today to be more efficient than those of 10 years ago? If so, what metrics exists for you to draw any conclusion regarding enhanced performance?
2. Are the current pharmaceutical quality management practices applied in a holistic fashion across the various functions within your organisation. Is there more cross-functional collaboration as a result? Does this hold true for your supply chain also?

3. Are the current pharmaceutical quality management practices driven by the lifecycles of the product(s) manufactured by your organisation (including steps undertaken by your external partners) or are there still some latent operational 'silos'?
4. Are the manufacturing strategies now employed, more scientifically based and if so, how?
5. Are all the *Critical Quality Attributes* (CQA's) as well as influential *Process Parameters* and material inputs for the products manufactured at your site identified and have they been universally communicated and understood by all?
6. Are the products manufactured by your organisation safer now (i.e. less associated risk) as a result of the quality assurance approaches and regulatory strategies currently employed? In essence, how much risk reduction has been achieved?
7. Do your current practices drive innovation and facilitate continual improvement and if so, how?
8. Are your qualification and validation activities now focused on maintaining a lifecycle state of control, and are emerging risks identified and appropriately managed?
9. Have you put in place *Process Performance and Product Quality* monitoring programs that will provide an on-going means of *Continued Process Verification* for the products you currently market?
10. Are the outcomes of your regulatory inspections better now than they were a decade ago?

Ultimately, can you confidently affirm that patient related risks associated with the product(s) manufactured or marketed by your organisation have been reduced due to the quality assurance approaches now applied within your organisation? If no, what do you think are the key factors impeding the reduction in patient risk? If yes, how do you currently measure, quantify and communicate this reduction in product and patient risk?

References

(2001) Parliament E Article 111(6) of directive 2001/83/EC. (EC), E. C., Ed

(2013) Eudra*GMP, Eudra*GMDP _European medicines agency on-line database for MIA's and GMP certs. EMA

Center EYGLS (2013) Closing the gap? Big pharma's growth challenge and implications for deals. January

Deloitte (2013) Global life sciences outlook 'optimism tempered by reality in a "new normal"'

Deming WE (2000) Out of the crisis. 1st MIT Press edn. MIT Press, Cambridge, p xiii, 507 p

EMA (2012a) Reflection paper on medicinal product supply shortages caused by manufacturing/good manufacturing practice compliance problems. Nov 2012

EMA (2012b) Guideline on process validation-draft. Agency, E. M., Ed. March 2012

FDA (2011a) A review of FDA's approach to medical product shortages. October 2011.

FDA (2011b) Guidance for industry, process validation: general principles and practices. Current Good Manufacturing Practices (CGMP) revision 1 edn. FDA Ed. January 2011, p 19
FDA (2011c) Advancing regulatory science at FDA: a strategic plan; August 2011
FiercePharma (2013) Top 15 drug patent losses for 2013. http://www.fiercepharma.com/special-reports/top-15-patent-expirations-2013#ixzz2QFdMc824. Nov 2012
Friedli T (2012) Mastering plant complexity and the impact of operational excellence. In: global pharma manufacturing summit. New Jersey
Grady Denise PA, Tavernise Sabrina (2012) Scant oversight of drug maker in fatal meningitis outbreak. Wall Street J. 06 Oct 2012
ICH Q-IWG (2012) Introduction to ICH and the new quality paradigm. In: Robert JL (ed) Integrated training programme. ICH, Washington, DC
ICH (2008) ICH harmonised tripartite guideline: pharmaceutical quality system Q10. ICH, Ed. June 2008
ICH (2009a) ICH harmonised tripartite guideline: pharmaceutical development Q8(R2). ICH, Ed. Aug 2009
ICH (2009b) ICH harmonised tripartite guideline: quality risk management Q9. ICH, Ed. Nov 2009
ICH (2012) Development and manufacture of drug substances (chemical entities and biotechnological/biological entities) Q11. ICH. 1 May 2012
Margaret A, Hamburg MD (2013a) Weaving new threads in FDA's global safety net. FDA. 22 Feb 2013
Margaret A, Hamburg MD (2013) Address to the annual meeting generic pharmaceutical manufacturers association on the prioritization of product quality. FDA. 22 Feb 2013
McLaughlin T (2012) New England compounding center, pharmacy linked to meningitis outbreak, files for bankruptcy. Huffington Post 21 Dec 2012
News C (2013) Lethal medicine linked to meningitis outbreak. 10 Mar 2013
Nonaka Ikujiro NT Knowledge emergence. Oxford University Press.
Nonaka I, Toyama R, Konno N (2000) SECI, Ba and leadership: a unified model of dynamic knowledge creation. Long Range Plann 33:5–34
O'Donnell K, Irish Medicines Board (IMB) (2012) Quality defect and product recall statistics, 2004–2011. IMB 'Industry Open Day' seminar 2012, 27 Sept 2012
ShaAvhrée Buckman-Garner M (2013) How FDA promotes partnerships to accelerate medical product development. FDA
Skibo AR (2013) Outsourcing & emerging markets v's quality and drug availability. In: Creating, implementing and sustaining a culture of quality-putting the c into cGMP. ISPE, Baltimore
Transfer Center for Technology Management (2012) U. o. S. G. operational excellence in the pharmaceutical industry. http://www.opexbenchmarking.com. Accessed Dec 2012
Woodcock J (2012) Reliable drug quality: an unresolved problem. J Pharm Sci Technol 66 (3):270–272

Chapter 6
A Look to the Environment and the Impact on OPEX

Thomas Friedli and Daniel Bellm

The objective of this chapter is to provide an overview about some of the driving forces on OPEX in the pharmaceutical environment. We separately look at two different perspectives:

1. *The business environment for pharmaceutical companies, and*
2. *The global dimension of today's business including the so called pharma-emerging markets*

Based on these perspectives we will derive the impact of the current developments on pharmaceutical production and pharmaceutical OPEX. We will come back to this in Part 4 of this book dealing with the future of pharmaceutical production.

The General Business Environment

With a glimpse to global stock markets, the pharmaceutical industry has performed poorly compared to other industries over the last 10 years.[1] Positive influencing factors like the strong growth in emerging markets (see Fig. 6.1), the aging population and influenza pandemics seem to be counterbalanced by other factors like increasing competition, the global financial and debt crisis, the patent cliff, an increasing complexity and a declining R&D productivity.[2]

[1] Cf. KPMG (2011), p. 2

[2] Cf. KPMG (2011), p. 2

T. Friedli (✉) • D. Bellm
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; daniel.bellm@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_6, © Springer-Verlag Berlin Heidelberg 2013

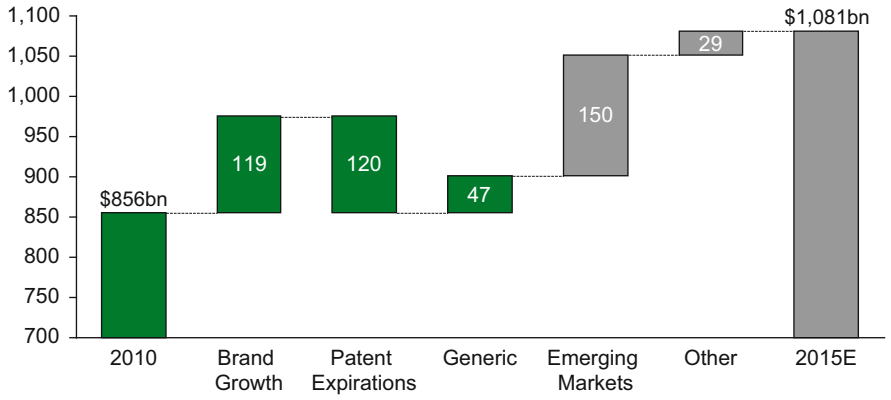


Fig. 6.1 Emerging markets are the key drivers of total spending (cf. KPMG (2011), p. 3)

We will describe some of these factors more detailed in the following parts and will derive the impact on OPEX and manufacturing at the end of this chapter.

R&D Productivity

In recent years, R&D productivity in the pharmaceutical industry has been widely discussed. There is no doubt that not only the long-term success and survival of a multitude of pharmaceutical companies, whether they are research driven or generics, depend on the output of their pipeline, but the future wealth of the entire mankind is also dependent on how successful these pharmaceutical companies are in developing new therapies for the unmet diseases and medical conditions.

Since 1950, FDA has approved about 1,350 New Molecular Entities (NMEs) (Munos 2009; EvaluatePharma 2012; FDA 2013). Of the more than 4,300 companies that are involved in drug innovation, only 6 % have registered at least one NME ever since. More than 150 companies that have delivered in total more than 600 NMEs have already disappeared from the pharmaceutical landscape, mostly through M&A activities (Munos 2009).

Productivity is typically measured as the ratio of output versus input. This, however, makes the measurement of the pure number of New Molecular Entities (NME) – although it is obviously easy to count – an imperfect measure of R&D productivity, as the mere number does not reflect changes in an increased output quality (Pammolli et al. 2011). Both input and output of the research process are influenced by various factors. The research and innovation processes lasting for several years, are determined by substantial knowledge spillovers, multiple, heterogeneous sources, and drain of knowledge due to employee turnover. Globally dispersed R&D of private and public organizations and numerous research

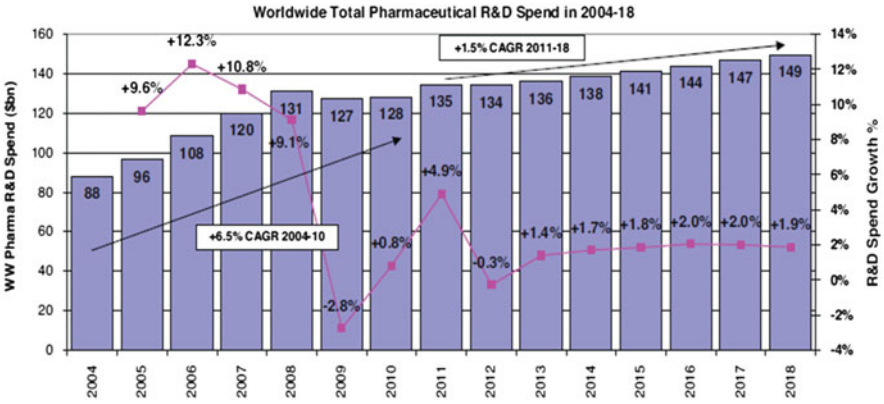


Fig. 6.2 Worldwide total pharmaceutical spend (EvaluatePharma 2012)

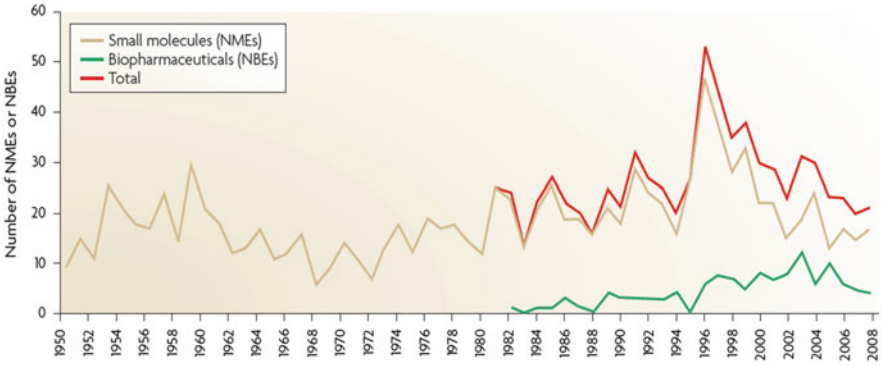


Fig. 6.3 Timeline of approvals of new molecular entities (NMEs) and new biological entities (NBEs) by the US food and drug administration (FDA) between 1950 and 2008 (Source: Munos 2009)

collaborations exacerbate a correct measurement of R&D productivity (Orsenigo et al. 2001; Owen-Smith et al. 2002; Pammolli et al. 2011).

However, it is widely acknowledged that R&D productivity in the pharmaceutical industry seems to be decreasing for the last couple of years (Paul et al. 2010). Although R&D investments have increased significantly during the years (see Fig. 6.2), the industry lacks an appropriate growth in its final output (see Fig. 6.3), the approval of new drugs as therapeutic innovations (Pammolli et al. 2011). Thus, one can arrive at a conclusion that therapeutic innovation in the pharmaceutical industry has become increasingly challenging. And, not to mince words, without an increase in productivity, the industry's survival and growth prospects are at an indisputable risk (Paul et al. 2010).

Several reasons for a declining R&D productivity can be found listed by practitioners and scientists. A growing complexity in science, pressures on pricing,

market access and tougher competition, as well as the hurdles on unmet needs, tighter regulation (Tollman et al. 2011) and market consolidation due to continuing M&A activities (LaMattina 2011) are some of those determining factors. R&D managers with sometimes inadequate leadership training, insufficient scientific medical expertise or even no profound experience in R&D, partially tend to over-manage or even micro-manage the R&D process, thus contributing to the industry's concerns. Moreover, the short-term goals of business-driven organizations and their sometimes aspirational objectives impede medical opportunism and scientific creativity (Paul et al. 2010). The introduction of new technologies and the continuous improvement of R&D processes have led to higher efficiency levels of certain process steps. Nevertheless, these efforts have not been able to overcome the forces mentioned above (Tollman et al. 2011).

In contrast, countries that maintain even more demanding regulations have promoted the innovativeness and competitiveness of their pharmaceutical sector. Recent studies show that companies operating in countries under the auspices of an exacting regulatory apparatus are more selective in the compounds which they pursue for future development. As such, R&D investment and thereby the emergence of the pharmaceutical industry have been positively simulated by making pharmaceutical research more risky and implementing rigorous regulatory requirements (Munos 2009).

Considering the pure number of truly innovative NMEs, opinions are quite consistent. Some argue that the number of NMEs has been stable for the last 5-6 years but the proportion of true revenue-generating drugs as a percentage of R&D expenditures has decreased significantly (Paul et al. 2010). Others even dramatize the picture distinguishing the past 5 years from the period between 1996 and 2004 when FDA has approved an average of 36 NME per annum (Oliver Wyman 2011). However, considering the historical average of around 31 launches per year since 1950 (see Fig. 6.2), the industry's current performance is not as dramatic as often thought. But we agree that a decline in the average 5th-year sale of nearly 15% between 1996 and 2004 and the period from 2005 till present (Oliver Wyman 2011) put an undeniably hard pressure on the industry. Additionally, the probability of about 21 % that a new drug will once achieve a blockbuster status has not changed for the last 20 years. This, unfortunately, does not apply for the investment in order to maintain such a formidable success rate (Munos 2009). As such, some clearly state that the pharmaceutical industry needs a significant increase in its R&D productivity in order to compensate the revenue loss due to patent expirations (Paul et al. 2010).

An outlook into pharma's future shows that growth of the global pipeline is currently stagnating. In 2009 the number of research projects from preclinical to Phase III had reached its peak with a total of 7,709 compounds, excluding biosimilars and reformulations, and shrunk down to 7,408 since (Berggren et al. 2012). The pipeline for preclinical compounds declined by 11 % between 2009 and 2011; in the same period also the pipeline for Phase I and II projects has shrunk. In contrast, the number of late-stage Phase III compounds has a yearly average growth rate of almost 9 % since 2009. Despite this observed slowdown, the status of the pipeline is promising. Currently it is still larger than it was during the

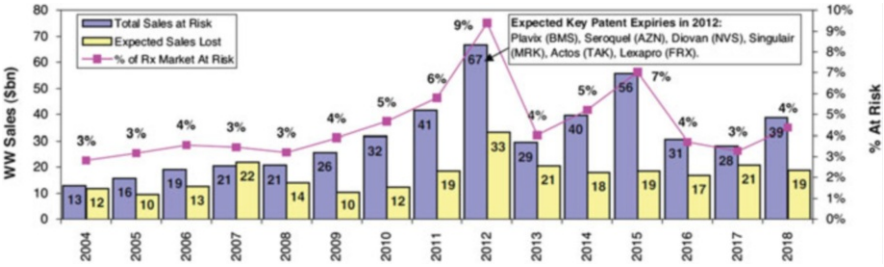


Fig. 6.4 Worldwide sales at risk from patent expiration (EvaluatePharma 2012)[3]

previous 5 years to 2011 (Berggren et al. 2012) when it brought nearly 31 NMEs per year to market (EvaluatePharma 2012). On an even optimistic assumption based on a stable success rate of 8.3 % from Phase I to launch, Berggren et al. (2012) estimate an average output of the pharmaceutical research pipeline of 35 launches per year until 2016.

The Patent Cliff

Beginning in 2010, the pharmaceutical industry has faced a historical high wave in drug patent expiration. This phenomenon is widely known as the "patent cliff" (DeRuiter and Holston 2012). With a significant number of top-selling drugs, like Pfizer's Lipitor® to treat and lower blood cholesterol, Bristol-Myers Squibb's Plavix® preventing platelets from coagulating, GlaxoSmithKline's Advair® for a treatment of asthma patients, or AstraZeneca's drug to treat schizophrenia and symptoms of bipolar disorder, Seroquel®, big pharma has experienced painful patent expirations, paving the way for their lower-priced generic substitutes. As such, the patent cliff is the result and aggregation of several successful products that have reached the end of their patent life and hence put substantial sales at risk (Fig. 6.4). The industry's tumble from the expiry of lots of patents is even intensified by the continued global economic crisis, which has health care payers in advanced countries in a state of disarray (Mullin 2012). It is noteworthy that the cliff that peaked in 2012 was mainly caused by drugs that have been discovered in the late 1980s (EvaluatePharma 2012). This, however, provided the concerned organizations with plenty of time to prepare them for the approaching sales drop. As eventually most pharmaceutical companies face similar situations, the industry put substantial effort in finding appropriate solutions to cope with these challenges

[3] (Patent analysis: 'Total Sales at Risk' represents the worldwide product sales in the year prior to patent expiry but allocated to the year of expiry. E.g. Plavix had sales of $7.1bn in 2011, this is shown above as 'At Risk' in 2012 (EvaluatePharma 2012)).

PROTECTION EXPIRY YEAR	US		JAPAN	UK	FRANCE	GERMANY
2012	Plavix® Seroquel® Singulair® Actos® Lexapro®	Diovan® Diovan HCT® Geodon® Boniva®	Nu Lotan Myslee® Preminent Haigou Seroquel®	Lipitor® Amias Seroquel® Aricept® Singulair®	Tahor Singulair® Pariet® Ixprim Aprovel	Seroquel® Atacand® Atacand® Plus Sortis® Aricept®
2013	Oxycontin® Aciphex® Zometa®	Xeloda® Opana®ER Asacol®	Diovan® Plavix® Livalo® Elplat®	Viagra® Xeloda®	Seretide® Coaprovel Xeloda® Micardis® Viagra®	Viani® Zometa® Atmadisc® Coaprovel Viagra®
2014	Nexium® Cymbalta® Celebrex® Symbicort®	Lunesta® Restasis® Evista® Sandostatin® LAR Actonel®	Prograf® Glivec® Abilify®	Abilify® Cipralex® Risperdal® Consta®	Seroplex® Abilify® Ebixa® Risperdal® Consta® LP	Axura Risperdal® Consta® Blopress Plus®
2015	Abilify® Copaxone® Gleevec® Namenda®	Provigil® Combivent® Zyvox® Prezista® Avodart®	Zyprexa® Adoair® Alimta® Spiriva® Symbicort®	Spiriva® Cymbalta® Alimta®	Alimta® Spiriva® Copaxone® Protelos® Cymbalta®	Spiriva® Copaxone® Alimta® Cymbalta®
2016	Crestor® Benicar® Benicar HCT® Cubicin®		Blopress Baraclude®	Glivec® Vfend®	Glivec® Cancidas® Vfend®	Glivec® Zyvoxid Vfend®

Fig. 6.5 Major protection expiries by country and year (Source: IMS 2012)

and to mitigate expected losses (Mullin 2012). Unfortunately, pharmaceutical companies do not yet have a good model at hand to get through such transitions (Jimenez 2012).

Due to substantial patent expiration, the pharmaceutical industry is losing its financial cushion (Fig. 6.5). Since 2006, patent expiry cost the industry an estimated $60 billion in sales. Even more, by 2015, market prognosis project this figure to raise up to $160 billion (Bloom 2012), with its heaviest burden in 2012 and 2013 (Jimenez 2012).

However, the patent cliff is mostly associated with research driven pharmaceutical manufacturers, expiry of their patents and the subsequent loss of sales. Especially for the reason that shortly after the generic substitutes have been launched, prices decline by an average of 40 % and lead in some cases to drastic reduction in sales of nearly 80 % (Denoon and Vollebregt 2010, see also Grabowski and Vernon 1992; Hemphill and Sampat 2011). Actually, in the short term, generic manufacturers will benefit from the patent cliff, as they rapidly acquire market share once branded products lose their IP protection. Starting in 2015, the generic industry is expected to also experience a slowdown in revenue growth as fewer branded blockbuster drugs will be coming off patent (DeRuiter and Holston 2012).

From Fig. 6.4 it is apparent that the pharmaceutical industry is approaching another patent cliff in 2015. With a predicted $33.5 billion sales at risk, this cliff nearly equals that in 2012 (see Table 6.1). However, there are some important differences worth considering. Many of these branded blockbusters that will come off patent are biologic drugs. And with biological drugs, it is expected that sales will not immediately fall of the cliff, unlike the small-molecule blockbusters did back in 2012 (EP Vantage 2013). The basic reason for this is that biosimilars, in contrast to generic small molecule drugs, may differ substantially from their original counterpart and therefore may require costly and long-lasting approval procedures (Frey et al. 2009).

Table 6.1 Top products going off-patent in 2015 (EP Vantage 2013)

Rank	Product	Company	US annual sales ($m) in 2014 (year before patent expiry)
1	Lantus	Sanofi	4,791
2	Abilify	Otsuka Holdings	3,876
3	Rituxan	Roche	3,610
4	Neulasta	Amgen	3,441
5	Copaxone	Teva Pharmaceutical Industries	2,678
6	Gleevec	Novartis	2,002
7	Namenda	Forest Laboratories	1,575
8	Lovaza	GlaxoSmithKline	882
9	Treanda	Teva Pharmaceutical Industries	746
10	Combivent	Boehringer Ingelheim	694
Other			9,320
Total			33,524

The End of the Blockbuster Era

For pharmaceutical companies nothing is quite as exciting as having a promising new molecule in their pipeline that – in the best case – targets some major unmet human health problem (Booz&Co 2012). In the past decades, the pharmaceutical industry continuously adapted its business model towards the development of *the* single drug that solves a common medical problem of tens of millions of people. Relying upon those annual blockbusters to drive a company's profits, the pharmaceutical industry applied this "one size fits all" approach ignoring a patient's unique biology (Jørgensen 2008). The model at present is based on high uncertainties as well as highly skewed distributions of revenue and profit; and shows several similarities with the production of cultural products like movies and their instability of profits (Collier 2011; Hannigan et al. 2013).

In 1987, Glaxo's Zantac® was the first global drug surpassing US$1 billion in annual sales (Rickwood 2012) introducing a new era in pharmaceutical history: the era of blockbusters. A decade later, six blockbuster drugs accounted for 12 % of annual sales in the United States (Aitken et al. 2009), the by far biggest pharmaceutical market at that time. In the following years, the number of blockbusters increased to 51 in 2001, contributing some 25 % to global sales and jumped to 116 blockbuster drugs since, providing 36 % of the global pharmaceutical market's value (Rickwood 2012). However, when the term "blockbuster" was coined in the late 1980s, a drug having that status accounted for about 0.74 % of the global annual pharmaceutical market (see Fig. 6.6). Due to inflation and overall market growth which nowadays provides products an increased number of opportunities for generating sales and to reach this former elite level of US$ 1 billion, the value of a drug that has reached the blockbuster status has significantly diminished by nearly 85–0.12 % of global market value (Rickwood 2012).

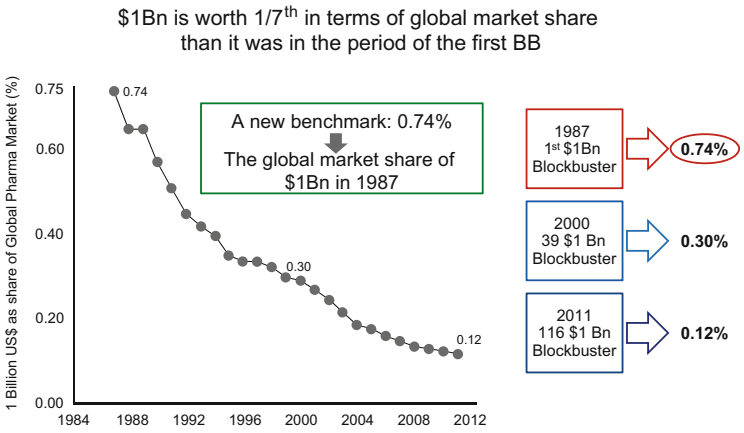


Fig. 6.6 The total value of a blockbuster 1987–2011

Furthermore, since their first emergence, the characteristics and identity of blockbusters have changed. Originally and predominantly applied in primary care, during the past decade the blockbuster model has shifted toward specialty therapies (Aitken et al. 2009; Rickwood 2012; Oliver Wyman 2011). According to Rickwood (2012) in 2002, 70 % of those drugs, traditionally defined as blockbusters were assigned to the group of primary care products. Five years later, the proportion of global drug spending that incurred for primary care drugs has diminished to 55 %. Thereof, 22 % amounted for the five top-selling therapeutic classes which comprised acid pump inhibitors, antidepressants, oral antidiabetics, lipid regulators, and respiratory agents. In contrast, specialist drug therapeutic classes like anti-epileptics, antipsychotics, autoimmune agents, erythropoetins, oncologics, etc. already accounted for 45 % of global drug spending (Aitken et al. 2009). Recently in 2011, the drug distribution was inversely rated with only 44 % of all blockbusters being primary care drugs (Rickwood 2012).

Along with the shift from primary care to specialist drugs a change of pharmaceutical companies' business model seems to be apparent. Several augur the end of the blockbuster era (Hill and Chui 2009; Collier 2011; Thomas Reuters 2011; Cooksey and Buffery 2012) and question, if pharma companies can actually survive, if they pursue their current business model without adaptations (Booz&Co 2012). Thus, following Porter's (1998) generic strategies, many pharmaceutical manufacturers are currently changing their focus from the once dominating mass markets toward smaller, vacant niche markets (Collier 2011). This becomes evident with the latest trends in orphan drugs (Sharma et al. 2010; Unknown 2010; Thomas Reuters 2011) and personalized medicine (Jørgensen 2008; Bates 2010). In accordance with such growing diversity and manifold demand in specialized medicine, traditional blockbusters are not exclusively reserved for the mass markets, but also drugs targeting at smaller patient populations start increasingly to exceed the billion dollar hurdle (Rickwood 2012). This is in line with Jeff Kindler's (former CEO of

Pfizer) statement "[...] we're changing the way we do business [...] we are still pursuing blockbusters, but we are also focusing on addressing many specialized needs of many smaller groups of people" (Kindler 2010).

The Debt Crises and Healthcare System Cost Reduction Programs

Unlike automotive, construction, semiconductor or machinery, the pharmaceutical industry is hardly marked by cyclic fluctuations. With the beginning of the financial crisis in 2008 – emanating from the United States and Europe – several thought that a non-cyclic industry as pharmaceuticals was immune to turmoil and recession, but the global economic crisis and the following downturn disabused them fast (Pharma 2012). In fact, although several countries were hit severely by the economic crisis, only a few of these suffered a considerable decline in pharmaceutical consumption. On a regional consideration, between beginning of 2008 and the end of 2009 South East Asia's consumption increased by nearly +28 %, the American region grew by some +12 % – only Europe had to recover from a −3 % decline, reached in the third quarter of 2009, to a marginal +2 % gain of pharmaceutical consumption by the end of 2009 (Buysse 2010). Recent investigations of the IMS Institute for Healthcare Informatics report a drop of the nominal US drug spending by 1 % in 2012 to US$ 325.8 billion (IMS 2013).

As a reaction of the global downturn, the subsequent sovereign debt issues, and reduced government budgets, beginning in 2010, many European countries imposed a multitude of cost-containment measures (Miller 2011; Vogler et al. 2011; Coker 2012). Besides, since that time, all countries appear to be permanently optimizing their pharmaceutical system (Vogler et al. 2011). The most commonly applied cost-containment were price reductions of pharmaceutical products (Vogler et al. 2011; Coker 2012), followed by changes in copayments, which most of the time led to increasing costs for patients to compensate lower reimbursement rates, adaptions of reference pricing systems, and policy changes that affected reimbursement procedures (Vogler et al. 2011). Moreover, several already weakened economies that suffered low demand, little tax revenues as well as high unemployment, were hit twice by initiated government austerity programs and reserved bank lending. Reduced government spending, higher interest rates, and difficulties in private-sector credits negatively affect those countries' overall economic activity (Miller 2011).

Pharmaceutical companies, heavily relying on the European market had to manage considerable effects on their financial performance due to pressures from the European deficit-led pricing as well as from above mentioned influences (Coker 2012). This, however, involved pharmaceutical companies of all business types. Tighter budgets at research driven companies led to reduced spending in R&D, putting depleting pipelines under additional pressure and forcing R&D leaders to

continuously justifying their investments (Deloitte 2011). Furthermore, the rising cost pressure in the health care industry induces governments to allow an earlier generic entry (Jimenez 2012). Pharmaceutical contract manufacturing organizations (CMOs) that supply the European market – which is dominated by national healthcare systems as the primary buyer and distributor of pharmaceutical products – have to put up with the deterioration of their operational performance as volume and price reduction evoke a sharp decline of drug expenditures (Miller 2011).

The Increased Competition

Macroeconomic and regulatory changes determine the competitive and operational environment of pharmaceutical manufacturers and their managers' tactical and strategic decisions (Rossetti et al. 2010). Prior to 1984, the pharmaceutical industry was dominated by research driven companies that barely felt the competition from generic product imitations. This came from costly requirements set by the Food and Drug Administration (FDA) that had to be met by generic drugs these days (Grabowski and Vernon 1992). Since September 1984 the Hatch-Waxman Act (formally known as Drug Price Competition and Patent Term Restoration Act) regulates the entry of generic drugs in the US, the world's largest pharma market (Grabowski and Kyle 2007). Most significantly, with the law becoming effective, an abbreviated process (Abbreviated New Drug Application (ANDA)) has been introduced to shorten the time for generic drugs to receive FDA approval. The law enables generic manufacturers to legally conduct the necessary tests of bioequivalence and to apply for FDA approval before the respective patent expiration (Frank 2007). Under certain circumstances, FDA approves a 180-day exclusive right for the first generic manufacturer that has filed an entitled ANDA. This exclusivity allows a generic manufacturer to compete solely with the patent owner before other generic competitors enter the market (Hemphill and Sampat 2011). Today those patent challenges occur increasingly earlier in a branded drug's life cycle than before (Grabowski and Kyle 2007). In the European market, generic drugs are often favored by government drug policy and as such their prescription is encouraged or has even become mandatory not to overtax drug budgets (Kanavos et al. 2008).

This said, it is quite obvious why Grabowski and Vernon (1992) could not provide evidence for any significant entry barriers into the generic market that has seen an explosive growth, from a market share of hardly 20 % in the mid-1980s, to about 70 % today (Frank 2007; Kanavos et al. 2008; Engelberg et al. 2009; Hemphill and Sampat 2011) and experienced intensified competition since (Saha et al. 2006; Grabowski and Kyle 2007). This fierce competition also unfolds to the biotech sector whose low entry barriers and companies with normally only a few products in the pipeline are considerably vulnerable towards competitors (Guo et al. 2004).

As mentioned earlier, such fierce price competition from generic substitutes and the effect of generic market entry constitute a real challenge for branded drugs and curtail the profits that are vital to fund their innovative activity (Frank 2007).

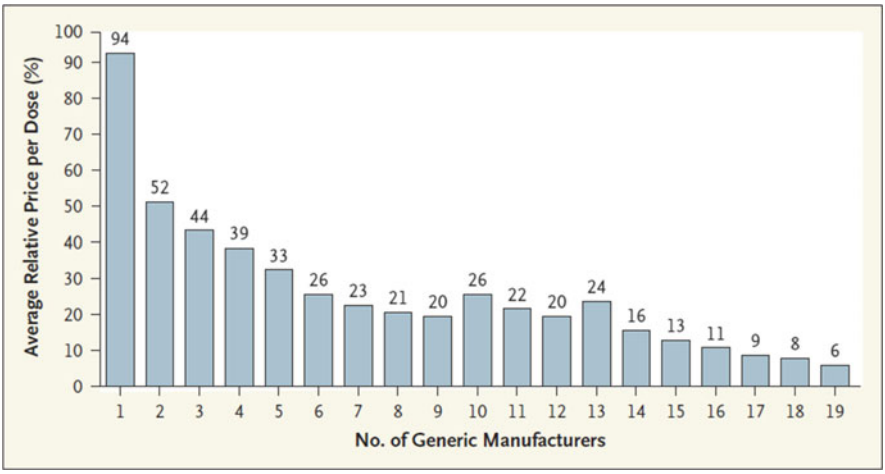


Fig. 6.7 Change in a drug's average relative price as the number of generic substitutes increases (Source: Frank 2007)

Yet generic entry does not only impact the branded drug business but also leads to increased price rivalry among generic companies themselves. The effect on average relative prices of drugs and such initiated fierce competition among generic manufacturer is illustrated in Fig. 6.7.

With the on-going market entry of generic manufacturers, increasing rivalry and competition between branded drug manufacturers and generic manufacturers is sure to ensue as competition shifts from monopoly-like markets towards competition based on price (Epperly 2013). This, in contrast to many other industries, tightens the challenges for research driven manufacturers such as the pharmaceutical industry, where the person who is consuming the product is not necessarily the person choosing and paying for it. In addition, decision making and payment are more complex within the pharmaceutical industry (Guha et al. 2008). In order to mitigate the rivalry from generics, some research driven pharma companies built up their own generic brand products or cooperate with generic manufacturers and thus try to utilize the 6-month exclusivity period by an authorized generic version of their own brand name drug. Besides, brand manufacturers participate in the price competition among others through different kind of promotions e.g. free samples or rebates. The latter often depend on a drug's sales volume that may decrease after generic entry. Guha et al. (2008) argue that volume-dependent reduction of free samples and lower rebates may result in considerable price increases as soon as generics have entered the market. Hence it might displease brand name drug manufactures that brand loyalty is rather low within the industry (MarketLine 2012). Additionally, to make matters worse, the US and European countries try to control cost, making future growth come by harder in the developed markets (Herper 2012).

With the rise of the emerging markets most pharma companies seek to participate at these new engines of pharmaceutical growth. The Agreement on Trade

Related Aspects of Intellectual Property Rights (TRIPS) regulates the protection of intellectual property (IP) at a minimum standard for all WTO members[4] (WTO 2013). Thus, research driven pharmaceutical manufacturers can make use of their patents also in countries apart of the advanced and familiar markets. Unfortunately, as latest events evidenced, TRIPS does not provide a full guarantee for fully granted patent protection in certain markets (Economist 2013). Besides some adventurous IP protection, emerging markets challenge pharmaceutical companies with a lack of reimbursement, deficient healthcare infrastructure, and the affordability of drugs due to a widely spread out-of-the-pocket spending (Bhattacharjya and Sapra 2008; Anderson et al. 2009; Booz&Co 2013). This leaves band name pharma in a state of uncertainty and further, unavoidable competition in markets that a dominated by generic manufacturers (Anderson et al. 2009; Campell and Maag 2010).

The Increasing Complexity

Pharmaceutical companies are more and more exposed to growing complexity. As such, they have to continue to find appropriate ways to handle these most diverse influencing factors. These external drivers of complexity are among the most challenging ones for pharma and are predominately characterized by economic volatility, varying customer behavior, or changes in technologies and the competitor base (Simplicity 2012). The increasing globalization and dynamic environment induce companies to expand and to accelerate their operations (Fockenbrock 2011). Beyond the unpredictable nature of pharmaceutical manufacturing, pharma companies are confronted with a high number and variety of consumption points and market intermediaries along the entire supply chain, thus leaving these organization in a muddle of interdependencies, contingencies, and uncertainties (Goetschalckx et al. 2002; Rossetti et al. 2010). In addition, the latest economic crisis intensified the already existing challenges pharma had to cope with, and brought evidence that flexible and agile companies handle these external shocks better than their sedate competitors (Fockenbrock 2011). With a number of drugs coming off patent and the drying up of steady revenues from blockbusters, many pharmaceutical companies avert from highly standardized products towards customized and low volume specialized solutions.

Only a few pharmaceutical manufactures solely rely on branded drugs. Most companies have expanded into other sectors like generics, biosimilars, diagnostics, consumer health, nutrition, or wellness (Booz&Co 2012). Thus, increasing customer demand for individually adapted products leads to the expansion of pharma's product

[4] WTO members can make use of different periods of time to delay the application of the provisions listed by TRIPS. For developed countries the period ended at 1 January 1996, for developing countries and countries in transition the period ended on 1 January 2000, for least-developed countries with regard to pharmaceutical patents the period will end on 1 January 2016. Country classifications are according to the United Nations (WTO 2013).

ranges. Without transparency of real cost allocation, marketing-fads and highly advertised drugs – often being a worst case scenario for manufacturing – are cross-subsidized by top-selling products and thus weathering revenues. High customer proximity affects a company's entire process of value creation; frequent customer interaction leads by trend to larger product portfolios and an increased complexity. Low similarities within the portfolio impede the utilization of economies of scale and deteriorate organization's efficiency (Friedli and Bellm 2012).

However, blind complexity reduction of e.g. SKUs will most likely not lead to the achieved target (see Chap. 19). Pharmaceutical manufacturers need to evaluate their right degree of complexity by balancing ultimate flexibility versus inability of supply. There are examples in the literature where companies rather preferred to increase their complexity than simplifying it down, while focusing on their core competences. Others however overestimate the added value of mergers and acquisitions and end up drowning in complexity due to poor organizational coordination and strategic misalignment of the newly built organization (Simplicity 2012).

Recent Quality Issues and Drug Shortages

In late 2007, the heparin case shocked the pharmaceutical community, when the contaminated product led to at least 81 deaths and hundreds of serious adverse events in various countries since (Briones 2008). Several established pharma companies had to also recall several batches of drug. Following these recalls, FDA officials traced the supply chain ending up at a Chinese facility that supplied the poor quality heparin active ingredient (Hedlund et al. 2012). As a matter of fact, quality issues have spread in global manufacturing despite the request of Article 2 of the WHO Constitution for setting global standards as to "develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products" (WHO 2007, p. 1).

Unfortunately, the described heparin case, even though it might be the worst one, not the only one of a kind, the pharmaceutical industry suffers from. Actually, there are far too many of these quality lapses within the industry over the past few years that have compromised public health (Eglovitch 2013).

Thus, poor product quality and numerous compliance issues brought the pharmaceutical industry easily additional costs exceeding US$ 700 million in fines since 2001 and billions more due to lost sales (McKinsey 2007). This might result from the pharmaceutical industry's legacy to apply science rather to the discovery of NMEs and rely on inspection of final product quality, than working on scientifically mastered manufacturing processes (see Chap. 29). However, it is quite reasonable that a knowledge-intense industry as pharma has recognized its shortages and trends like transparency in manufacturing and several beneficial business practices became requirements for pharmaceutical companies (Pharmtech 2009). Unfortunately, do not all pharma companies continuously strive for changing to a science-driven approach to pharmaceutical manufacturing; still

Table 6.2 Drug GMP warning letters by category from 2005 to 2012 (Source: Eglovitch 2013)

	FY 05	FY 06	FY 07	FY 08	FY 09	FY 10	FY 11	FY 12
Oral solid		6	2	4	7	16	9	7
API	2		1	3	7	8	17	8
Oral liquid	1	1	1		3	6	4	
Topical	2	1	2	3	4	6	6	6
Miscellaneous	3	4	1		6	5	4	9
Injectable	2	3	6	2	3	4	13	9
Inhalable	2		1					
Repacker	3	1	1	1	2	2		
Testing lab						1		
Veterinary	2	4	2	1	1	1		1
Biologics	1		2	1	1			
Total	18	20	19	15	34	49	53	40

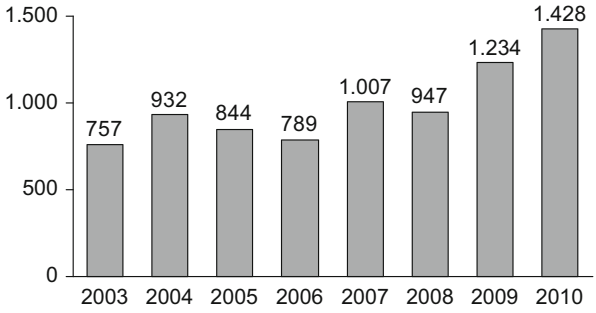


Fig. 6.8 FDA's foreign drug inspection accomplishments (FDA 2011)

too many companies are lacking behind in implementing outstanding practices and seem to hardly feel an imperative for changing their behavior until a significant compliance issue occurs (McKinsey 2007). This reluctance for change is partially reflected in Table 6.2, illustrating the development of drug GMP warning letters issued by FDA.

No doubt, the increase of warning letters sent by FDA is surely influenced by the agency's increasing number of site inspections that are no longer focused on domestic manufacturing facilities only but continuously expanding to foreign locations as illustrated in Fig. 6.8 (Eglovitch 2013).

Yet, more frequent site inspections should not be seen as scapegoats for the industry's shortcomings and an increased submission of warning letters or 483 s in the worst case. Many pharma companies still have to learn the application of latest manufacturing practices and the capability to manufacture quality rather than controlling it. This goes in line with Eglovitch (2013, p. 1) quoting an industry observer that the recent decrease of warning letters by 23 % from 2011 to 2012 is "more of a 'statistical anomaly' than an actual indication of waning enforcement."

Therefore, regulatory agencies like FDA adjusted their focus to no longer simply monitor the outputs of inspected manufacturing sites but also their processes and systems (McKinsey 2007).

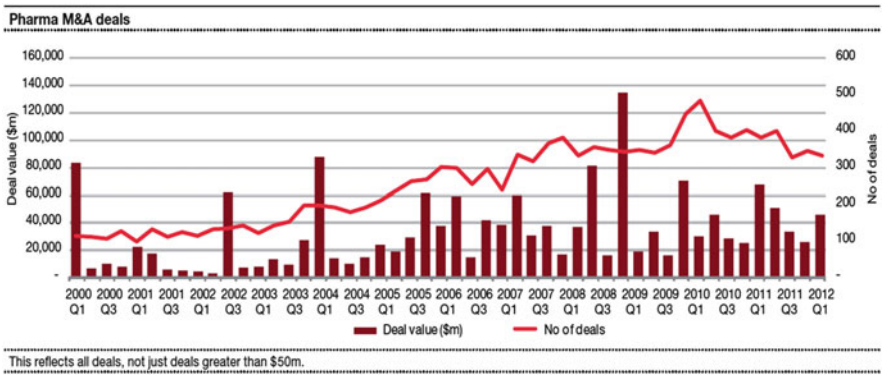


Fig. 6.9 Global M&A deals from 2000 to 2012 (Source: PwC 2012)

As long as the market does not reward quality and e.g. generic competition is predominantly based on prices (Woodcock and Wosinska 2013), it is reasonable that quality problems will continue or even become more frequent especially on a global scale. With the industry's shift to emerging markets, evidence brought by several studies that such problems are more common at pharma's offshore operations (Staton 2011), and the same problems surfacing year after year, it is – unfortunately – apparent that we will see more quality issues if global pharma stays on its current track.

Mergers & Acquisitions

For many years, technology intense industries like the pharmaceutical industry have been characterized by ample merger and acquisition (M&A) activities. Several studies reveal the effects of industry structure and characteristics on M&A deals and document evidence that such deals are driven by industry-wide shocks like deregulation or technological advances (Mitchell and Mulherin (1996); Hall (1999); Andrade et al.(2001); Andrade and Stafford(2004); and Harford (2005)). As a matter of fact, most of today's big pharma companies are the result of at least one major M&A deal (Duflos and Pfister 2007)

In the pharmaceutical industry M&A intensity grew in the mid-1980s strongly influenced by the threat of upcoming patent expirations. Due to a rising competition from generic manufacturers and potential declines in sales, some research-driven pharma companies seek to cut costs by merging their efforts for R&D, manufacturing, marketing etc. (Ramrattan and Szenberg 2006). Others pursue an increase of their product portfolio, access to certain markets or a filling of their pipeline gaps (Duflos and Pfister 2007; Collier 2011; PwC 2012). As Fig. 6.9 depicts the pharmaceutical industry has seen an almost constantly increase in both value and number of M&A deals for the past decade.

However, the rising number of deals that the industry has already witnessed and is still facing, has left its marks. The decline in the total number of big pharma companies has led to an increasingly concentrated market especially among those companies that are considered as the engines of pharmaceutical R&D (LaMattina 2011; Comanor and Scherer 2011; Bruce 2012). And such consolidation does not spare the generic market either (DeArment 2012). In accordance with a shrinking number of research-driven companies, the industry sees fewer parallel research efforts which lead to a reduced rate of pharmaceutical innovation (Comanor and Scherer 2011). With the emergence of few big, and simultaneously the vanishing of plenty of small and agile companies, the danger rises that the industry's pace would slow down due to inert companies and their slow decision-making processes (Bruce 2012). Furthermore, those vertical and horizontal integrations threat to transform the industry into an oligopoly (Gagnon 2013). From a different point of view (McKinsey 2011) argue that rumors about market consolidations are most likely conventional wisdom and that the industry over the years has become even more fragmented and the total number of pharmaceutical companies has more than doubled.

Analyzing the characteristics of M&As over the years, the number of deals targeting on small molecules and biologics has remained relatively unchanged, but their percentage of overall deals has declined from about 40 % in 2007 to some 22 % in 2011. Besides, as depicted in Fig. 6.10, companies of the vaccines sector and generic manufacturers gained importance and increasingly became the target of latest M&A activity. In the same period where veterinary deals declined, big pharma further diversified into sectors like consumer health/OTC and diagnostics looking for synergies with their existing product portfolio (Ignjatovic 2012). With the beginning of 2012 the industry has seen several M&As of Big Pharma heading for biotech companies with promising research focused on oncology (Mullin 2012).

The increasing importance of the fast-growing emerging markets for pharma is depicted in Fig. 6.11. From 2007 to 2011, M&A deals in developed countries have predominately been focused on small molecule and biological branded drugs (36 %). Furthermore, almost 87 % of all deals that targeted on diagnostic or medical device companies comprised manufacturers located in developed countries. In contrast, emerging market deals mainly focused on generic manufacturers (50 %), consumer health (23.3 %), and vaccines (13.3 %) providing evidence for big pharma's continuing global expansion and the recognition of the advantages of involving local partners in emerging market operations (Ignjatovic 2012).

As Big Pharma has not yet recovered from the recent patent cliff and some more blockbusters will come off patent soon (see Fig. 6.4), companies still seek to fill up their pipelines and benefit from latest advances in areas like immunology or oncology (Staton 2013).

However, the question arises, where pharma will go next? The pharmaceutical industry is a relatively young industry compared to e.g. automotive. Considering the number of big automotive OEMs it is a significantly smaller number than Big Pharma currently comprises. Nevertheless, even in automotive some argue there are

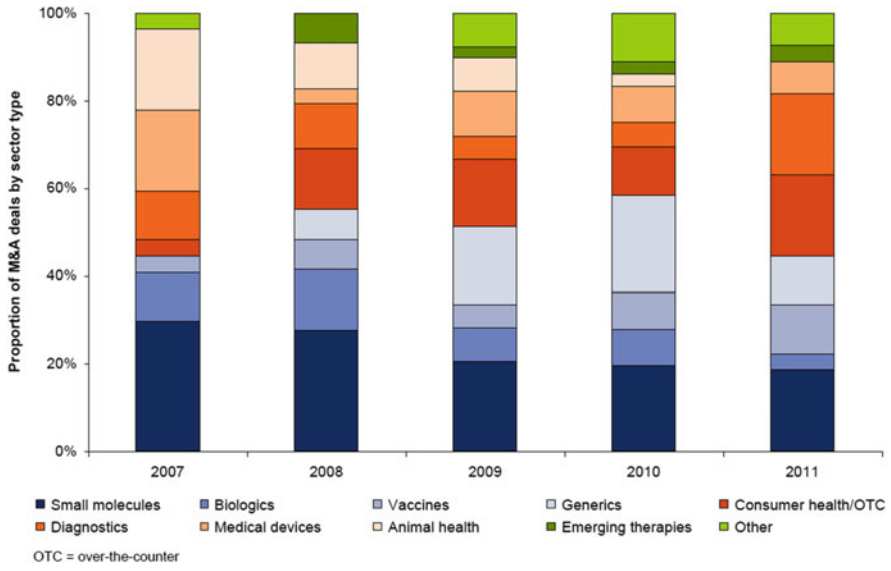


Fig. 6.10 Top 10 pharma companies' M&A deals from 2007 to 2011 by sector (Source: Ignjatovic 2012) (Ignjatovic (2012) considers the top 10 pharma companies as Pfizer, Novartis, Sanofi, Merck & Co., Roche, AstraZeneca, GlaxoSmithKline, Eli Lilly, Johnson & Johnson, and Abbott laboratories)

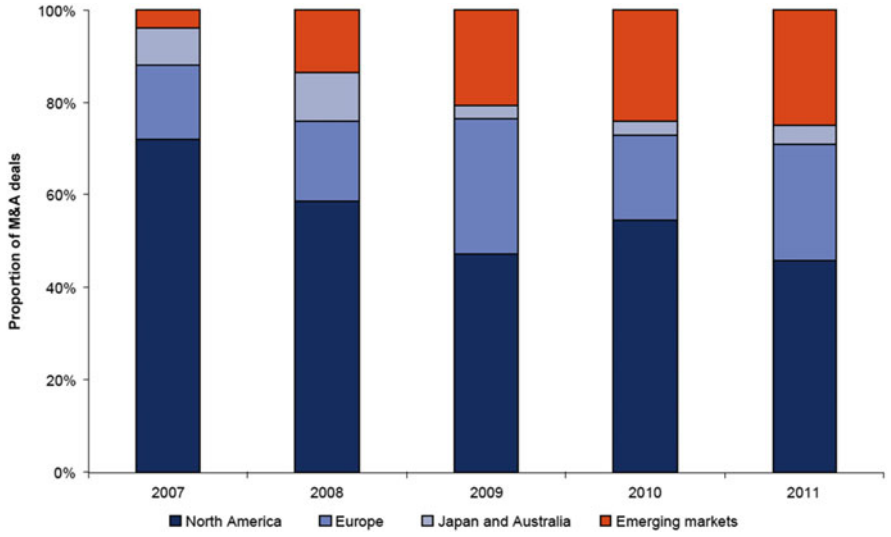


Fig. 6.11 Top 10 pharma companies' M&A deals from 2007 to 2011 by geography (Source: Ignjatovic 2012) (Ignjatovic (2012) considers the top 10 pharma companies as Pfizer, Novartis, Sanofi, Merck & Co., Roche, AstraZeneca, GlaxoSmithKline, Eli Lilly, Johnson & Johnson, and Abbott laboratories)

still too many OEMs in the market and that further consolidation will continue (Roland Berger 2009).

Overcapacities

For some time the pharmaceutical industry suffers sever overcapacity. Several factors that have been discussed in detail above e.g. R&D pipelines running dry, the patent cliff or continuous organizational restructuring to improve operational profits by cutting costs and maximizing productivity contribute to or even worsen pharma's problem. Recent M&A's like Pfizer-Wyeth, Merck-Schering Plough, Roche-Genentech, and the marriage of Sanofi-Aventis and Genzyme have led to a consolidation of the pharmaceutical sector. In addition, larger companies have bought out several mid-sized and small companies or incorporated them into their operations. These activities have resulted in numerous redundant manufacturing facilities and thus led to the industry's overcapacity and exceeding global demand by approximately 40 % (Frost and Sullivan 2009).

Facilities of leading pharmaceutical companies that lack manufacturing flexibility and which are primarily designed for the production of high-volume, high-margin, patent-protected small molecule APIs become obsolete when their original purpose loses patent exclusivity and is subjected to competition from generics overnight (Tse and Jakobs w/o date).

In their desperate search of a margin improvement many leading pharmaceutical companies enter into the CMO business offering their idle manufacturing capacity for other players (Tse and Jakobs w/o date). In order to avoid negative publicity or huge severance costs in case of a facility shut down, multinational pharma companies in the past preferred to transfer their spare facilities to private-equity firms or to management teams that continue to run the sites as CMOs. Although this approach brings relief to brand name manufacturers, it merely shifts the problem. Moreover, it provokes an unsustainable situation for the global CMO industry (Miller 2011) and on a longer term perspective such approach creates an imbalance within the entire pharmaceutical industry (Frost and Sullivan 2009).

The Global Dimension

The Emerging Market Opportunity

Globalization is considered as one of the most critical challenges companies face in their daily operations (Khanna et al. 2005; Burgess and Steenkamp 2006). Even though not new to companies and their managing teams globalization gathered pace especially since the late 1980s and thus intensifying global competition. After the

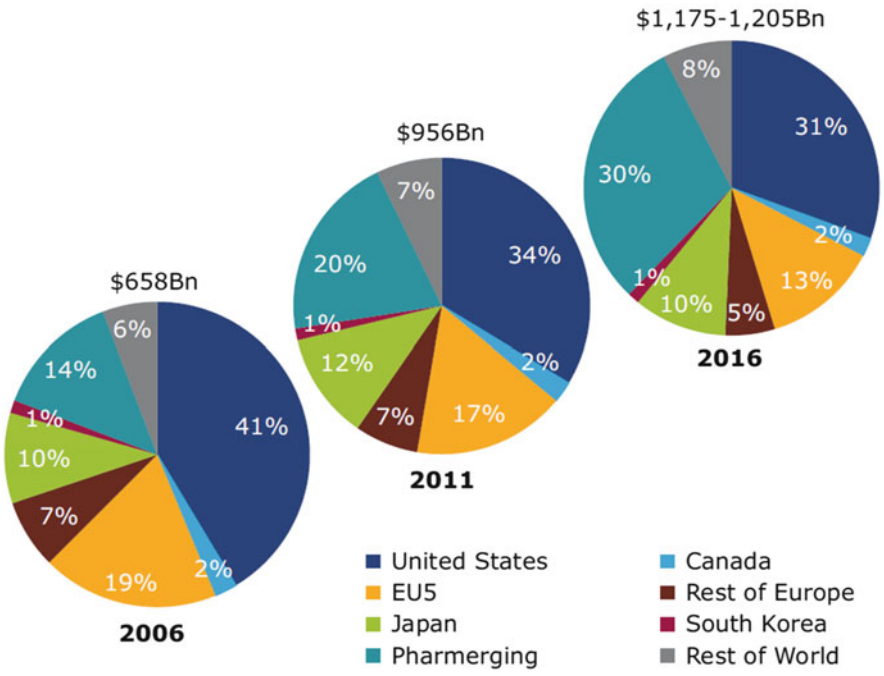


Fig. 6.12 Pharmaceutical spending by geography (Source: IMS 2012)

collapse of the Soviet Union along with other Eastern Asian countries a notable number of the world's population elided from a state-controlled and central planning to a global market economy. The revolution of information technology and the companies' willingness to outsource their operations led to global partnerships and supply chains (Hayes et al. 2005; Yip 2002). Moreover, the establishment of international trade agreements like GATT (1941); WTO (1995) as well as economic pacts like EFTA (1960); ASEAN (1967); Mercosur (1991) and NAFTA (1994) continue to drive the trend of transnational manufacturing (Ferdows 1997; Dangayach and Deshmukh 2001; Mora-Monge et al. 2008) facilitating global sourcing and distribution (Khanna et al. 2010) and spur global competition (Sheth 2011). This is also entails a rapidly changing pharmaceutical landscape on a global scale.

Historically, advanced countries have been the largest market for multinational pharma companies and will continue to do so in the future. However, with the advent of globalization the contribution of emerging markets to pharmaceutical sales will gain significant importance in the next decades (see Figs. 6.12 and 6.13).

As competition in the developed world is considerably high and pressure on prices is expected to continue, manufacturing companies are on the lookout for new sources of low cost labor (Hayes et al. 2005) and access to new markets. By establishing their operations in low labor cost countries like China, Eastern Europe, India, and Latin America (Hayes et al. 2005) by mistake companies often adopt a mind-set of "less developed countries". As such, they expect that these countries

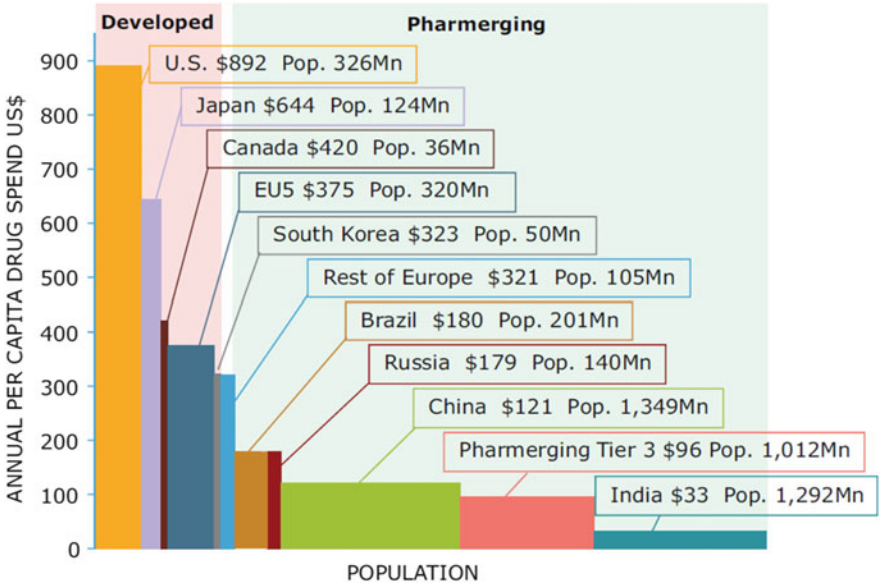


Fig. 6.13 2016 pharmaceutical spend per capita 2005$ and population (Source: IMS 2012)

follow an equal development path as followed by industrialized countries yet at an earlier stage, erroneously assuming "that the game is therefore one of catch-up, and that market evolution patterns seen previously in developed economies will be replicated in the (emerging markets) EMs" (Arnold and Quelch 1998, p. 9). The statement is supported by Khanna et al. (2010), arguing in their recent investigation that there seems to be a common sense of emerging markets to converge with already industrialized countries. However, they emphasize not only to distinguish operations in emerging markets from developed markets but also to distinguish emerging markets individually from each other (Khanna et al. 2010).

That said, it is quite obvious that these markets have to be treated differently. Familiar approaches and often highly standardized programs that work well in advanced countries for years will need country-specific adaptions to reveal their full potential in a new environment. This also comprises OPEX programs of especially Western pharmaceutical companies that have evolved from and are tailored to the culture and behavior of their country of origin.

Outsourcing for Cost Savings

In their struggle to contain fixed costs, most pharmaceutical companies are currently searching for opportunities to reduce their internal capacities in manufacturing, R&D, and even marketing. As such, pharmaceutical companies of

all sizes increase outsourcing of their operations in order to gain productivity and efficiency, and to convey solving their problems to one of the numerous service providers. Moreover, the global competitive environment, forces many organizations to especially streamline their pharmaceutical manufacturing – most affecting the manufacture of small molecule generic drugs. This trend has even been strengthened by the latest financial crisis (Zhang 2012).

In order to realize significant cost savings, many drug companies have already started or stand in a late stage consideration of outsourcing their manufacturing to e.g. Eastern Europe, China, and India (DeRuiter and Holston 2012). Pursuing their model of "more achievements for less cost" Western pharma companies enter these emerging markets utilizing both low cost manufacturing and access to these markets. Thus, many multinational drug companies looking for partnerships with domestic companies in these markets that already possess the required technical capabilities (Zhang 2012).

However, top-level executives are often blindsided by the numerous benefits of offshoring operations and may too easily refuse the downsides, taking operational risks serious. Offshore manufacturing locations pose additional quality risks, especially when partnered organizations possess employees with different culture, i.e. language and values. Thus, it is the challenge for companies outsourcing in those regions to transfer and maintain their knowledge that is required to operate and manufacture their products correctly to mitigate the quality risk (Gray et al. 2011).

It is expected that the outsourcing trend will continue for the next years and that the pharmaceutical supply chain will disaggregate compared to the automotive industry (McKinsey 2011). Moreover, the demand for outsourcing services will also be carried on by pharma companies that pursue personalized medicines and will thus increasingly rely on the outsourcing opportunity in order to handle their product portfolios becoming more diverse (Zhang 2012).

Summary and Conclusions

The Pharmaceutical Industry has undergone tremendous change over the last years, having seen the deterioration of its former blockbuster business model. An increased global competition combined with the described productivity crisis in pharmaceutical R&D and record high losses of patent protection for major drugs have led to a huge cost pressure on every single activity within a pharmaceutical value chain. The regulatory environment on the one hand makes needed changes more difficult, having a history of avoiding or at least complicating them. On the other hand, the latest regulatory requirements are based on a process-oriented understanding and continuous verifications fostering a more science-based approach to pharmaceutical production. But still a legacy of no-change culture has to be overcome on the way to true excellence. The third dominant factor is the globalization of the business and the globalization of value chains increasing again

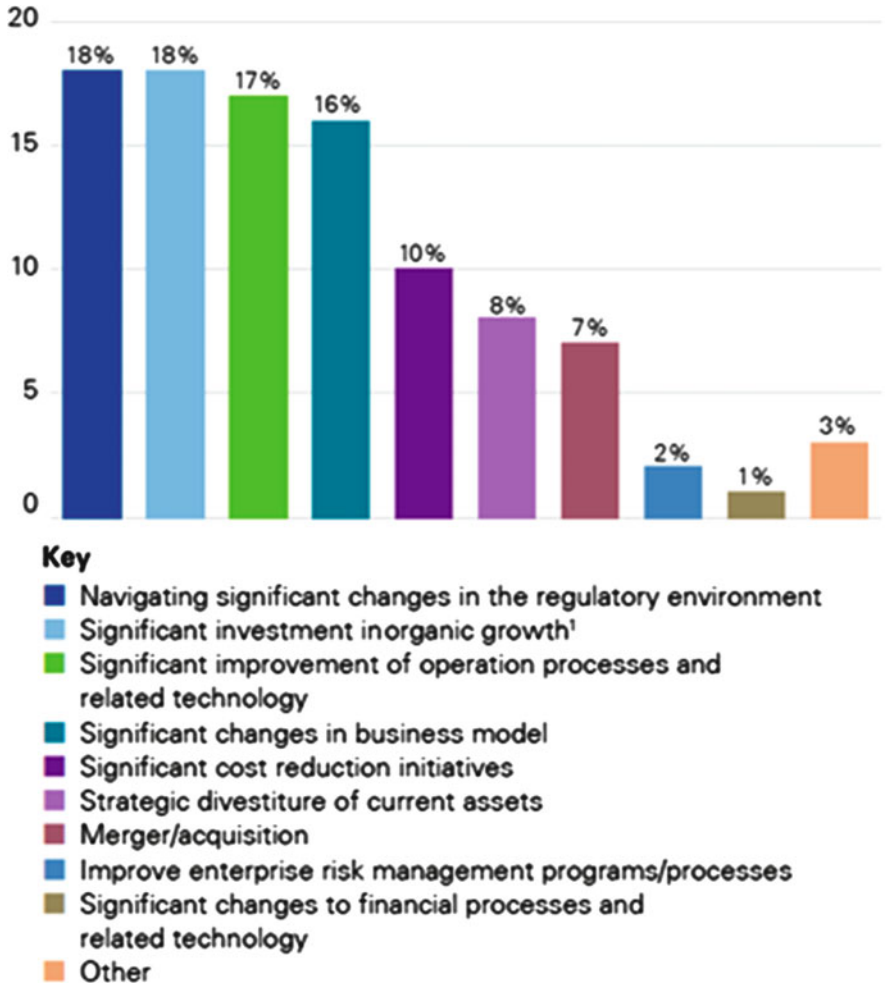


Fig. 6.14 Top initiatives on the mind of management (Source: KPMG 2012)

the complexity of the business. The global production network has to be managed from a true network perspective in the future to ensure competitiveness. We will come back to this at the end of the book in our part 4.

As illustrated in Fig. 6.14, the highest ranked priorities of top management in the pharma industry are all related to operations. Therefore to be successful in the future the pressure of changing to a continuous improvement culture ensuring a steady increase of productivity while keeping the quality level will become a mandatory prerequisite for pharmaceutical companies. Additionally, OPEX will more and more have to work as well in the emerging countries as production capacities are currently shifting. A new generation of OPEX will have to deal with the global logic of today's healthcare business.

References

Aitken M, Berndt ER, Cutler DM (2009) Prescription drug spending trends in the United States: looking beyond the turning point. Health Aff 28(1):w151–w160
Anderson T, Olson J, Sobelman D (2009) Assessment of the opportunities for pharmaceutical manufacturers in emerging markets. J Manag Care Pharm 15(5):396–402
Andrade G, Stafford E (2004) Investigating the economic role of mergers. J Corporate Finance 10:1–36
Andrade G, Mitchell M, Stafford E (2001) New evidence and perspectives on mergers. J Econ Perspect 15(2):103–120
Arnold DJ, Quelch JA (1998) New strategies in emerging markets. Sloan Manag Rev 40(1):7–20
Bates S (2010) Progress towards personalized medicine. Drug Discov Today 15(3/4):115–120
Berggren R, Møller M, Moss R, Poda P, Smietana K (2012) Outlook for the next 5 years in drug innovation. Nature Rev 11:435–436
Bhattacharjya AS, Sapra PK (2008) Health insurance in China and India: segmented roles for public and private financing. Health Aff 27(4):1005–1015
Bloom J (2012) Should patents on pharmaceuticals be extended to encourage innovation? http://online.wsj.com/article/SB10001424052970204542404577156993191655000.html#. Accessed 9 Apr 2013
Booz & Co (2012) Big pharma's uncertain future, Booz&Co, issue 66 Spring 2012
Booz & Co (2013) Pharma emerging markets 2.0 – how emerging markets are driving the transformation of the pharmaceutical industry
Briones S (2008) Heparin recall: another crisis for China & the FDA
Burgess SM, Steenkamp J-BE (2006) Marketing renaissance: how research in emerging markets advances marketing science and practice. Int J Res Mark 23(4):337–356
Bruce I (2012) Interview with future medical chemistry's US senior editor, Iwao Ojima. Future Med Chem 4(16):2019–2022
Buysse IM (2010) Impact of the economic recession on the pharmaceutical sector. http://www.pharmaceuticalpolicy.nl/Publications/Reports/Buysse_report%20impact%20recession_2010.pdf. Accessed 5 May 2013
Campell D, Maag G (2010) Zeitenwende im internationalen pharmamarkt: "Aufstrebende Regionen" gewinnen an Bedeutung. Pharmind 72(4):614–618
Coker V (2012) Outsourcing to emerging markets: the effect of the European economic crisis. Pharm Technol 36(2):s34–s42
Collier R (2011) Bye, bye blockbusters, hello niche busters. C M A J 183(11):697–698, August 2011
Comanor WS, Scherer FM (2011) Mergers and innovation in the pharmaceutical market. HKS faculty research working paper series RWP11-043, John F.Kennedy School of Government, Harvard University
Cooksey K, Buffery D (2012) The 2012 pharmaceutical pipeline, American health & drug benefits. Spec Feature 5(3):51–55
Dangayach GS, Deshmukh SG (2001) Manufacturing strategy: literature review and some issues. Int J Operations Prod Manag 21(7):884–932
DeArment A (2012) Chain pharmacy generics – mergers among generics cos. On the rise. Drugstorenews, 24 Sept 2012
Denoon A, Vollebregt E (2010) Can regererative medicine save Big Pharma's business model from the patent cliff? Regen Med 5(5):687–690
DeRuiter J, Holston PL (2012) Drug patent expirations and the "patent cliff". US Pharm 37 (6):12–20, Gray et al. 2011
Deloitte (2011) Measuring the return from innovation – is R&D earning its investment?
Duflos G, Pfister E (2007) Searching for innovations? The technological determinants of acquisitions in the pharmaceutical industry

Economist (2013) Drug patents a fool's game, Schumpeter business and management http://www.economist.com/blogs/schumpeter/2013/04/drug-patents. Abgerufen am 23 May 2013, 20 Uhr
Eglovitch JS (2013) After issuing 40 drug GMP warning letters in FY 2012, FDA aims to improve drug quality this year, the gold sheet, pharmaceutical & biotechnology quality control 47(3)
Engelberg AB, Kesselheim AS, Avorn J (2009) Balancing innovation, access, and profits – market exclusivity for biologics. N Engl J Med 361(20):1917–1919
EP Vantage (2013). http://www.epvantage.com/Universal/View.aspx?type=Story&id=384778&isEPVantage=yes. Retreived 22 Apr 2013
Epperly L (2013) Generic drug manufacturers, the Henry fund, Henry B. Tippie School of Management
EvaluatePharma (2012) World preview 2018 – embracing the patent cliff
FDA (2011) Division of foreign field investigations. www.fda.org. Retreived 6 May 2013
FDA (2013). www.fda.gov. Retreived 6 May 2013
Ferdows K (1997) Made in the world: the global spread of production. Prod Operations Manag 6 (2):102–109
Fockenbrock D (2011) Die neue Dynamik auf den Märkten. www.handelsblatt.de Abruf am 10 May 2013
Frank RG (2007) The ongoing regulation of generic drugs. N Engl J Med 357:20
Frey D, Frei D, Pfister K (2009) Biosimilars – Status quo und quo vadis? Schweiz Med Forum 9 (5):97–100
Friedli T, Bellm D (2012) Leistungsdefinition im internationalen Vertrieb – Zwischen Kundennähe und Komplexitätsfalle. In: Binckebanck L, Belz C (eds) Internationaler Vertrieb Grundlagen, Konzepte und Best Practices für Erfolg im globalen Geschäft. Wiesbaden, pp 499–514
Frost & Sullivan (2009) Global active pharmaceutical ingredients market: an outlook
Gagnon JP (2013) The research manufacturing pharmaceutical industry. In: Smith MI, Wertheimer AI, Fincham JE (eds) Pharmacy and the US healthcare system, 4th edn. Pharmaceutical Press, London.
Goetschalckx M, Vidal CJ, Dogan K (2002) Modeling and design of global logistics systems: a review of integrated strategic and tactical models and design algorithms. Eur J Oper Res 143 (1):1–18
Grabowski H, Kyle M (2007) Generic competition and market exclusivity periods in pharmaceuticals. Manage Decis Econ 27:1–12
Grabowski HG, Vernon JM (1992) Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 Drug Act. J Law Econ 35(2):331–350
Gray JV, Roth AV, Leiblein MJ (2011) Quality risk in offshore manufacturing: evidence from the pharmaceutical industry. J Oper Manag 29(2011):737–752
Guha R, Lacy AM, Woodhouse S (2008) Analyzing competition in the pharmaceutical industry. Econ Committee Newsletter 8(1):6–9
Guo R-J, Lev B, Zhou N (2004) Competitive costs of disclosure by biotech IPOs. J Account Res 42 (2):319–355, May 2004
Hall BH (1999) Mergers and R&D revisited, prepared for the quasi-experimental methods symposium, Econometrics Laboratory, UC Berkeley, 3–7 Aug 1999
Hannigan T, Mudambi R, Sfekas A (2013) A longitudinal analysis of blockbuster pharmaceutical drugs, DRUID Academy 2013 at Comwell Rebild Bakker, Rebild/Aalborg
Harford J (2005) What drives merger waves? J Financ Econ 77:529–560
Hayes RH, Pisano GP, Upton DM, Wheelwright SC (2005) Operations, strategy, and technology: pursuing the competitive edge. Wiley, Hoboken
Hedlund K, Coyne D, Sanford D, Huddelson J (2012) The heparin recall of 2008. Perfusion 28 (1):61–65, 2013 Jan
Hemphill CS, Sampat NS (2011) When do generics challenge drug patents? J Empirical Legal Stud 8(4):613–649

Herper (2012). http://www.forbes.com/sites/matthewherper/2012/07/12/the-global-drug-market-will-swell-to-1-2-trillion-while-big-pharma-treads-water/. Abgerufen am 23 May 2013, 17 Uhr
Hill R, Chui M (2009) The pharmerging future. The Business Magazine of Pharma 29(7):6–9
Ignjatovic T (2012) Key findings pharmaceutical diversification trends 2012
IMS (2012) The global use of medicines: outlook through 2016 conclusion. www.imshealth.com. Retreived 6 May 2013
IMS (2013) IMS health study points to a declining cost curve for U.S. Medicines in 2012. http://www.imshealth.com. zuletzt abgerufen am 13 May 2013, 15 Uhr
Jimenez J (2012) How I did it. . . Harv Bus Rev 90:39–42
Jørgensen JT (2008) Are we approaching the post-blockbuster era? Pharmacodiagnostics and rational drug development. Expert Rev Mol Diagn 8:689–695
Kanavos P, Costa-Font J, Seeley E (2008) Competition in off-patent drug markets: issues, regulation and evidence. Econ Policy 23:499–544
Khanna T, Palepu KG, Sinha J (2005) Strategies that fit emerging markets. Harv Bus Rev 83:63–76
Khanna T, Palepu KG, Bullock RJ (2010) Winning in emerging markets: a road map for strategy and execution. Harvard Business Press, Boston
Kindler J (2010) Pfizer CEO: the end of the 'blockbuster' era. http://www.cnbc.com/id/37543532). zuletzt abgerufen am 3 May 2013, 15 Uhr
KPMG (2011) Future pharma, five strategies to accelerate the transformation of the pharmaceutical industry by 2020
KPMG (2012) Pharmaceuticals & life sciences industry outlook survey: executives focus on growth despite regulatory challenges
LaMattina J (2011) The impact of mergers on pharmaceutical R&D. Nat Rev Drug Discov 10:559–560
MarketLine (2012) MarketLine industry profile, global generics, reference code: 0199–0334
McKinsey (2011) A wake-up call for Big Pharma. McKinsey Q, Dec 2011
McKinsey (2007) Improving quality in pharma manufacturing. McKinsey Q. Sept 2007
Miller J (2011) The EU debt crisis and CMOs – the EU debt crisis portends of possible negative repercussions for the dose CMO industry. BioPharm Int 24(9):26–28, Sep 2011
Mitchell M, Mulherin J (1996) The impact of industry shocks on takeover and restructuring activity. J Financ Econ 41:193–229
Mora-Monge CA, González ME, Quesada G, Rao SS (2008) A study of AMT in North America: a comparison between developed and developing countries. J Manufact Technol Manag 19 (7):812–829
Mullin R (2012) Beyond the patent cliff. Chem Eng News 90(50):15–20. http://cen.acs.org/articles/90/i50/Beyond-Patent-Cliff.html. Accessed 22 Apr 2013
Munos B (2009) Lessons from 60 years of pharmaceutical innovation. Nat Rev Drug Discov 8:959–968, December 2009
Orsenigo L, Pammolli F, Riccaboni M (2001) Technological change and network dynamics lessons from the pharmaceutical industry. Res Policy 30:485–508
Owen-Smith J, Massimo R, Fabio P, Walter WP (2002) A comparison of U. S. and European university-industry relations in the life sciences. Manag Sci 48(1):24–43, Special Issue on University Entrepreneurship and Technology Transfer (Jan., 2002)
Pammolli F, Magazzini L, Riccaboni M (2011) The productivity crisis in pharmaceutical R&D. Nat Rev Drug Discov 10:428–438, June 2011
Paul SM, Mytelka DS, Dunwiddie CT, Persinger CC, Munos BH, Lindborg SR, Schacht AL (2010) How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Rev 9:203–214
Pharma IQ (2012) The big pharma recession report
Pharmtech (2009) Q&A with Thomas A. Silberg. Pharmaceutical Technology, Mar 2009
Porter ME (1998) Competitive strategy. Techniques for analyzing industries and Competitors, 2nd edn. The Free Press, New York

PwC (2012) Diagnosis of a steady pharma deal flow. Pharma M&A Insights
Ramrattan L, Szenberg M (2006) Global competition and the United States pharmaceutical industry. Am Econ 50(2):65–82
Rickwood S (2012) Redefining the blockbuster model: why the $1 billion entry point is no longer sufficient. http://www.pharmaphorum.com/2012/09/11/redefining-blockbuster-model-1-billion-entry-point-no-longer-sufficient-part-1. Abgerufen am 29 Apr 2013
Roland B (2009) Truck industry 2020: the future is global
Rossetti CL, Handfield R, Dooley KJ (2010) Forces, trends, and decisions in pharmaceutical supply chain management. Int J Phys Distrib Logis Manag 41(6):601–622, 2011
Saha A, Grabowski H, Birnbaum H, Greenberg P, Bizan O (2006) Generic competition in the US pharmaceutical industry. Int J Econ Bus 13(1):15–38, February 2006
Sharma A, Jacob A, Tandon M, Kumar D (2010) Orphan drug: development trends and strategies. J Pharm Bioallied Sci 2(4):290–299
Sheth JN (2011) Impact of emerging markets on marketing: rethinking existing perspectives and practices. J Mark 75(4):166–182
Simplicity (2012) True cost of complexity in the pharmaceutical sector – and what you should be doing about it
Staton T (2011) Study: quality problems more common at offshore plants. www.fiercepharma.com/story/study-quality-problems-more-common-offshore-plants/2011-09-07. Retrieved 4 June 2013
Staton T (2013) Drugmakers, get ready for bigger, faster dealmaking, Moody's says. http://www.fiercepharma.com/story/drugmakers-get-ready-bigger-faster-dealmaking-moodys-says/2013-04-23. Retrieved 6 June 2013
Thomas R (2011) The changing role of chemistry in drug discovery
Tollman P, Morieux Y, Murphy JK, Schulze U (2011) Identifying R&D outliers. Nat Rev 10:653–654
Tse & Jakobs (w/o date) Consolidation and differentiation key drivers of change in the global pharmaceutical manufacturing industry
Unknown – Pharmaceutical technology Europe 22(5): 10–10, 2/3p, May 2010
Vogler S, Zimmermann N, Leopold C, Joncheere KD (2011) Pharmaceutical policies in European countries in response to the global financial crisis. South Med Rev 4(2):69–79
WHO (2007) Quality assurance of pharmaceuticals – a compendium of guidelines and related materials, vol 2, 2nd updated edn, India
Woodcock J, Wosinska M (2013) Economic and technological drivers of generic sterile injectable drug shortages. Clin Pharmacol Ther 93(2):170–176, 2013
WTO (2013) Frequently asked questions about TRIPS. http://www.wto.org/english/tratop_e/trips_e/tripfq_e.htm#Who%27sSigned. Abgerufen am 23 May 2013, 20 Uhr
Wyman O (2011) Beyond the shadow of a drought – the need for a new mindset in pharma R&D
Yip GS (2002) Total global strategy: updated for the internet and service era, 2nd edn. Prentice Hall, Harlow
Zhang J (2012) New global pharmaceutical outsourcing trends. http://www.lifescienceleader.com/past-issues/item/3912-new-global-pharmaceutical-outsourcing-trends/3912-new-global-pharmaceutical-outsourcing-trends?list=n. Abgerufen am 8 June 2013, 10 Uhr

Chapter 7
Barriers and Success Factors in Managing Operational Excellence

Thomas Friedli and Daniel Bellm

In our previous book, *The pathway to Operational Excellence in the Pharmaceutical Industry*, we developed a model that aimed at the sustainable implementation of Operational Excellence (OPEX) initiatives. Over the last 10 years, we have witnessed and examined several more OPEX programs, and this chapter will tie in these insights with our previous work. Knowing success factors and barriers in managing OPEX can provide guidelines as to how to design, review and adapt an excellence program. Thus, the first part of this chapter will discuss aspects that should be taken into consideration when launching an OPEX initiative. The subsequent part provides insights into challenges OPEX managers of more mature initiatives are likely to face. At the same time, this section serves as a bridge to parts II and III of the book by giving insights into practical applications in the industry, mostly written by industry leaders themselves.

Challenges in Managing OPEX: Getting the Initiative Started

Launching a successful OPEX initiative is not easy but a complex and multi-faceted procedure. Luckily, ever since the first programs came up in the industry about a decade ago, many more were to follow, giving ample opportunities to learn from failures and successes. The pharmaceutical landscape comprises companies that truly managed to create promising OPEX programs. These companies structured their initiatives well, placed emphasis on certain elements of the programs where necessary, and created optimal conditions to thrive their initiatives step by step. In a nutshell, they did their homework. Unfortunately, we have also seen OPEX programs that were doomed to fail. In such cases we frequently observed a lack

T. Friedli (✉) • D. Bellm
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; daniel.bellm@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_7,

of exactly those attributes that supported the successful OPEX implementation at other companies. However, there is no bad example that may not also serve as a good example. Thus, this chapter will provide insights from both success stories and failures in the implementation of OPEX initiatives.

Stating a Long-Term Focus from the Beginning

All too often people prefer to tread a beaten track. It is easy, convenient, and often a matter of routine. This reluctance to change can be a big issue for any company introducing OPEX. Murmurs may spread within an organization and recalcitrant employees may start to look for ways to work around new managerial ideas. Overcoming this inertia is a demanding challenge that can be mastered by purposeful communication. To prevent employees from trying to sit out a new initiative, it is important to clearly emphasize its long-term focus right from the beginning. It should be a clearly communicated commitment, of the company and especially so of its Top Management, that sets direction for the organization's upcoming future.

Having and Communicating True Excellence Instead of a Pure Cost Focus

There are many ways to introduce OPEX on a corporate or plant level. Ultimately, the chosen way will shape a program's success and determine the ease with which people can be included within an OPEX initiative. We have seen OPEX implementations that were not only launched, but also communicated as a broader cost-cutting program. As a consequence, the initiative was seen as annoying add-on to the job rather than a promising contributor to a company's sustainable long-term success. However, there are smart ways to bring the program to life, e.g., by engaging the workforce in optimizations, and sharing the program's earnings with employees [see Chap. 9]. This, however, has to be paralleled with our understanding of OPEX as described in Chap. 2. Of course *costs* constitute an important part of every OPEX initiative, but they have to be looked at in conjunction with *quality* and *time*. The balanced management of these three integral parts will later determine the acceptance and success of the program. An OPEX initiative that is solely designed – consciously or unconsciously – as a cost cutting tool will certainly fail in the end, and can have serious drawbacks. Some of the quality issues we have seen in plants all over the world are certainly rooted in the tremendous cost pressure that has been built up in such ill-designed cost cutting exercises.

In recent years, the priorities for launching OPEX initiatives have partially changed within the industry. Since 2007, the St.Gallen OPEX Benchmarking investigates reasons for implementing OPEX in the pharmaceutical industry on a

site level. Priorities are being assessed by asking to indicate how much a statement applies to a particular plant on a 5-point Likert scale, ranging from (1) *not at all*, over (3) *partially,* to (5) *completely*. Categories like "increase employee empowerment", "reduce lead times and inventory", or even "to launch a broader cost cutting program" reveal only a negligible difference in importance between 2007 and 2012 data. In contrast, the perception of consequences and implications of modern OPEX programs and what these programs are capable of has changed notably. In 2012, 80 % of the benchmarking participants indicated to have launched their OPEX initiative in order to initiate a cultural change for continuous improvement, compared to only 57 % in 2007. Likewise, 2012 data show that companies pursue an increased employee involvement and cost awareness with their implementation of OPEX programs.

Visibly Allocating Resources to the Initiative

It is not enough to merely focus on communicating an initiative's long-term focus. Instead, words have to be followed by visible action – providing training in basic tools and methods of problem solving, teaching people when to apply which tool (see Chap. 18) and the qualification of experts. Employees will have to familiarize themselves with new concepts and approaches, and this will take time. Depending on the company's size, this also requires a substantial financial effort. Yet, care has to be taken to prevent OPEX from being seen as a hindrance to daily work. It is vital to immediately have dedicated people working on OPEX and delivering visible results on a site level. OPEX experts and their colleagues in line functions need to have sufficient time in order to get the ball rolling and contribute to the initiative's success (see Chap. 16 for a deeper understanding of OPEX structures).

Alignment with All Other On-Going Initiatives

A manufacturing site is like a pool for a multitude of different projects and initiatives, most of which will be targeting an improvement of the plant's performance. Thus, managers are constantly dealing with multiple initiatives, such as Lean Production, Six Sigma, QbD, PAT and others. Introducing OPEX to a plant will thus bring up the challenge of avoiding the "just another initiative"-character. To overcome such preconceptions an initiative has to be aligned with all other on-going initiative-based activities at corporate and plant level. We have seen that introducing OPEX as an umbrella initiative that supports the structuring of all other activities will not only persuade site management, but also all other employees that are involved in OPEX. The main reason for this is that management can explain the "why", i.e. for what reasons specific actions are taking place. The understanding of

causes, the "why", is a necessity to get a buy-in of the shop floor. Anecdotal evidence shows that summarizing several stand-alone initiatives around a central OPEX cornerstone emphasizes a company's pursuit of superior operational performance and paves the way towards excellence.

Getting a Buy-In on All Levels

An OPEX initiative will only succeed if people feel familiar with the program's scope and purpose, and accept it as meaningful for the company and the plant. In order not to remain a mere theoretical exercise, it is essential for the initiative to get a buy-in from people on all levels. Therefore, the objectives of the initiatives have to be linked to the overall business strategy, as well as to the site's manufacturing strategy. And, most importantly, objectives have to be communicated. Communication within an OPEX initiative is vital and needs to change according to the program's maturity level. At the early stages it is the basic idea (or logic behind) an OPEX initiative and the number of projects launched or to be launched that are communicated. Later on, people usually will rather be interested in the impact and quality of a project, as well as their own contribution to the company's competitiveness. A commonly shared language, i.e. clearly defined terms and definitions, are key to success. By ensuring that people understand the initiative and its value, personal commitment is promoted.

Establishing and Communicating a Direct Link Between Competitiveness, Strategic Objectives for Manufacturing and the Initiative

Besides its alignment with other on-going projects, an OPEX initiative must also be in line with an organization's manufacturing strategy. Based on the manufacturing strategy, strategic objectives for operations are derived to maintain and increase corporate competitiveness. This in the following leads to a strategic profile of an OPEX initiative and determines priorities and foci. To achieve employees' acceptance it is necessary to visibly communicate how such an initiative is integrated into the company's targets. People will question what the initiative might be good for, or how it fits into their daily work. OPEX is more than simply employing a selection of tools to improve some processes on shop floor. Rather, it strives for the transformation towards, and preservation of, a plant's sustainable long-term success. The initiative's overall purpose, how it is linked to the targets of the company, and how the program is meant to affect competitiveness needs to be disseminated among employees.

Appointing Senior Managers as Key People

Another key to getting OPEX started is appointing the right leaders. Their skills are crucial to iron out obstacles, overcome initial inertia, and to motivate people. As such, it is senior managers that should be appointed – they are well-rooted within the company structure and experienced in the organization's operations, thus having the required political power and self-assertion to bring the initiative on its way, and to discuss with site managers on eye-level. Their experience, achievements and power within the organization lend them the credibility and authority to enforce necessary measures. Young managers, also young potentials, often lack these capabilities and authority.

Challenges on the Road: Sustain the Initiative

After an OPEX initiative has been launched effectively, its management and certain key focal areas will need to change. This does not mean that factors relevant for an initiative's successful take-off should be disregarded. They should be further stressed, but complemented by taking into account new barriers, and utilizing upcoming opportunities.

Leadership & Management Commitment

A successful OPEX initiative lives from true managerial commitment on all levels, down to the shop floor. Not only do managers provide the framework that provides the rules of the game, they also have to make their honest commitment to OPEX visible whenever possible. This ought to start at a corporate level and connects the hierarchical pyramid down, via the site leadership team on plant level, to the workforce on the shop floor. Corporate commitment is essential, especially when an OPEX is first implemented. At these early stages intense efforts are usually inevitable. We decided to deal with this topic in the second part of this article, as we think that ongoing leadership and management commitment is especially relevant once the initial euphoria fades away. Looking at our OPEX model (Chap. 2) it is obvious that during the early days an initiative's focus is rather on creating an effective system and implanting a vision rather than harvesting the fruits of efficiency. Without managerial commitment, necessary investments most likely will not be approved and the program is meant to nip in the bud before it has even started. However, corporate commitment is just the first step and still a far cry from success. It is vital to sustain and even amplify managerial commitment in order to keep the momentum of the program. At plant level, it is the site leadership team that promotes the OPEX initiative and provides middle management and the workforce with support in introducing, achieving, and maintaining excellent operations.

Developing One's Own Customized Program

Liker (2004) described Toyota's unique approach to lean management, and pointed out the failures of companies that solely implemented selected lean tools without a holistic understanding. These companies often neglected the interrelation of, and synergies between these tools, and ultimately missed the power of the Toyota Production System (TPS). They merely copied. We have seen similar approaches in the pharmaceutical industry when companies first touched OPEX (Gronauer et al. 2010, p. 175f). Several years later, and despite the industry having gained experience in designing OPEX programs, we still observe copy-paste approaches: Some companies still seek a shortcut towards excellent performance. In doing so, they overlook two major facts. First, one of the best examples for lean production, TPS itself, evolved over a period of more than 60 years. Second, tacit knowledge is everything. Starting an OPEX program is more than simply following a recipe by applying explicit procedural knowledge. It requires a type of knowledge that a company gains from experience and continuous reflection (Liker and Meier 2006, p. 5). In order to maintain a successful OPEX initiative, a company has to design its own unique program over time, and tailor it to its specific environment and culture. By doing this, the initiative nourishes the company's strengths and assists in overcoming its weaknesses, making OPEX a truly competitive weapon. Identification with the OPEX program throughout the organization will increase, ensuring the acceptance needed for its sustainability.

Choosing the Right People, and the Right Projects

Making OPEX work is a management challenge. Improvement projects that are run under the umbrella of operational excellence usually require a strong collaboration of cross-functional teams, and frequently follow standardized procedures. Therefore, OPEX is less a technical or methodical challenge; rather, its success is dependent on the managers leading an initiative and associated projects. Managers who successfully start OPEX initiatives and who are able to cope also with stormy times are totally committed to the program. They are deeply rooted and well-known in the company, and bring along a broad range of social and managerial skills. Such skills are also needed in directing and leading people within line functions, thus creating a certain kind of trade-off when well-trained and skilled managers leave the OPEX organization or high potentials are not considered for OPEX as they are already engaged in a lot of other activities. Another challenge lies in carefully selecting appropriate improvement projects, that is, projects that fit into the overall long-term objective and current status of an OPEX initiative. It is important to start a project not for the project's sake and to, e.g., finally run projects only to qualify new Green Belts without any relation to the business needs. The selection of projects has to be based on criteria that are derived from the business objectives

and clearly defined. It is important that these criteria are transparent – if people do not understand why/based on which criteria improvement projects are initiated, they will struggle to see their benefits.

Taking into Consideration the Different Maturity Levels and Capabilities Within a Global Network

Most of the multinational companies we are collaborating with run a global department for their OPEX initiative. Managers of these departments are on a daily basis confronted with their plants' different maturity levels and the different capabilities that individual plants bring into the company's global network of manufacturing sites. Companies that have not yet established such an OPEX department but manage scattered manufacturing sites face exactly the same challenges. In a (global) network, OPEX cannot be managed with a default target-setting for all sites. There are simply too many site-specific factors affecting plant level performance that have to be considered. Some plants, for instance, may have started with OPEX a couple of years ago, thus already having achieved a relatively high performance level. In contrast, other sites may have just started with their OPEX activities recently. To set a yearly target achievement on a level that can only be reached after several years might be as discriminating for one site, as expecting a yearly performance increase that is only easily accomplished if a site is just about to start with OPEX is for another. Thus, the OPEX target needs to be customized to a plant's current level in order to meet the right balance between the possible and the unattainable. Moreover, defining site-customized OPEX target provides OPEX managers with the opportunity to foster the communication and knowledge exchange between network sites. In most cases, the more advanced sites will already have developed solutions to the challenges OPEX newbies have yet to encounter.

Having Key People Who Go Where the Action Is, Motivating and Engaging People (Management as Caring & Coaching)

Leading OPEX is not a desktop exercise – no matter what size the company, successful leadership requires going where things happen. As discussed above, a lot of prerequisites need to be in place to successfully start and sustain such an initiative. Ultimately, however, the program will only reveal its full potential if key people are physically available where change is taking place. Especially for managers who are responsible for global or regional OPEX programs this implies time-consuming and often exhausting travels. Similarly to shop floor or plant level, managing OPEX on this global level is also about motivating and engaging people. In-person caring and coaching across borders has paid off in every single case we have witnessed to date.

Leaving the Implementation Responsibility in/with the Line Functions

OPEX fulfills a supporting and enabling function. OPEX specialists focus on providing methodical, technical, and scientific support. On plant level, it is the plant leadership team that is responsible for outcomes; on a network level this responsibility lies with the management of the business. We know from the history of quality management that it can jeopardize an initiative's impact to work with divided responsibilities or even to give the responsibility to the support function. The result will be that the rest of the organization does not show the needed engagement. Thus, strong personal involvement of line employees will strengthen commitment and increase the understanding of the initiative.

Establishing Transparent Mechanisms Throughout

We have already discussed the importance of establishing and communicating a direct link between the initiative, competitiveness, and strategic objectives for manufacturing in introducing OPEX to a manufacturing plant. Such communication is paving the way for a buy-in of an organization's workforce. In order to sustain the workforce's commitment in the long run, coordination mechanisms ought to be established transparently. Decisions need to be comprehensive, and their contribution to a company's strategic goals must be clear.

Ensuring Involvement

Training people in methods, tools and practices applied within OPEX programs is always resource-consuming. Clearly, it takes a certain time to train people and to achieve the state of awareness and mindset that ensures they are devoted to the program. People need to deploy and practice their skills continuously. Involving people from all hierarchy levels in the initiative, and building cross-functional teams, strengthen the sense of unity of the workforce and solidarity with the overall program.

Enabling People to Do What Is Required by the Initiative

Companies that already run an OPEX program, quite often face a challenge when it comes to devoting sufficient resources to the initiative. Besides providing basic training in OPEX tools, an important part of enabling people to participate in and contribute to the initiative is to make sure that they really have the chance to apply their knowledge. Even though people are part of the program and integrated in related

work or project teams, their daily business will determine a substantial share of their working time, often leaving little room for additional projects. This sort of pressure can quickly lead to frustration and resignation. It is the managers' task – both of line functions and OPEX programs – to allocate the time needed to work on OPEX projects. It is their responsibility to enable people to do what is required by the initiative and to provide people with support in order to lead the project to its success.

Conclusion

Excellence initiatives aim at enabling the continuous improvement of an organization – a complex challenge. As such, excellence initiatives themselves – and their management – are rather complex. We have found *comprehensiveness* of an OPEX initiative to be the most important success factor throughout a program's entire life cycle. Comprehensiveness is dependent on a self-contained set of four determinants, i.e. structure, activities, behavior, and a controlling approach. For an in itself comprehensive presentation of these determinants, we rely on the *St.Galler Management Concept* (Bleicher 1995).

The St.Galler Management Concept is based on system theory. The system approach enables the *integration* of different management hierarchies and aspects, and counteracts unilateral "top down" or "bottom up" views that usually come to use in management science and practice (Bleicher 1995). Here, we use this system approach as a reference framework for a management concept that fosters the understanding of a leadership style that is deliberately dealing with an increasingly complex and dynamic environment. The core element of the system approach is the holistic consideration of a multitude of diverse influences within a network of relationships (Bleicher 1995).

The St.Galler Management Concept distinguishes three dimensions to derive differentiated solutions coping with today's challenges in management: A *normative*, *strategic*, and *operative* level, thereby discriminating separately defined problem areas. It is important to note that these three dimensions do not refer to a division of labor or responsibility for diverse management categories. Moreover, according to the St.Galler understanding that has been strongly influenced by Bleicher (1995), in the sense of an *integrated management* the assumption is based on the mutual pervasion of all differentiated dimensions. Figure 7.1 visualizes the relationship of normative, strategic and operational management.

The dimensions illustrated in Fig. 7.1 can also be looked at from a different perspective: On the vertical axis, different management aspects are distinguished, which we too observed as being crucial for the comprehensiveness of an OPEX initiative: activities, structures, and behavior. These aspects operationalize the integration between the initial conceptual and creative intent, and its subsequent implementation by performance and cooperation. *Activities* result from the realization of norms turning missions into programs that are finally turned into orders. *Structures* are defined by the organization's constitution as well as organization and

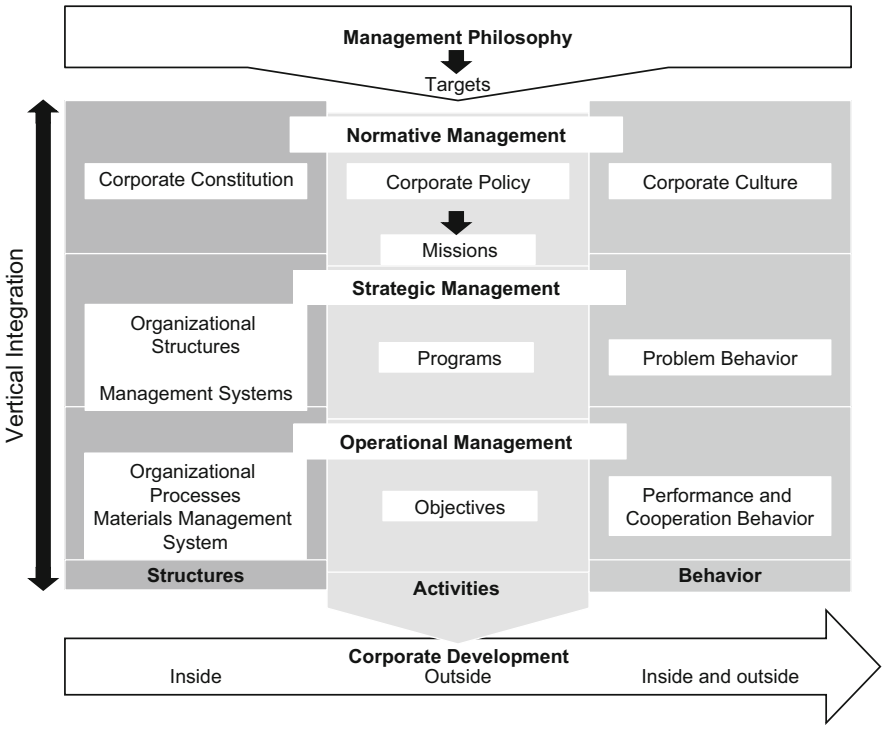


Fig. 7.1 The St.Galler Management Concept – the connection between normative, strategic, and operational management

management systems across all three dimensions. Both aspects are means to influence human behavior in an interplay between moral concepts and strategic thinking (Bleicher 1995). Applied to OPEX programs this means:

- Activities: At the normative level, corporate missions are developed to be later used as a guideline for strategic and operational action within the organization. Such missions are operationalized by programs and assigned to responsibilities. These programs have a long-term character and comprise diverse aspects to grow, exploit, and maintain an organization's success factors. On an operational level, these programs are translated into defined assignments. As such, activities govern the content and number of projects and training programs run by an organization's manufacturing sites.
- Structure: The corporate constitution legitimizes the management at the normative level. By designing organizational and management systems the structural aspect is further substantiated at the strategic level. On an operational level structural aspects are represented by processes controlled by scheduling and planning systems. This defines how an OPEX program is embedded in the organizational structure. As there is no uniform organizational structure that supports an excellence initiative constantly well, structure will change with an

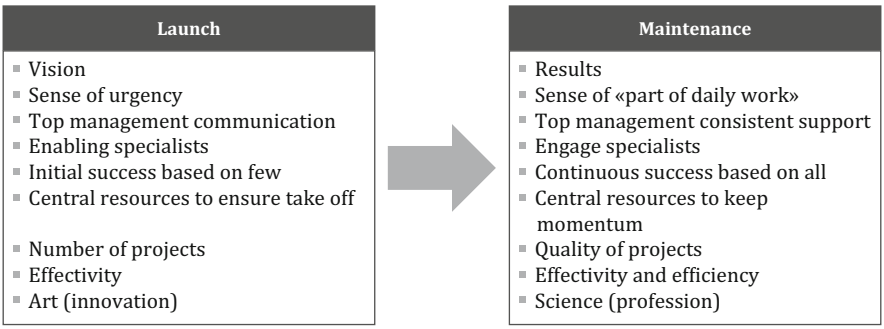


Fig. 7.2 The development of an OPEX initiative's focal areas over time

increasing maturity level. Therefore, structure is adapted to actual needs over time (see Chap. 16 for a better overview of OPEX structures)

- Behavior: At the normative level, the future behavior of an organization's people and how they strategically and operationally act is determined. Whereas the normative dimension gives the reason for a defined behavior, at the strategic level responsibilities are assigned with regard to people's competence and behavior in problem solving. Thus, it is the task of the strategic management to set a leading example for behavior. The operational level is realizing behavior and concentrates on performance and cooperation behavior.

We mentioned *behavior* as the third determinant that has to be taken into consideration when it comes to managing an OPEX initiative. Indeed, most OPEX managers we have met think hard about how to lead the program, and especially about how to foster a culture that leads to the aspired work results. However, it is not behavior that molds work and processes – rather, behavior follows work! Thus, first the processes need to be designed and people motivated to do the work as it should be done; their behavior will then adapt accordingly.

- A controlling approach: Every OPEX initiative should include a controlling approach that measures and balances input and output of the program. Targets for a network's sites are set individually, and strengths and weaknesses of each site need to be assessed. A useful OPEX controlling ensures steady improvements, discloses the best practices within the network and enables the company to share knowledge between sites.

That said, it is obvious that excellence initiatives have to be aligned with an organization's overall manufacturing and supply strategy. A constantly changing environment and increasing maturity of the manufacturing sites and the program itself require a time-based change of the OEPX initiative's focused priorities – new focal areas arise, while existing focal areas need to be adapted. Figure 7.2 summarizes the latter aspect, stressing the importance of developing focal areas in the long run.

These success factors will be constantly challenged by the people involved in the program. The more employees are engaged in and identify themselves with the initiative, the more they will question its purpose, challenge their leaders, and weigh the program's cost-benefit ratio.

As each OPEX initiative is shaped by an individual company's culture, OPEX programs can vary to a large extent – there is no universal recipe. Moreover, it is the task of the OPEX leader to balance the program and prepare it for future challenges.

References

Bleicher K (1995) Das Konzept integriertes Management, 3. Aufl. Campus, Frankfurt a. M

Gronauer T, Friedli T, Götzfried M (2010) The roadmap to operational excellence – pattern and elements of OPEX programs. In: Friedli et al (ed) The pathway to operational excellence – overcoming the internal inertia. Ed.-Cantor-Verl, Aulendorf

Liker JK (2004) The Toyota way: 14 management principles from the world's greatest manufacturer. McGraw-Hill, New York

Liker JK, Meier D (2006) The Toyota way fieldbook, 1st edn. McGraw-Hill, New York

Part II
Leading Operational Excellence: Outstanding Practices

"Victory comes through hard – almost slavish – work, team play, self-confidence, and an enthusiasm that amounts to dedication."[1]

This part of the book is intended to provide an overview of selected integrated approaches to managing Operational Excellence on a global scale, and to give insights into the most important aspects that should be focused on in professionalizing pharmaceutical OPEX. Five leading pharmaceutical companies share how they have reached the current stage of their OPEX programs, and explain the driving forces behind their decisions. We deliberately abstain from promoting the idea of an ideal OPEX program, as we believe that a successful framework has to be tailored to the very specifics of a company. By describing five quite different OPEX frameworks, we intend to supply readers with inspirations on how to design or enhance their own company's program: We suggest readers take over those parts of successful practices that appear to be most suitable for their own journey to Operational Excellence.

In the second half of this part we provide insights into conditions and constraints in building up a new plant in India, outlining today's possibilities of infrastructural ramp-up of pharmaceutical manufacturing. We proceed with valuable experience from a major global consultancy, the Boston Consulting Group. We use their approach to highlight aspects that need to be considered if an organization looks for real change instead of mere short-term impacts.

Another focus lies on the organizational framework that is necessary to truly embed OPEX in a company, a topic that has not yet received sufficient attention. Even OPEX-advanced industries like the automotive and electronics industry lack profound knowledge of the right degree of centralization of OPEX programs or the optimal number of respective experts in a global company. The final chapters of this

[1] General Dwight D. Eisenhower, cited from Korda, M. (2007): Ike – An American Hero, New York, P. 94.

part are dealing with integrated process development, matching problems with tools, plant complexity and knowledge management. Altogether, they provide the reader with empirical examples as wells as a solid scientific foundation for the re-consideration of own OPEX programs or parts of it.

Chapter 8
From Process Stabilization to Plant Network Performance: Pfizer's Journey to Operational Excellence

Colin Seller and Richard Davis

Introduction

Pfizer is one of the world's leading research-based pharmaceutical companies; discovering, developing, manufacturing and marketing innovative medicines. The company was founded in 1849, and by 2012 it had grown into a $59 billion global enterprise with more than 88,000 employees and an annual R&D spending of $7.9 billion.

Pfizer has a long and distinguished manufacturing history. In a notable example, the company responded to an appeal from the US Government during World War II to manufacture penicillin to treat soldiers. By 1944, Pfizer had become the world's largest producer of that medicine.

Pfizer Global Supply (PGS) is a critical element of Pfizer's success. PGS remains focused on its Fundamental Value Proposition – the balance between a challenging operating environment and our unwavering commitment to quality, compliance and supply.

The 22,000 colleagues in PGS make certain that the entire range of Pfizer products – the more than 3,000 formulations of its prescription-only and consumer healthcare products, offered in more than 175 markets – are produced to the highest standards, in complete compliance with all applicable regulations, and always available when they are needed.

Pfizer currently operates more than 50 internal manufacturing sites around the world and has a distribution network of about 190 sites serving its major markets. Nearly 200 transportation providers move essential products from factory to pharmacy or retailer.

C. Seller (✉)
Pfizer, Sandwich, Kent, UK
e-mail: colin.m.seller@pfizer.com

R. Davis
Pfizer, Groton, Connecticut, USA
e-mail: richard.m.davis@pfizer.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_8, © Springer-Verlag Berlin Heidelberg 2013

To complement its internal manufacturing, Pfizer works with a network of more than 400 supply partners to help produce active ingredients, secure packaging, and entire lines of its medicines. Pfizer holds all manufacturing and supply partners to its high standards of excellence and invests heavily in the people, processes and technology to assure the quality people expect when they select a Pfizer medicine.

Operational Excellence: Taking the First Steps Toward Continuous Improvement

Compared to other manufacturing industries, notably the automobile sector, the pharmaceutical industry was initially slow to focus on operational excellence practices and adopt a continuous improvement mindset. Pharma had launched a limited number of programs by the late 1990s, but they were not widespread until the first decade of the 2000s. Within a short time, however, the focus on operational excellence showed a significant impact on pharmaceutical manufacturing and business processes.

As an industry leader, Pfizer Global Supply (PGS) has been at the forefront of a decade-long, industry-wide movement to drive performance by embracing the goals of Operational Excellence and fostering a continuous improvement culture throughout the organisation. These efforts began with the *Right First Time* (RFT) strategy launched in 2003. RFT, like subsequent Lean initiatives, has become a core component of PGS's strategies to ensure cost competitive, quality products that service the customers' needs.

In 2003, PGS's performance was at least comparable to pharmaceutical industry standards. However, the newly formed RFT team was well aware, that other industries were more advanced in terms of process capability and fostering a continuous improvement mindset. The slow uptake of operational excellence practices within pharma was influenced by a number of factors including:

- Pharmaceutical manufacturing had traditionally focused on *end-product quality* and delivering a quality product to the patient, but with limited effort spent on understanding and improving the *effectiveness and efficiency* of manufacturing processes.
- The pharmaceutical industry had not focused on developing a *deeper understanding of their processes beyond that needed for normal operations*. This led to small, but unwanted, numbers of process failures resulting in the materials not meeting the high internal standards of Pfizer and hence not released for supply to the patients.
- Pharmaceutical manufacturing processes were often *complex* and included many *non-value-added activities*.
- Pharmaceutical manufacturing tended to view individual sites independently. There was little *overall end-to-end process understanding* of the flow between suppliers, active pharmaceutical ingredient (API) plants, drug product sites, and other external suppliers/ingredient sites.

Structuring Teams for Success

Right First Time (RFT) was the first phase of the Operational Excellence process at Pfizer. Its aim was to systematically reveal true root cause of unwanted variations in manufacturing processes. The ultimate goal was a scientific approach to foster systemic, ongoing, and value-added change.

The pharmaceutical industry, including Pfizer, recognized that any fundamental change could not be a top-down initiative. Employees needed to be broadly involved in enhancing processes and driving continuous improvement. As a result, the RFT strategy emphasized the need to:

- Create a culture of continuous improvement
- Promote leadership behaviors among all employees in PGS.

For RFT to succeed, PGS colleagues had to believe that it was more than "just another corporate initiative." Senior PGS leadership took a number of steps to address this including:

- The PGS mission and strategy were aligned to demonstrate the commitment of PGS and site leadership to the RFT initiative. Site leaders made clear from the beginning that the *robustness of processes* was the main focus of the initiative.
- *A central corporate support organisation was established* within PGS.
- RFT champions were appointed at each site, reporting directly to site leaders. In most cases, these champions were members of the site leadership team.
- Placing the right tools in the hands of the right people, and convincing PGS colleagues to use these tools.

Lessons and Successes from the Initial RFT Rollout

Pfizer learned a great deal through the process of implementing the initial RFT strategy. For example:

- Overall effectiveness in manufacturing requires commitment at the site and shop floor levels. For this reason, RFT gave all PGS colleagues the necessary tools to understand, develop, and implement improvements of the capability of processes.
- Success was dependent on connecting the strategy to the Vision *and* on the way individual sites implemented the initiative. It was crucial for every site to embrace continuous improvement as an overall organizational capability, adopting new approaches and practices in a fast, reliable, and sustainable way.
- A visible commitment by the site leadership was essential to motivate participants and support the strategic role of the program. The decision to anchor the RFT champions in the site organisation, rather than in corporate functions, contributed to a sustainable implementation.

- It was important to link the project to corporate and site strategy, rather than position it as a cost-cutting exercise. As the RFT program began to tackle efficiency issues, the challenge was not to lose focus on quality. By continuing to stress the importance of robust, high-quality processes, the team was able to achieve sustainable process improvements which also helped to align the people with the project.

As the RFT rollout continued, the results of the optimisation efforts drove variability from core processes. Processes consistently delivered a level of performance between 4 and 5 sigma, up from recorded variability levels of 2 to 3 sigma when the project began. As a result, process output was more consistent, there were fewer recurring problems, costs decreased, and process speed and reliability increased. The increased predictability of processes also enabled buffer inventories to be decreased.

By 2008, PGS integrated the application of RFT with Lean Principles and Technology & Innovation into its strategy. RFT and Lean initiatives became a core component of PGS's strategies to ensure cost competitive quality products that service the customers' needs.

To ensure continued success of Operational Excellence, the company needed to identify a way to truly integrate Lean with RFT while making use of the current support organisation. To address this need, the RFT team added the Method IV module to the existing training curriculum. This module trained colleagues in Lean principles. By 2008, most colleagues had received one-day training in enhanced problem-solving skills, enabling them to tackle the myriad of issues that occur across PGS every day (Method I). In addition, approximately 10 % of the organization had a working knowledge of various improvement methodologies, including Six Sigma, the application of Lean Principles, and Human Error analysis (Method II & III).

Linking RFT and Lean provided additional opportunities to optimise process efficiency. At PGS, this linkage led to enhanced performance in terms of efficiency, lead time, and reduced inventory. For example, applying the Lean approach to an expanding list of key product supply chains led to improvements of more than 50 % in the lead-time for product supply (Fig. 8.1).

Pfizer also designed its Lean Toolbox to enable improved efficiency and better management of complexity. Value stream mapping (VSM), was used to identify and prioritize opportunities. Additional tools and tactics that were used to advance Lean goals included standard work plans, spaghetti diagrams, cell design, and pull principles (in which product is produced to service the immediate needs of customer orders, rather than the traditional approach of pushing supply of product to meet long-term forecasts). Lean tools and principles combined to establish a firm foundation for continuous process improvement.

In addition, PGS added the use of a Balanced Scorecard to measure progress across key parameters in four mission performance elements (i.e., Internal Process, People, Financial Performance, and Customer Service).

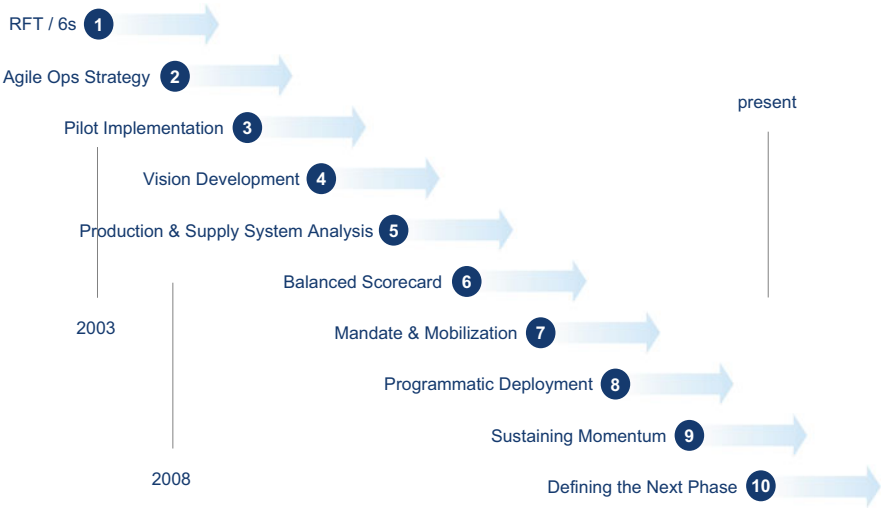


Fig. 8.1 Steps along the continuous improvement journey

Defining the Next Phase of Strategy to Build on Initial Progress

The journey that began with the deployment of the Right First Time strategy continues today as Pfizer develops a high performing internal and external supply organization. While PGS had made significant progress during the early period of its journey toward operational excellence, sustaining momentum is even more important today. The pharma industry sector faces an environment that is rapidly evolving. Trends impacting the pharma sector include:

- Increasing pricing pressure
- Rising competition
- Rising portfolio complexity
- Shifts in product pipelines and products
- Rising emerging market demand
- Shifts in reimbursement policies (Fig. 8.2)

Given an increasingly challenging industry landscape, Pfizer identified the need for a holistic transformation effort to meet the changing needs of the business. RFT and Lean had been the focus for the previous decade, and achievements had been significant. However, these efforts were generally focused on independent projects. To truly transform the organization, PGS realized its need to build on the current progress and its key delivery commitments of controlling costs and optimizing site performance. To achieve the goal of becoming a world class supply organization,

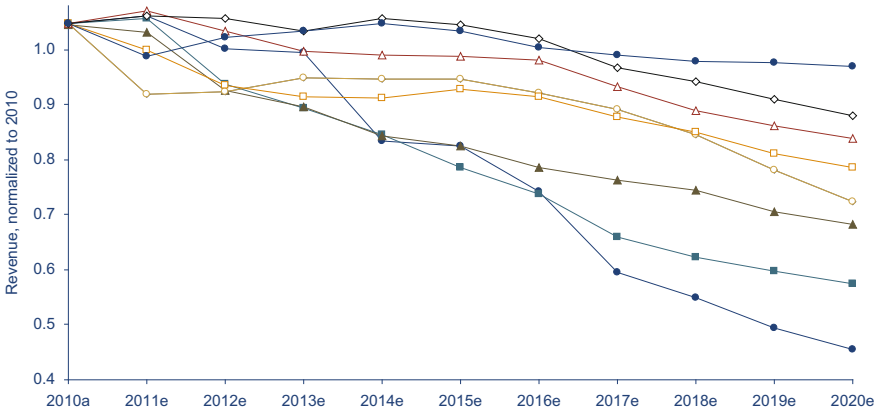


Fig. 8.2 Pharma revenue growth projections exclusive of new products pipeline for major pharma companies (Bernstein Research 2011)

the next phase of the strategy required significant step changes in performance while building sustainable capabilities across PGS.

Pfizer leadership realized a compelling *reason for change* must be identified and key supporting organizational mechanisms had to be in place to transform the PGS organization. PGS identified that their transformation journey required:

- A clear picture of the starting position, market, customers, and evolution needed – *the compelling reason for change*
- A thorough understanding of business goals and aspirations
- Shared leadership view and understanding of the goals
- Leader ownership for achieving the goals
- Clear communication to the organization
- Alignment on a defined path for achieving the vision
- A detailed plan for how to achieve objectives and milestones
- An environment that was ready for, and enables change
- Resources and investments where needed
- Incentives and rewards to build focus and encourage change

PGS leadership also noted that reliance on single point process improvements, the type typically achieved in the early phases of RFT/Lean programs, needed to evolve into a *full system approach*. PGS's current Operational Excellence Transformation program moved from the single point process approach used with RFT/Six Sigma, through Value Stream Mapping (VSM), to a full system approach with top down focus on the highest value initiatives identified across the PGS internal and external supply network. Moreover, the full system approach recognizes that focusing on costs while forgoing capability building within the organization will lead to unsustainable results (Fig. 8.3).

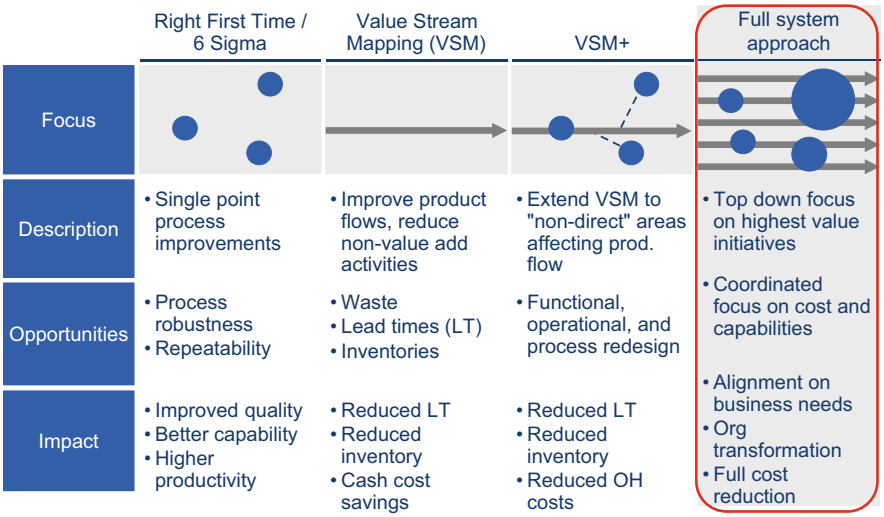


Fig. 8.3 Full system approach to operational excellence transformation

Transformation: A Journey to High Performance

Transformation is a conscious transition to a sustainable way of working at a significantly higher level of business performance based on fundamental shifts in: ambition; collective self-beliefs; behaviors and culture; and underlying capabilities, systems and processes. Transformation is intended to produce significant leaps in performance, not simply incremental improvements. The improvements are also intended to be sustainable and maintained over time (Fig. 8.4).

Transformation begins with the understanding that change happens one person at a time, and that it is the linkage between technical and cultural elements that produce real and sustainable improvement. Transformation is ambitious in both the aspirational "breakthrough" or "step-change" targets set by leadership, as well as its aim to change how colleagues think, act, and do their work on a daily basis. While discrete operational and systemic improvements are identified and realized, a major focus is also on developing colleague capabilities and engagement for sustained improvement at all levels.

Transformation is not a single event, but a process of embedding continuous improvement, initially within deep focus areas, or workstreams, but ultimately extending across the entire organization. It incorporates and extends beyond traditional Operational Excellence to include deliberate cultural change beginning with leader behaviors, change management, and appreciation for value creation. The transformation approach provides a common language and methodology for PGS to build standardized platforms for improvement, leveraging best practices and network learning.

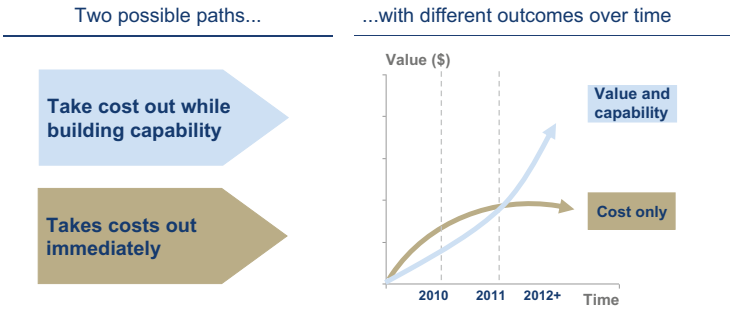


Fig. 8.4 Transformation adding value *and* capability

Transformation is focused on four key elements:

- *Business Requirements*: Alignment of operations with business strategy to manage costs while maximizing quality and supply reliability. A segmented approach to product management is also a key component of this element.
- *Operating Systems*: Deployment of agreed performance principles and platforms for plants, products, and functions. This element also includes configuration of demand, flow, capacity, and supply chain footprint to create value and minimize loss. (Performance principles, approaches, and platforms will be discussed in detail further in this chapter).
- *Management Infrastructure*: Establishment of a formal organizational structures process as systems to support the transformation is critical. Infrastructure is also supported by deployment of performance management practices (e.g., Balanced Scorecards) that identify goals, metrics, and targets for high performance at the site and supply network level.
- *Mindsets and Behaviors*: This element strives to fully align mindsets, behaviors, and capabilities of the organization with the business strategy and goals. Development of colleague skills and capabilities is also a key part of this element.

Network Performance Principles: A Common Framework for Transformation

To support the transformative, full system approach, a common set of principles was needed to align transformation strategies at every level of the organization. The Network Performance Principles (NPP) began as a common framework to align efforts to improve the way that PGS operated. They were intended to set guiding principles to define and drive PGS as a high performing supply network. Based on benchmarking with high performing supply organizations across many sectors, the Network Performance Principles (NPPs) defined:

- How operations and supply chains should operate in an ideal state
- How elements within and across PGS will operate together

- How balanced metrics drive high performance
- How highly capable colleagues deliver operational performance

In addition, the Network Performance Principles described an ideal state that best in class companies strive for including:

- Supply and delivery strategies tightly linked to customer needs and business requirements
- Organizations and functions aligned on how global supply chains function and decisions are made to optimize performance
- Engaged colleagues understand customer needs and have the capabilities to deliver the highest performance and drive continuous improvement
- Harmonized processes and systems in place to enable consistent network delivery

The NPPs were also designed to be flexible and configurable to the specific business needs. Production and inventory strategies may vary by product and demand profile, product lifecycle, facility needs, and competitive requirements. For example, one product launch might require a production strategy enabling market coverage upon regulatory approval with ability to scale up production quickly while also avoiding investment risk due to potentially slow sales. In contrast, an older established product line might face declining pricing and margin, and a potentially short lifecycle, thereby requiring the operations to manage cost, complexity, variability in contracts, and changes in volume in a careful and flexible manner. By taking a segmented approach in the context of the Network Performance Principles, PGS can optimize performance across the product portfolio.

Network Performance Principles apply on a PGS Network-wide level and individual site level, but to varying degrees. Not all principles were intended to have equal importance at both levels. For example, the principle: "Align supply chain strategies with sales strategies" asks the network to address customer needs from a product perspective. Although this principle has some impact at a site level, the majority of the effort takes place at the PGS Network level.

On the other hand, the principle: "Match production and inventory strategies to product segments" asks a site to optimize operations based on the characteristics of different product segments they manage. This principle affects how the network operates, but the impact of the principle is applied primarily at the site level.

Finally, some principles are foundational to high performance, and impact both sites and network equally. For instance, the principle: "Leaders engage and enable colleagues to optimize performance" applies to all leaders and colleagues across the operating network.

The NPPs are grouped into five key focus areas:

- Customer focus
- Supply Strategies
- Delivery Capabilities
- Engaged colleagues/leaders
- Key Enablers

While these principles make up the current core NPPs at PGS, they are updated and added to, as appropriate, to adapt to changing trends, business strategies, and through benchmarking with other high performing companies.

Measuring Progress: The Network Performance Assessment (NPA)

The Network Performance Assessment (NPA) serves as a qualitative measurement of site performance against Network Performance Principles (NPP). The NPA supports an assessment of where a site is in the transformation process, which elements are progressing, and which elements should be prioritized when developing the transformation plan (Fig. 8.5).

NPAs are a key input for structuring and guiding current transformation efforts as well as future transformation initiatives and are conducted in a one day workshop by a multi-disciplinary team from the site, and facilitated by a Network Performance Lead or Operational Excellence colleague. The NPA supports the NPPs, and as the NPPs evolve over time, so will the NPA.

Rationalizing Activities: The Creation of Standard Network Approaches

While the Network Performance Principles and Assessment serve as the backbone for the transformational efforts, simply having principles in place will not ensure a consistent and optimized approach to the process. An organization can be faced with a number of challenges to implementation of the transformational activities including:

- Strategic alignment: Beginning the transformational journey with different visions of the future state can result in sub-optimal results and significant effort re-aligning priorities and programs
- Resourcing: Transformational teams, supported through existing Operational Excellence resources, need to be staffed. In addition, the colleagues leading the transformational programs may have little codified guidance and have untested capabilities.
- Competing Priorities: Pursuing organizational transformation in a business environment that is rapidly evolving or during periods of major business evolution (e.g., acquisition and divestiture of business segments), can raise conflicts with prioritization and resource availability and focus.
- Organizational Maturity: Implementation of truly transformational operational performance principles requires an organization to be much more transparent than it may have been previously. Identified opportunities for operational

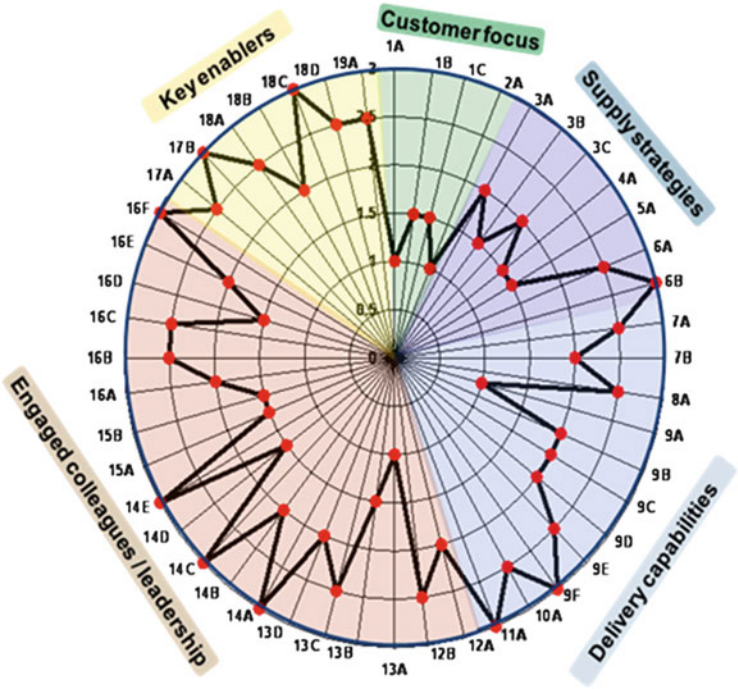


Fig. 8.5 The network performance assessment (NPA) measures performance and maturity against the network performance principles (example)

improvement can potentially be viewed negatively, with the on-going concern that the transformational process will be used primarily to support consolidation of operations, rather than operational improvement.

- Development of Enabling Processes: One of the key elements of transformation is development of a cultural mindset that focuses on operational transformation rather than the traditional focus on local optimization and spot improvements. To be successful, creation of new tools to support and manage change and track progress is essential. At PGS, this need prompted the development of Standard Network Approaches (SNA).

Standard Network Approaches are standard work for globally relevant activities that when developed, codified, and applied in a common way, the benefits in implementing across the entire organization yield compounding transformational or continual improvement results. Standard Network Approaches (SNA) leverage proven good practice processes and methodologies that drive high value, step-change improvements within PGS and its extended supply network. SNAs are not intended as one-size-fits-all approaches and are implemented based on the opportunity and the needs of a site or function within the business.

The following SNAs are used at PGS to support transformational activities. While identification and codification of Standard Network Approaches are ongoing

activities, these key approaches help to drive step change and sustainable transformational improvements in performance.

- **Diagnostics**: Diagnostics provide a sustainable solution to identifying and scoping step improvement opportunities. Diagnostic teams assess the current operations state, develop a future state, identify gaps, and propose an implementation plan, and address mindsets and behavior.
- **Production System Redesign (PSR)**: Production System Redesign supports the design of an end-to-end, integrated planning and scheduling, production, and inventory strategy. PSR enables manufacturing sites to better manage segmented production models.
- **Constrained Assets and Overall Equipment Effectiveness (CA/OEE)**: This Standard Network Approach is an industry recognized methodology for identifying and eliminating sources of loss. This approach allows the prioritization of improvement drivers to maximize process throughput with the current asset base and resources. CA/OEE is a key element in improving supply performance, customer services, and competitiveness. CA/OEE is typically applied in situations where:
  - Capacity constraints are causing supply issues that could potentially drive capital expenditures to correct these deficits
  - Products or processes are filling a high portion of facility capacity
  - Products are under high external cost pressure
- **Global Reliability Program (GRP)**: The Global Reliability Program (GRP) is a Lifecycle Asset Management Program that focuses on building reliability into site maintenance processes and systems. The Global Reliability Program is used to instill a culture of reliability in the utilization and maintenance of physical assets including:
  - Ensuring quality and compliance of maintenance operations
  - Increasing asset availability and performance and improving customer service
  - Promoting leadership in maintenance organizations and increasing job satisfaction
  - Delivering cost improvements
- **Hoshin Strategy Development**: Hoshin is a means to develop and deploy strategy. It encompasses a cyclic approach utilizing strategic intent and associated goals to prioritize and manage activities in support of achieving those goals and monitoring the results. By its nature, the Hoshin process employs a feedback mechanism to ensure that the most important activities are undertaken at the right time in order to produce optimum results. (From "Hoshin Kanri for the Lean Enterprise, Jackson, 2006)
- **Organizational Redesign**: Organizational Redesign is employed to support site and functional organizational effectiveness and efficiency improvements.

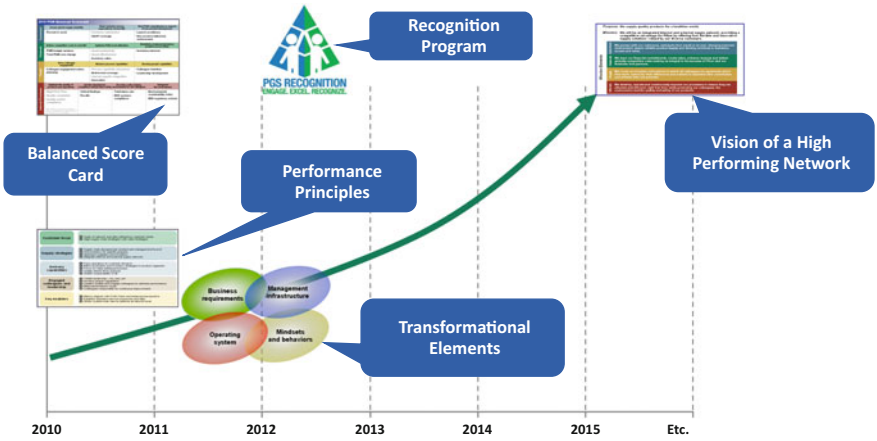


Fig. 8.6 The transformational journey

Conclusion

The journey that began with the deployment of the Right First Time strategy in 2003 continues today at PGS with the *Transformation* process. The transformational approach is based on the need to align business strategy, deploy agreed performance principles, establish a formal organizational structure and process to support the transformation, and align mindsets, behaviours and capabilities of the organization with the business strategy and goals (Fig. 8.6).

Transformation is supported through the development of *Network Performance Principles*. The intent is to define and drive PGS as a high performing supply network through a common set of performance standards. The Network Performance Principles (NPPs) describe the vision of best in class performance including:

- How operations and supply chains should operate in an ideal state
- How elements within and across PGS will operate together
- How balanced metrics drive high performance
- How highly capable colleagues deliver operational performance

The *Network Performance Assessment* supports these principles by providing a qualitative measurement of site performance against Network Performance Principles (NPP). The NPA supports an assessment of where the site is in the transformation process, which elements are progressing, and which elements should be prioritized when developing the transformation plan.

Finally, *Standard Network Approaches* are deployed across the organization yielding compounding transformational and continual improvement results.

Transformation is a conscious transition to a sustainable way of working at a significantly higher level of business performance. Moreover, the improvements are

also designed to be sustainable and maintained over time. The alignment of these transformational approaches with Operational Excellence practices can produce significant leaps in operational performance.

Reference

Bernstein Research (2011) The long view: is there light at the end of the pharmaceutical "patent cliff" tunnel? New models to 2020

Jackson TL (2006) Hoshin Kanri for the lean enterprise: developing competitive capabilities and managing profit. CRC Press, Boca Raton. ISBN 978-1-56327-342-1

Chapter 9
Ten Years with OPEX as a Brand: cLEAN© in Novo Nordisk Product Supply

Kasper Mejlvang

The Birth of cLEAN®: Why and How?

The predominant focus for Novo Nordisk during the second half of the 1990s was quality and regulatory requirements setting the agenda in Novo Nordisk Product Supply (PS) up until 1998.

From 1998 demand began to increase to the extent that PS' supply capabilities came under pressure, and since the efforts to improve quality had been successful, supply capability gradually took over as a focus area. From 1998 to 2003 capacity was expanded through investments and the number of employees in PS doubled from approximately 4,000 to 8,000. In spite of this, the company still struggled to keep pace with the growth and PS Management therefore began to discuss which other measures could be taken to overcome the supply challenge.

Asking how to increase capacity without investing more quickly led to talks about 'lean' and 'waste reduction' and on October 31st 2003 Product Supply Management launched cLEAN®. The name "cLEAN®" was chosen to reflect two aspects of the ambition. First, the 'c' refers to 'current' as the 'c' in cGMP, recognising from the start that the LEAN-journey would evolve over time. Second, the word LEAN was chosen and interpreted broadly as a 'lean philosophy', i.e. the principles of continuously optimizing processes by reducing waste.

"It was important for us to have our own approach and our own system. We didn't copy, but we did exploit any useful inspiration no matter whether it was called lean, Six Sigma, TQM, TOC, etc. What we launched wasn't merely a project but a production philosophy; from day one cLEAN® was framed as 'The way we operate'," explains Niels Luntang Christensen, Project Director, Product Supply, who was responsible for the implementation of cLEAN® in 2003.

K. Mejlvang (✉)
Novo Nordisk, Chartres, France
e-mail: ksme@novonordisk.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_9,

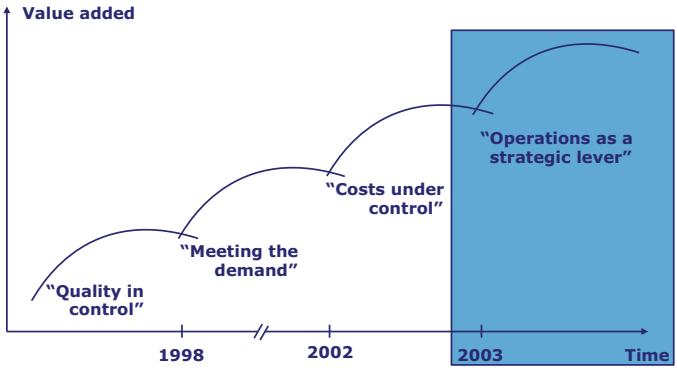


Fig. 9.1 The transformation of Novo Nordisk's operations

In the period around 2000 Product Supply experienced challenges which occasionally required emergency intervention caused by cases of back orders, long delivery times, low operational efficiency, delayed investments and budget overrun. During that period, forecast precision was limited and new product launches were delayed. But in 2003 PS was characterized by relative stability and deliveries, investments and budgets all met the targets. Further, Product Supply had acquired a low cost manufacturing company in Brazil.

From that perspective, the timing was optimal for defining a long term strategic goal and to invest in long term measures and solutions for the organization to get ahead of the game and help increase the value of Novo Nordisk.

"Roughly speaking, now that Novo Nordisk had quality, supply capability and costs under control, the time was right to embark on the fourth phase 'operations as a strategic lever'" (see Fig. 9.1)

Explains Per Valstorp, Senior Vice President, Product Supply, Novo Nordisk: "Therefore, we launched the ambition to develop the most efficient pharmaceutical production system in the world. We called it cLEAN®, had it patented as a registered brand to protect it and to indicate that we were serious about it. We launched an array of measures all under the cLEAN® name, and we launched the goals that within five years we should double production while maintaining costs – and by that improve our COGS." Per Valstorp continues: "It was a whole-hearted launch from my side. It was a mission that I backed up 100 percent and which was initiated, conceived and financed by me and my management team. From the outset, we were quite comfortable that this was the road to take and that it would and should take us far."

The transformation process was anchored in a central cLEAN® Office with 25 consultants who were in charge of driving and supporting the change initiatives. Each production unit appointed its own cLEAN® coordinator, and all departments dedicated employees to cLEAN® activities. Globally, approximately 1 % of the organization was dedicated to cLEAN®.

COGS20: The Target

In 2003, COGS (cost of goods sold) in Product Supply was 28.3 % and increasing. At that time, the average in the pharmaceutical industry was around 22 %, and although this covers a broad spectrum of business models as well as market conditions and COGS varying from 10 % to 34 %, there was no doubt that the Novo Nordisk COGS of 28.3 % needed to be reduced to improve competitiveness.

Therefore, PS Management established the goal of achieving a COGS of 20 % within 5 years. The goal was launched as "COGS20" and although many people in the organization considered it to be an unrealistic goal, after some time it was generally accepted.

A key reason for the buy-in that was obtained over time was that the COGS20 goal was launched together with an "Invest in the Future" guarantee and a job guarantee through a Job Transfer Center (JTC).

"Invest in the Future" implies that cost savings from the cLEAN® efforts on the way towards the COGS20 goal would be invested in research & development as well as sales & marketing activities. In other words, these savings were not converted into share holder dividends but re-invested in developing and growing the company to become more healthy and stronger against competition – and hence they also safeguarded jobs in PS for many years to come. The guarantee of investing in future jobs addressed the need for job security felt by many employees in PS, particularly in Denmark. It contributed to the acceptance of cLEAN® in the organization and created a good foundation for the optimization and change efforts. The employees were told that the process would entail changes and that flexibility was a necessary prerequisite. A guarantee was issued that all good employees would be able to maintain a job in PS, but there was no guarantee that all employees could keep exactly the same job they had at the time. The Job Transfer Center was set up to match available employees with new roles as changes were implemented.

The COGS20 goal was defined in October 2003 and the "sound barrier" of the 20 % was broken in Q1 2010. A broad array of measures all implemented under the cLEAN® programme contributed to this. It took place with a broad involvement throughout the PS organization, supported from the central cLEAN® Office as well as external consultants. Achieving COGS20 led to the reward of an extra week of vacation for the approximately 10,000 employees in PS. Many observers of and participants in the cLEAN® process from that time emphasize the following factors as important for the success of COGS20 in spite of initial scepticism.

- Keep it simple: "Simple goal that was easy to understand for everybody."
- Confidence: "Invest in the Future" and "Job Transfer Center" guarantees created strong motivation throughout the organization.
- Level of ambition: "We have introduced goals that we did not even dare to dream about a few years ago and which we did not know how to reach up front."
- Persistence: "We have held on, and now it works. Only few people believed in this when we first set sails" (Fig. 9.2).

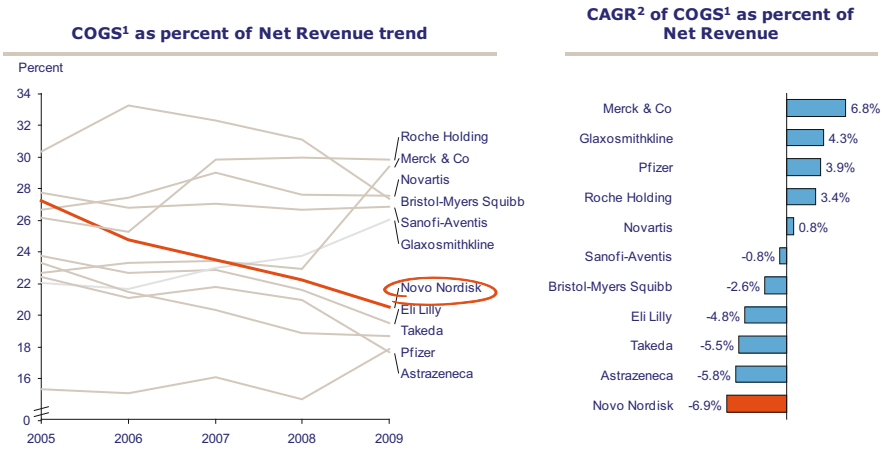


Fig. 9.2 Novo Nordisk in comparison to its competitors
Note: Pfizer data includes effect of Wyeth acquisition and Merck data includes Schering-Plough acquisition
Source: Compustat; Annual Reports
[1]Cost of sales incl. Depreciation and Amortization
[2]Compounded Annual Growth Rate in local currency

Academy: The Tools

One of the initiatives that paved the way for the accomplishment of the ambition was the training and education program called "cLEAN® Academy". The cLEAN® Academy consists of four levels called:

- Basic (100 % of the organization).
- 1 star (50 %).
- 2 star (5 %).
- 3 star (2.5 %) (Fig. 9.3).

Basic is the fundamental level where all of the 10,000 PS employees have received or will receive a 1-day basic training in the cLEAN® mind-set and tools in order to contribute to the creation of a culture of continuous improvement and to help sustain achieved results 'in a cLEAN® way'.

"cLEAN® basic made me aware of wasteful or unnecessary parts of my daily tasks. It encouraged me to consider the small improvements I can implement in my everyday life to ensure that everything I do at work makes a difference", explains one Basic module participant.

The 1 star module consists of a 3 day training, aimed at making the employee capable to participate actively in cLEAN® workshops or project teams. It involves subjects such as performance management, PDCA, process mapping, bottleneck theory, OEE, VSM, 5S, SMED, etc. The aim of the 2 star course is to enable the individual participant to structure, drive and facilitate a practical improvement

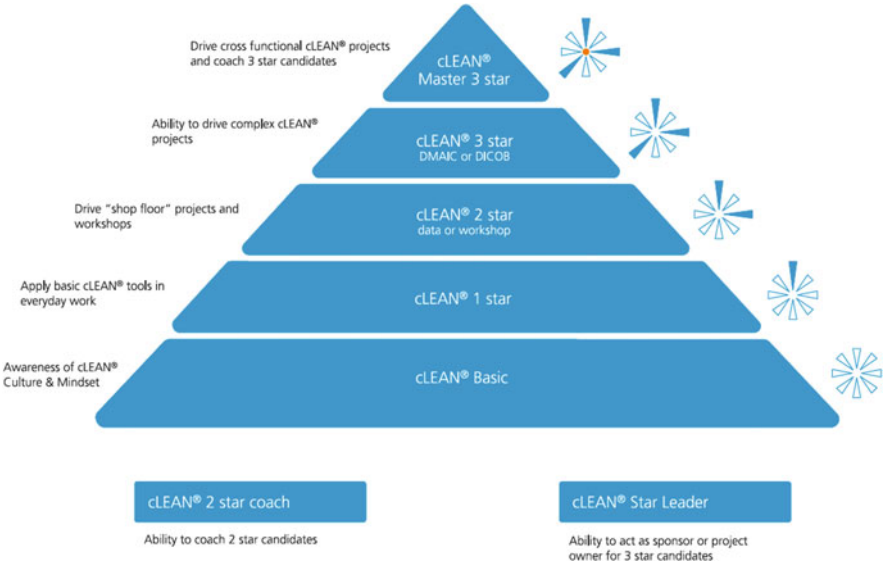


Fig. 9.3 The four levels of Novo Nordisk's cLEAN® Academy

project using cLEAN® principles and tools. It consists of a 3–4 month project and occupies up to 25 % of working hours. The 3 star course is a full time black belt course lasting approximately 6 months.

The Academy has ensured critical mass in terms of basic awareness and knowledge of cLEAN® in across PS, enabling continued momentum on the cLEAN® journey. It has created a common language and frame of reference which in turn has paved the way for specific projects and practical improvements in the day-to-day business.

"cLEAN® Academy has structured and standardized training in PS leading to the creation of both alignment and a consistent knowledge across the organization", explains Andrew Finnegan, who was in charge of the setup and roll out of the first phase of cLEAN® Academy. He adds: "You cannot create a culture without first introducing tools. Culture doesn't just evolve. You need to handle the practical world using concrete tools and projects. The cultural element gradually grows as a layer on top of the tools if you continuously emphasize the thoughts behind the tools. Everybody needs to be aware that the tools are means to achieve a higher goal: to create a healthier and more competitive PS."

In 2010 cLEAN® Academy was adapted to the new goals that have replaced COGS20 and Invest in the Future, namely "2014 Fast to Market", which focuses on reducing leadtime through the supply chain. About the same time, the cLEAN® Academy was supplemented by a fifth level called "Master 3 star." Further, the curriculum of the 2 star and 3 star courses have been updated to address the new targets as well as to integrate the insights acquired since 2003. As cLEAN® maturity has increased over time, the need for more tailored and higher level training has also increased, and the Academy aims to update the courses on an

ongoing basis to address those needs and hence stay 'current' as a key foundation to the cLEAN® transformation process.

PS@ShopFloor: The System

In 2004 and 2005, PS launched a series of so-called Modelline projects at a number of sites which had identified specific performance issues to be addressed. The Modelline projects will be described more in detail in the following section (2.4). While some Modelline projects worked as planned, others did not. The root cause analysis of this variation concluded that the decisive success factor for a "Modelline-project" was the level of buy-in from line management at the project site. At some sites buy-in to the project was low, because the cultural process had not reached a certain level of maturity. Culture, management behavior and attitude were not ready for the changes and the pace of change envisaged by the Modelline concept.

This led to the launch of a new measure which was introduced under the cLEAN® programme. The new initiative was called PS@ShopFloor,[1] *and* the main objective of the program was to focus even more on the leadership part of cLEAN® – to train management to support value creation on the shop floor. See Fig. 9.4.

Until then, lean leadership in the cLEAN® system had manifested itself mostly as good management of the performance board meeting held every morning at three different organizational levels. During these meetings the problem was identified, but management did not have the time to follow up on the problems with solutions on the shop floor because they were occupied the rest of the time by a busy meeting schedule.

As a consequence PS@ShopFloor introduced a radical change with a decision by Product Supply Management that all team leaders and department managers were allowed (and expected) to spend 4 h every day on the shop floor. In practice, the managers' schedules were controlled by their Outlook calendars. With PS@ShopFloor 4 h were set aside every day in the managers' busy schedules for them to dedicate time to supporting their organisations in solving the most pressing problems of the day and process confirming that solutions to problems worked according to intentions. The idea behind the program was to create a problem solving culture where any problems are addressed immediately, 24/7 which over time will remove the root causes of operational disturbances and create a stable, operationally excellent business.

This was a big change. The PS@ShopFloor program was designed to prepare managers for their new roles as problem solvers and coaches. It is a 14 week implementation followed by a 14 week 'sustainability phase'. During the entire period the manager is followed by a coach for some hours every day on the shop

[1] From the start, in 2007, this initiative was called 'Adrenalin Shot', however, it soon matured into a concept focusing more on sustainable change at shopfloor. Since 'Adrenalin' and 'Shot' were assessed to yield the wrong associations for this, the program changed name in 2010.

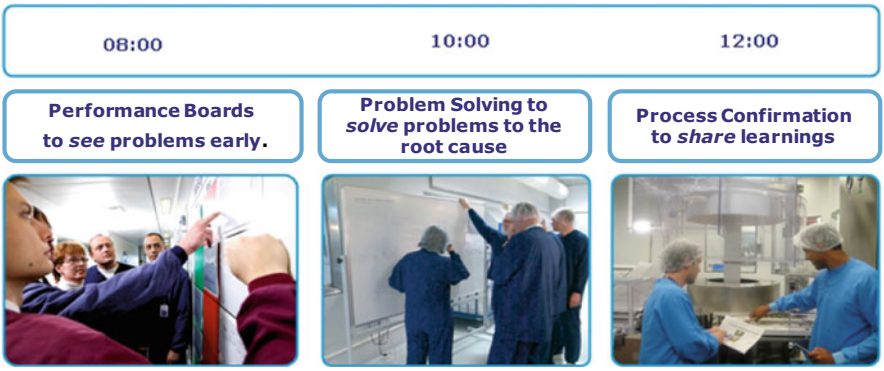


Fig. 9.4 The daily schedule of PS@Shopfloor

floor providing systematic feedback on the manager's behaviour and people management. The program focuses specifically on problem solving and practical distinction between symptoms and root causes. The managers are taught how cut through the many layers of explanations as to why a problem has occurred, in order to help employees arrive as directly as possible at the root causes. The aim is to establish a new standard for the activity or process in question in order to prevent future repetitions of the problem and create more stable processes. One system to support this is the application of the See–Solve-Share method through which the problem is visualized, then solved to root cause and finally shared across the organization e.g. by means of a new, detailed and easy to understand standard.

"We found that manager workshop training isn't enough. We need to follow the managers during their day-to-day activities, where practical leadership takes place. The PS@ShopFloor course therefore consists of an initial workshop followed by 28 hours of coaching over a period of 14 weeks. And we can see that it is in fact working. We can see that both on 'before and after' videos with the managers as well as on the business KPIs which for 95 percent of the cases have improved after only 14 weeks. We trust that this will create even bigger impacts in the longer term," says Director in cLEAN® Office Jan Kristensen, who has been in charge of the PS@ShopFloor program.

"There are always problems in a business like ours. We may succeed in optimizing the batch changeover time only to be met shortly after with a new cGMP standard requiring us to develop a whole new process. Previously we had a few excellent problem solvers, but with PS@ShopFloor we are spreading the problem solving capabilities across the organization so that we can address the problems fast and on site as they appear", says Jan Kristensen.

Senior Vice President Flemming Dahl is responsible for the Biopharm production area in PS and as such a user of the management development program PS@ShopFloor. He says: "The program has not been easy to implement. It's a dramatic change when you take out four hours of a manager's working day, and we certainly have seen changes in management because of this. But there is no doubt it works; our focus on what is important and what is not has become much sharper.

It's a big help for managers that they can let their behaviour and time be controlled by what creates value in the production. Today our approach to production is guided by the question: If this was my own company, what would I do today?"

PS@ShopFloor is an attempt to anchor the tools in our management behaviour and in the management systems, directly related to the end goal which previously was COGS20 and today is 'Fast to Market'. PS' barrier to achieving an even better Fast to Market performance is instability. And in order to reduce the instability the whole culture must be geared to solve problems fast and efficiently at the level of occurrence in order to ensure that fewer problems occur and output gradually increases. "We have examples of increases in output of more than 50 percent in a production unit, so there is no doubt that management development has a positive effect on our productivity," continues Flemming Dahl.

If Academy is the broad distribution of tools across the PS organization, PS@ShopFloor is the system needed to tie the tools together so that they may be applied in the right way at the right time to support the desired goals.

Modelline: The "Perfect Solution" That Did Not Work

PS launched several Modelline projects in 2004 and 2005. This was done with heavy support from external consultants. Modelline is a compressed project in which you have very short time to obtain significant productivity improvements on a production line. It is a kind of a laboratory exercise where you focus efforts on a clearly defined area for a limited period of time in order to create a well-defined effect; an exercise in which the aim to speed up the change momentum by showcasing what you can ideally achieve with cLEAN®. One of the places in which Modelline was launched was a filling line in a Danish site; a site with a long history and a big potential for improvement. A team of qualified and experienced consultants worked for 6 months on the implementation of Modelline – a proven and well documented concept, which has demonstrated its ability to create great results in many types of businesses. PS and the external consultants also implemented Modelline in two other Novo Nordisk production sites at which the results, contrary to those obtained in original site, were satisfactory. However, in this particular site the Modelline project failed to deliver on the targets for improving productivity, quality and supply capability. However, the valuable learning points that came from the project were key to the success of the following and the start of the PS@ShopFloor programme.

Plant manager at that time, Peter Mohan Christiansen explains: "We didn't reach our goal, but we did learn a lot of lessons," and he adds: "Modelline was a good example that we didn't have the human and organizational foundations in place prior to attempting the implementation of change. We were really good at handling the tools, but we forgot to work with the organization and the involvement of both line management and employees. Modelline was an important contribution to the cLEAN® maturation process in PS".

The experience with Modelline is one of the factors that led to the development and roll-out of the program PS@ShopFloor. Its aim is to build the human and organizational basis in order to facilitate the implementation of new tools, optimization projects, changes, etc. In turn, new tools and changes will iteratively influence the organizational foundation and contribute to the development of a continuous improvement culture.

"With Modelline we learned a lot in a very short time. It was a strong booster of the process of accelerating the cLEAN® journey. We did commit errors en route, but they paved the way for the solution to the enigma of how to continuously improve our productivity," says Peter Mohan Christiansen.

Consultant Anders Arnum Jensen, who participated as an internal consultant in the Modelline projects, supplements Peter's evaluation: "There was nothing wrong with the concept as such, but our approach was too fact and tool focused, and we forgot to get the organization onboard. But there is no doubt that our experience with Modelline has been paramount for the later development of cLEAN®.

Take-Aways

It is always difficult to evaluate which of your own experiences may be useful for others; but below is an attempt to describe eight take-aways which we believe have facilitated PS' cLEAN® journey to date.

1. **Consistency of purpose**. During the years, cLEAN® has helped shape one explicit direction towards a more competitive company, even though specific initiatives and tools that have been introduced along the way have been very different. All 10,000 employees in PS know the brand cLEAN® and as a minimum they have a basic understanding of what cLEAN® stands for and what that implies in terms of expectations to each employee. cLEAN® is by no means a project. It is a timeless concept and a mission. This is a strength because it has created a sense of purpose and coherence across PS for managers as well as employees and allowed for a more seamless sharing of better practices across organizational boundaries.
2. **Consistency in top management and strong personal ownership**. PS has had the same Senior Vice President since cLEAN® was launched in 2003. This has allowed for a seldom seen consistency in the support to the programme and it has been backed up by strong personal engagement throughout the period. Hence, the organization has moved beyond the feeling of 'yet another top management OPEX program being launched' every 2–3 years; the first kilometres of a marathon have been passed long ago, and when PS launches new projects and measures within the cLEAN® framework, the organization already has a basic understanding of what it is all about, hence saving a lot of initial change management efforts. This strength has been amplified by the fact that PS Management consists of members with strong ownership of cLEAN®, with most members having been part of the cLEAN® journey since 2003.

3. **New inspiration every 2 or 3 years**. Although the overall direction and purpose has been consistent throughout the period, the cLEAN® journey has regularly been re-energized by means of new programs addressing the needs of the business while keeping momentum in the cLEAN® journey. These programmes have been launched through the central cLEAN® Office based on input from the organisation, ensuring that cLEAN® lives up to the lower case 'c' for 'current' indicating that the target continuously moves and that the means therefore also need to evolve. These programs have carried names such as cLEAN® Temple, Modelline, cLEAN® Academy, cLEAN® Leadership, Flow, Adrenaline shots, PS@ShopFloor, etc. and have played their part for a shorter or a longer time each contributing to the cLEAN® journey in its own way. The assessment has been that these new programs have been needed continuously in order to add inspiration and energy to the continuation of the journey.
4. **Right balance between tools and culture and between infrastructure and results**. Culture requires tools, and without culture tools have only little effect. The same relationship applies to what you could call infrastructure or foundation and results or performance. It is of vital importance to focus on both aspects when a company wants to improve its own way of operating for the long term. It is easy to create results, but difficult to make them sustain. Along the way, many errors have been committed and many successes have been created. Modelline was an example of placing too much weight on tools and short term results at a time when the culture and infrastructure were too immature; however, without the lessons learned from Modelline, PS@ShopFloor would probably not have gained enough support for its strong focus on infrastructure and culture. And to get the balance right, PS@ShopFloor still needs to ensure a harsh focus on delivering on hard business KPIs during each project.
5. **There are no shortcuts to maturity**. The cLEAN® process has taught PS that things take time and that the journey is like a staircase at which it is not possible to skip a step. It is necessary to take all the steps in order to secure an appropriate foundation for future measures. During the early phases the organization needs to focus on fire fighting and symptomatic treatments with a relatively short time horizon. As the organization matures, it becomes capable of investing in efforts to nail root causes and making solutions sustainable.
6. **Focus on the basics**. It is becoming more and more evident that the basis needs to be in place and that you cannot spend too much time strengthening the basic tools and principles. In our work with cLEAN® we have discovered that maturity brings about even more focus on the basics rather than on new and more 'flashy' concepts. As cLEAN® managers become more experienced they increasingly spend their time on basic tools and principles, now with a gained insight about everything that could be achieved with that tool (e.g. VSM) that was never realized in the past. The idea is that there is always room for improvement of the foundation.
7. **Set high standards and ensure results are visible to all stakeholders**. A high level of ambition is a prerequisite for great results, and the creation of results is a prerequisite for keeping a process like the cLEAN® journey alive and ensuring

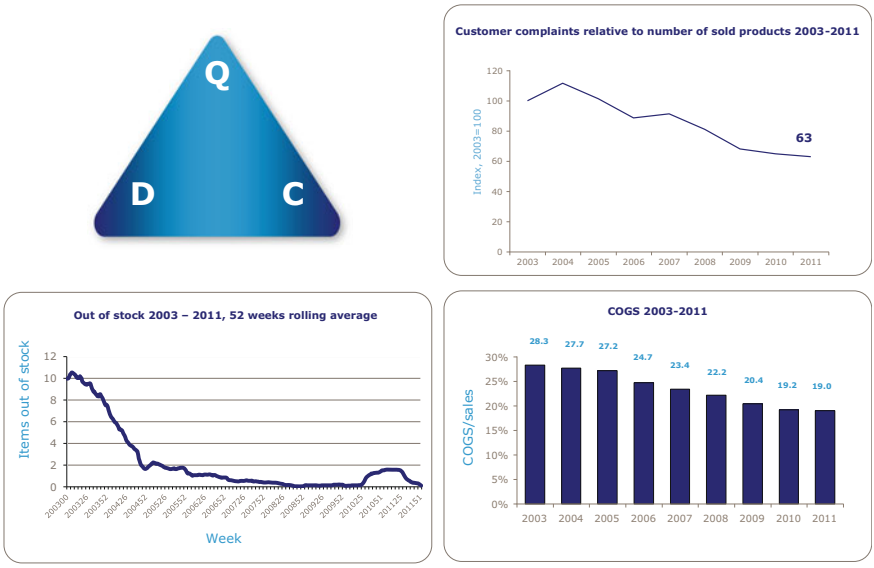


Fig. 9.5 Illustrates the results created by PS on delivery, quality and cost during the period where cLEAN® has been the primary driver for development within PS

its continued acceptance. Results and the communication of results are necessary both to maintain support from top management, but also to maintain engagement throughout the organization. During its existence from 2003 until today cLEAN® has matured significantly and delivered significant business results along the way, as illustrated in Fig. 9.5. This makes it increasingly easy to successfully implement new cLEAN® initiatives.

8. **There is no silver bullet – only hard work**. Look at the past 10 years with cLEAN® in PS, it is clear that nothing has come for free. The different phases and the goals that have been achieved so far are not the result of a master plan which has been carefully worked out by PS Management from the beginning. Rather, it is the result of an overall shared sense about where we want to head for the long term, combined with dedication and alertness to what – in a given year – is needed for the next couple of years in order to continue the journey from current state, based on the insights achieved in the past couple of years. And a lot of very hard work from everybody who has been involved along the way.

Next Steps

The PS cLEAN® journey has consisted of a series of phases during which different initiatives have provoked different waves that sooner or later have been replaced or supplemented by a new wave. It is hard work to improve. It requires visionary top

managers, capable middle management and engaged employees that are provided with a good framework and clear guidance. Improvements are not something you can just delegate through the organization. Much more is needed than the mere implementation of a new set of tools or the influence of a charismatic leader. Improvements require a cultural transformation leading to every single employee as well as middle and top management being actively engaged in creating small and big improvements every day. We believe that we have come some of the way towards this cultural transformation. It has been initiated, and we have moved through the first phases of the transformation process. But, we are also aware that we still have a long way to go and that we need to be alert in order to maintain the momentum. We need to remember to respect the little 'c' in cLEAN® which stands for 'current' and which tells us that the target is continuously moving.

As always we are currently considering what the next steps should be on the cLEAN® journey. We can see that with cLEAN® Academy we focused on covering the organization widely ensuring that all employees are equipped with an elementary understanding of the improvement process. We can also see that with PS@ShopFloor we focused on the middle management segment which is in the process of being prepared to take on a new leadership role widely based on employee coaching to improve the organizations ability to solve problems systematically and become more focused on the concrete shop floor processes. In that sense, the cLEAN® transformation has been guided from the top, but taken place bottom-up.

Therefore, the next logical step could be to focus more on senior management and train the top management segment in how to support the next phases. It may sound contradictory, since top management started the journey. However, we have gained many insights on the way, many of them pointing to the need for top management to be 'leaders as teachers' and being crisp on which management systems to implement to help the organisation drive performance in a sustainable way.

Until now the most successful cLEAN® efforts have been the ones setting goals (COGS20), implementing tools (cLEAN® Academy) and establishing systems (PS@ShopFloor), that combine tools to create a result creating behaviour. These efforts have created great results. But the efforts have also led to improved process stability – an important feat because it creates a better basis for the continued work with improvements.

With the improved maturity the realization has come that operational excellence long term can only be achieved if the whole production system fits together to support sustainable performance in all units. It is not enough to focus on production lines in isolation as they are part of support organisations and systems that all impact how they need to operate. Manufacturing Development defines standards for new processes. Quality Assurance defines systems for handling of non-conformities and change requests; HR defines systems for competency and performance management, Supply Chain defines systems for flowing products across sites, etc.

Making the different units of best practice play more effectively together in a production system is a natural next step to ensure that continuous improvement

takes place across the supply chain, not just in each unit, and to ensure that it supports all aspects of operating effectively, strengthening both compliance, delivery and cost performance.

Anchoring the principles of operational excellence in the systems supporting daily operations will also ensure that the PS mission of becoming the best in a cLEAN® way is achieved, independent of specific persons, tools or programmes.

Chapter 10
Lean in Novartis Pharma: Sustainability Through a Five Step Deployment Methodology

Steve Dreamer and Pav Niewiarowski

Origins of Lean in Novartis Pharma

Novartis Pharma began its most recent chapter in Operational Excellence in 2004 achieving tremendous results in productivity, cycle time reduction and working capital optimisation. Much of these achievements have been sustained since the inception of the Innovation Quality & Productivity program which began back then. This journey was described in the first book "Operational Excellence in the Pharmaceutical Industry", with a description of the balanced approach in addressing waste through Lean, and variation through Six Sigma. The approach to Lean was developed and piloted in response to the business imperatives of the time, to drive improvements along the extended value streams of the strategic brands running through the API and Finished Product manufacturing network.

Evolution of Lean: Learning & Responding to a Changing Business Environment

In 2010, Novartis Pharma passed a significant milestone in its strategic trajectory, a vision which had been set in 2005 to become the "Toyota of the Pharmaceutical Industry". A major element of the realisation of this strategy, was the deployment of Lean throughout the strategic brands. Another important aspect to be addressed was the successful implementation of an empowered organisation to own, run and

S. Dreamer (✉)
Novartis, Basel, Switzerland
e-mail: steve.dreamer@novartis.com

P. Niewiarowski
Novartis, Walton on Thames, UK
e-mail: pav.niewiarowski@novartis.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_10,

continuously improve the processes and practices that have been established as a result of Lean transformations. The advent of a new strategy and new challenges for Novartis Pharma highlighted the opportunity to reflect on the successes and lessons from the previous 5 years of experience in deploying Lean. This reflection comprised among others the refreshment of the approach as to ensure it continues to fit the purposes in and the requirements of an ever-changing business environment as well as to serve as a platform for Continuous Improvement.

In this period of reflection, a number of broad changes were identified that had taken root throughout the period of Lean deployment. Those changes were believed to have a profound impact on the longer term success of Novartis' Lean approach:

1. Complexity had grown significantly; there are now fewer high volume brands with dedicated value streams and more low volume brands with highly potent drug substances
2. Sustainability of "Lean solutions" varied between sites
3. There had been a significant though normal turnover in business leaders, from those that had led the transformations, to those who inherited operations where Lean solutions had been driven by predecessors

This led those who had been charged with deploying Lean throughout TechOps to reflect on the underlying causes and consequent opportunities, to embed Lean practices for sustained operational performance.

1. **Complexity** – the "one size fits all" approach of transforming a brand makes sense for that brand, but more often than not little sense for a complex work centre which typically processes multiple products and variants. To the process owner, the process needs to consistently perform throughout its full portfolio of products, a brand prioritisation could easily result in a 'fast track' mentality, whereby the benefits realised on a strategic brand, are "paid for" by compromising the remaining portfolio of products, rather than through true elimination of waste and variation. This becomes more apparent as the product portfolio continues to diversify, in line with what is seen throughout the industry.
2. **Sustainability** – the transformational approach undertaken and consistently rolled out since 2004 was extremely successful in making the case for and orchestrating a stepped change in performance in the principle Lean Key Performance Indicators (KPIs), those being cycle time, productivity and right-first-time. The change was initiated by intensive project work that came directly out of the value streams known as Process Units. Within these units implementation was strongly driven by a select group of senior leaders. Beyond those highly visible and intensive project efforts, there lies a risk that the significance of the transformational effort would in some instances be lost with the advent of new priorities. Besides, unless fundamental practices to operationally manage, sustain and improve performance were in place, some units would find themselves reinventing solutions to previously solved problems periodically.
3. **Turnover in Leadership** units which lacked the mechanisms to ensure sustainability and evolution of their processes in line with changes in the business environment, sometimes found that with new leaders, in the absence

of a consistent management system to sustain Lean, other priorities could take precedence with the consequence being an unconscious lowering of Lean standards set previously.

In response to these challenges, the Lean model should evolve, as an approach:

1. **To deal with Complexity** – cover the full portfolio of brands running through a Process Unit, though still with a strong emphasis on securing optimal performance for the brands which would add the most value, those typically being new launches, growing brands and those demanding the highest degree of involvement and resource utilisation.
2. **To assure Flexibility** – ... refresh the deployment approach, to ensure flexibility to accommodate and refresh Lean solutions in line with the ever changing demands of the business.
3. **To ensure sustainability through organisational changes**... install a Lean Management System to help orchestrate the daily activities in support of achieving daily performance targets, rather than solely focussing on a project driven approach of making stepped changes to specific bottleneck challenges. This will help ensure that Lean practices become a way of working and irreversible, working any other way will no longer be an option.

Although conceptually a radical refresh of the Lean methodology, this approach had already been well established in the QC Laboratories, where a number of business critical bottlenecks were avoided. This was achieved through a comprehensive **Lean Lab** approach (versus a mono-brand focussed solution) with a heavy bias towards established operational control in the laboratory, characterized by the use of visualisation, performance management practices around the visualisations, standardisation, 5S workplace organisation and establishing a routine of constantly challenging and eliminating waste and variation. This approach to achieve improved performance in QC laboratories started in Novartis Pharma in 2008 and by 2010, was well established and rolled out successfully through much of the QC Laboratory network.

The approach developed and rolled out as part of the **Lean Lab** program, became the model to be applied within the Process Units, making it a **Lean PU**.

The Five Step Lean Methodology

The methodology developed within Lab operations, together with the positive learnings and opportunities identified from the first phase of Lean deployment, resulted in a refreshed approach to Lean deployment, covered in a five Step Lean Methodology. The focus of this approach is to take an organisational unit through a full transformation and apply the most applicable tools on that journey, with a strong focus on a Lean Management System. The approach always begins with a true understanding of the vision based on the true customer demand and demonstrated capability and thus a solution is built to enable a brand independent flow, which is resilient to the anticipated regular peaks in demand.

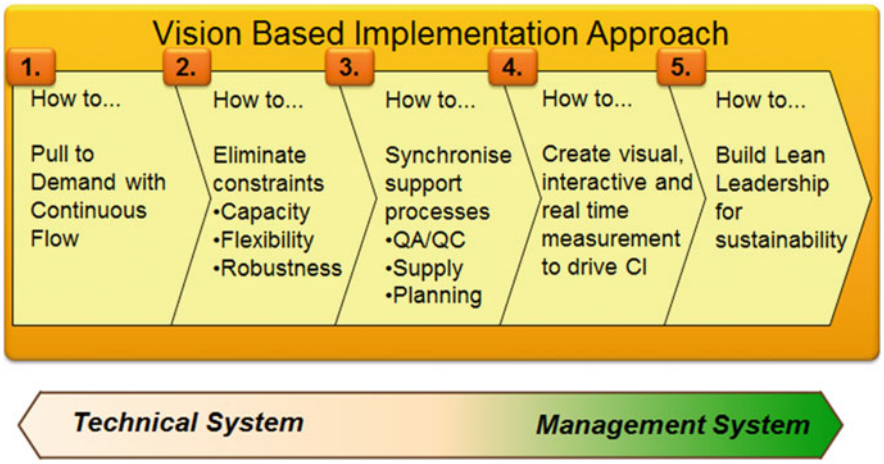


Fig. 10.1 The vision based implementation approach

The five steps are outlined in Fig. 10.1. The first three steps are primarily focussed on identifying the major constraints to enable a resilient flow which matches the customer demand. This is referred to as the "Technical System", because it results in projects focussed on enabling a stepped change in performance around bottlenecks which prevent the Process Unit from achieving its Practical Vision (PV) – the PV is the aligned Future State derived from the Vision. The Management System, steps 4 and 5 are primarily concerned with implementing operational management practices, to focus operations on short interval control, whereby shift targets are managed continuously within the shift, with support mechanisms in place to resolve issues, rebalance resources, solve issues and equally to act on improvement opportunities – with a strong bias to those improvements being managed within the operational team. Each step is summarised below, with a deeper focus on step 4.

The Lean process as illustrated in Fig. 10.2 is designed to only respond to actual customer demand and avoid anticipation of future demand. The PV is designed for maximum responsiveness and flexibility. The steps undertaken are to analyse and understand true customer demand, conduct a walk through to build a process or value stream map of the end-to-end process, develop an uninhibited Blue Sky Vision based on the potential if only the value adding steps were implemented, with infinite and instantly available capacity and consequently a practical concept of flow is designed, taking into consideration Lean performance benchmarks and the complexity of the product portfolio.

In step 2, the Practical Vision is analysed to identify all constraints and performance factors which currently prevent realisation of the designed flow concept (see Fig. 10.3). This is done by identifying the throughput rate required from each unit operation and the critical production path revealing the constraints to achieve that

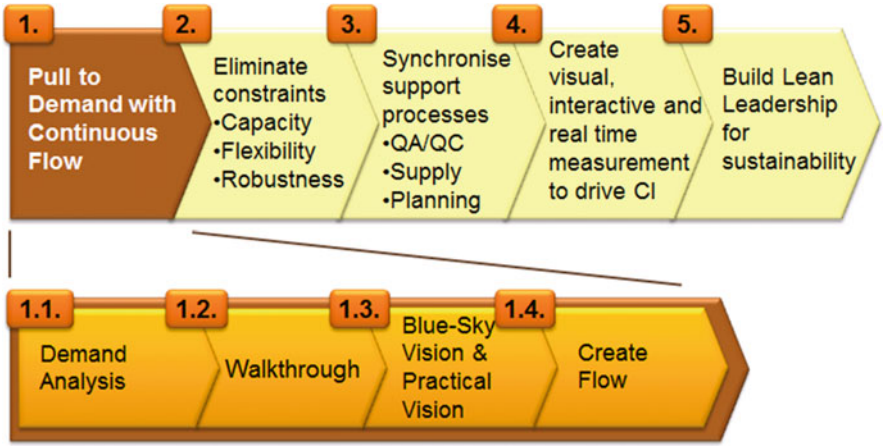


Fig. 10.2 Step 1 – pull to demand continuous flow

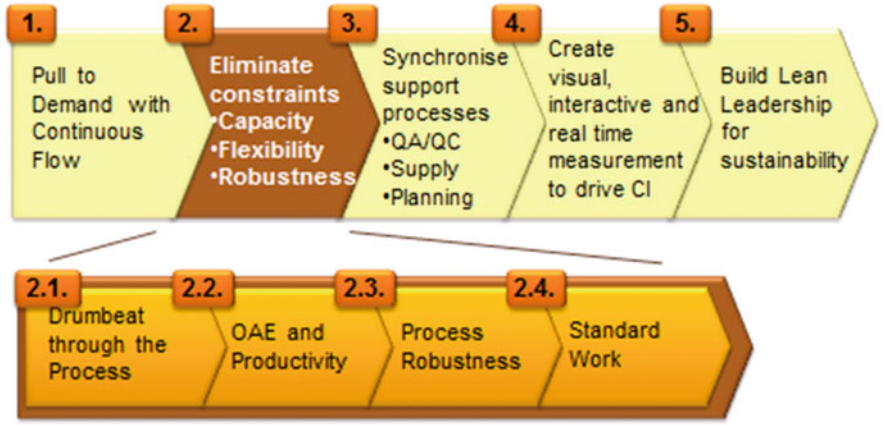


Fig. 10.3 Step 2 – eliminate constraints

rate of production. Those constraints can be categorised into two broad buckets, those being:

- **OAE (Overall Asset Effectiveness) and Productivity** – the typical focus of Lean waste elimination activities
- **Process Robustness** – causes of deviation from standard processes which result in processing delays whilst deviations are investigated and remedial action is taken, sometimes also resulting in yield losses or batch rejections

The final element, a focus on Standard Work, is to ensure that processes which must be performed in a standardised approach to ensure a predictable performance are done so and that this is clearly understood, visualised and adhered to by all.

Figure 10.4 depicts step 3. This step acknowledges and ensures that all support processes, though not necessarily on the critical path for achieving the PV from the

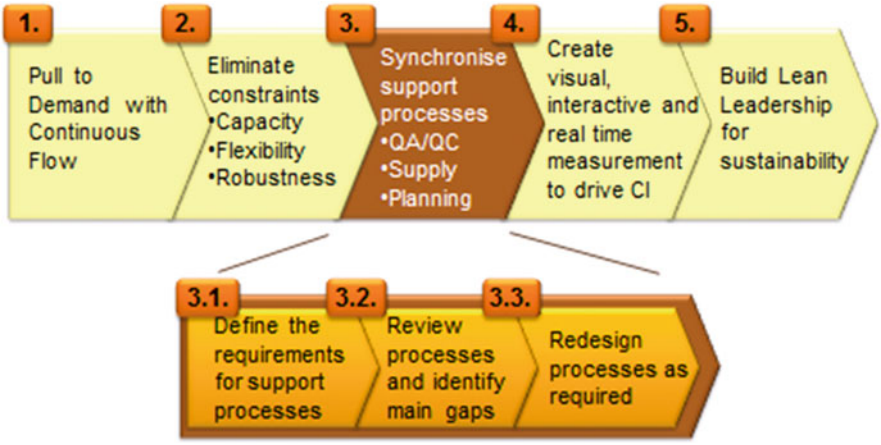


Fig. 10.4 Step 3 – synchronise support processes

outset, are a potential constraint and could easily become a bottleneck if left unchecked. This approach essentially re-runs steps 1, 2 and then 4 and 5 for the entire support unit, e.g. a QC Laboratory or a QA release process, though this time the demand rate is taken from production and the Lean standards are such that these support processes will never become a variable constraint and consequently should always synchronise with production needs (Fig. 10.5).

Visualization of process performance is the first of the main steps which can be run independently of the remainder, as this is now considered to be a foundational practice in running manufacturing operations. Visualization helps empower all process owners in understanding and driving process performance constantly, in real time against realistic and agreed performance standards. It helps define a "good hour" versus a "bad hour" and helps set clear boundaries as to when and how to take remedial action in order to achieve the shift target. The concept works from the shop floor upwards rather than top down. The shift is "saved" by visualization of performance by the hour. Daily performance is "saved" by the Process Unit's visualization of performance by the shift and consequently the week is "saved" by visualization of the Process Unit's performance and improvement priorities.

Visualization must be developed by the people who run the process. There is a belief and expectation that the visualization will develop alongside the key priorities and challenges for that work centre or Process Unit and consequently the visual solutions can look very different from area to area. What is important, is that key elements of visualization are addressed, those being that the unit represents the following:

- Process Performance – output versus target
- Work Scheduling – what to do, by when and by whom
- Waste Capture – evaluation and execution of identified improvement opportunities

. . . in three dimensions, those being

- Real Time – visuals should be relevant for now, this hour, this shift

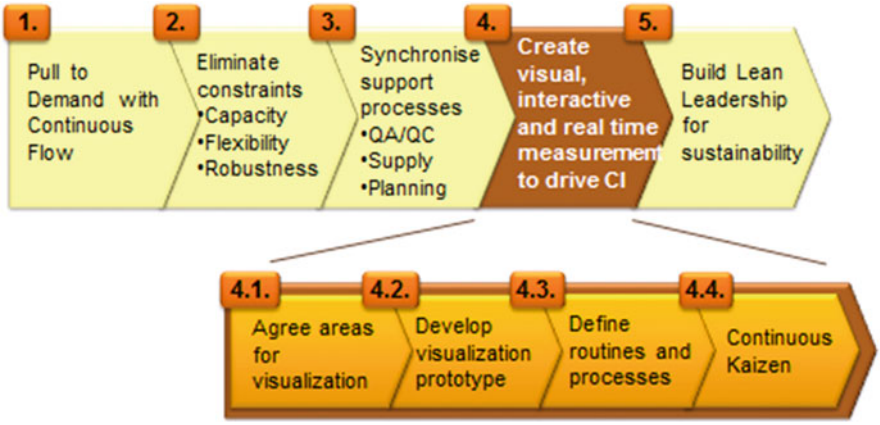


Fig. 10.5 Step 4 – create visual, interactive and real time measurement to drive continuous improvement (CI)

Shop Floor Visualisation Grid			
	Real Time	**Inter-active**	**Predictive**
Process Performance (Flow, Quality, Drumbeat)	Deviations versus work standards	Signalling for support interventions	Alert if cycle time or drumbeat at risk
Work Scheduling	Exact batch status (numerical, count)	Dynamic work centre schedule adjustment	Alert if schedule at risk
Waste Capture	Continuous waste capture	Fast actions & escalation	Anticipate risks for next batch

"I can better understand which is the importance of my role in the chain, and when & why is the moment to push additionally the production"

"The visualization gives me awareness on the performance of my daily work and which is the progress of production during the month"

"It makes me more committed on the daily scheduling and on the resolution of issues that occur, avoiding waste of time"

"We can all see who is doing what, it helps us balance the workload in our team"

Fig. 10.6 Three dimensions of visualization

- Interactive – visuals should prompt a behaviour in response to deviation from a standard or the plan
- Predictive – visuals should allow process owners to anticipate the impact of current performance on the output compared to target

these three dimensions are outlined in the visualization grid below. This tool helps teams to enhance and further develop their visuals. Visualization is seen as an iterative process, embedded use of visualization results in refinement and reinvention by process owners for years to come (Fig. 10.6).

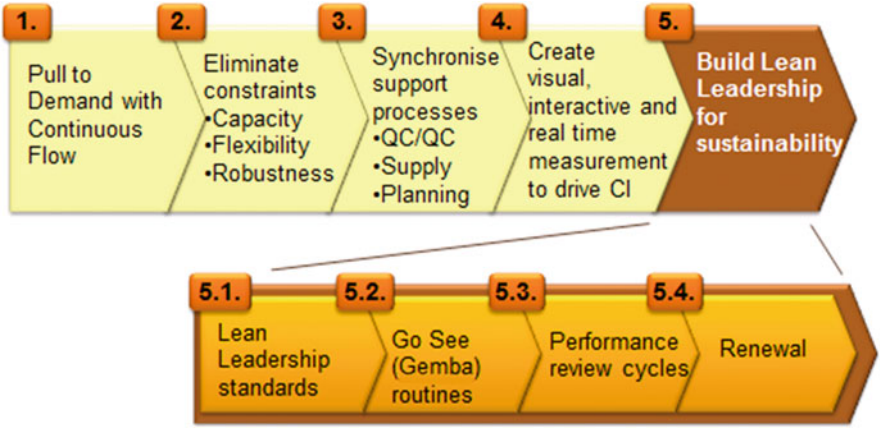


Fig. 10.7 Step 5 – build lean leadership

Step 5: Build Lean Leadership

The tangible elements of visualization are often those most easily implemented and copied. The easily overlooked though critical success factor for managing process performance is through the regular interactions on the shop floor, be it in a manufacturing process, a transactional area, a QA release office or a QC laboratory. Leaders should regularly be visible and asking consistent questions regarding messages derived from the visualizations: "Did we meet our target? If not, did we follow the standard? If not, why can it not be followed, what is needed to be improved? If yes, then where is the weakness in the standard? What help is needed to ensure the impact on the shift target is mitigated? What improvements are necessary to ensure the standard is robust, can be followed consistently and that adherence will ensure realisation of the PV?" (Fig. 10.7).

Lean Leadership consequently is about enabling the organisation to interpret, manage and positively respond to the signals presented by the process to ensure sustained performance, to help the organisation learn how to solve problems and to keep the PV fresh and relevant for today's business needs.

Conclusions

This refreshed approach to deploying Lean ensures that the Lean methodology is truly embedded in operations. This comes through application of a structured transformational approach with a strong, underpinned emphasis on building a Lean Management system., The approach is designed to considerably reduce the need for future "transformational" efforts, whilst ensuring process performance is owned and managed consistently at all levels of the organisation.

Chapter 11
Abbott Pharmaceuticals Journey of Business Excellence Standards

Valentin Starke and Joseph Kumor

Abbott: A Leading Diversified Global Healthcare Company

Abbott is a global healthcare company devoted to improving life through the development of products and technologies that span the breadth of healthcare. With a portfolio of leading, science-based offerings in diagnostics, medical devices, nutritionals and branded generic pharmaceuticals, Abbott serves people in more than 150 countries and employs approximately 70,000 people.

Business Excellence: Abbott's Approach

The roots of Abbott's Business Excellence program for the global pharmaceutical side of the business began in 2002. Contrary to the approach followed by many other pharmaceutical companies, Abbott did not start with Six Sigma or with Lean.

Abbott had a well-established reputation for strong operations and commercial execution. To ensure alignment between both activities, Abbott launched a formalized Integrated Business Planning (IBP) program in 2002 focusing on integrating commercial operations with manufacturing by enforcing the application of a number of key business processes on both ends of the supply chain. This

On January 1, 2013, Abbott completed a separation of its proprietary pharmaceuticals business, creating a new, independent biopharmaceutical company, called AbbVie.

V. Starke (✉)
Abbott, Allschwil, Switzerland
e-mail: valentin.starke@abbott.com

J. Kumor
Abbvie, North Chicago, Illinois, United States of America
e-mail: Joseph.Kumor@abbvie.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_11,

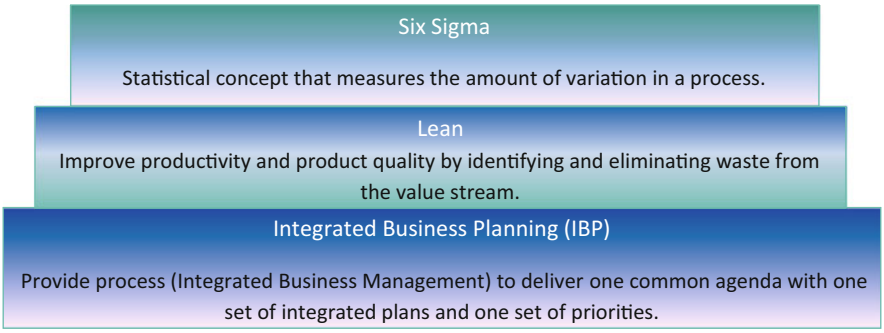


Fig. 11.1 Elements of Abbott's Business Excellence journey

program quickly led to significant improvement in terms of inventory levels and service levels.

When Abbott participated in various industry benchmarks in 2005, the data showed that manufacturing sites performed well in terms of customer service measures, but they had room to improve in productivity measures and unit price. During this time, Abbott's manufacturing sites embarked on a journey (Fig. 11.1) to build upon the Integrated Business Planning process by involving Lean Manufacturing and Six Sigma to reduce variability and non-value added work.

Between 2005 and 2011, the following programs were run independently:

- Become Effective: *Integrated Business Planning* helped provide one common agenda with one set of integrated plans and one set of priorities to continuously balance demand and supply.
- Become Efficient: *Lean* helped improve productivity and product quality by identifying and eliminating waste from the value stream.
- Become Consistent: *Six Sigma* helped measure and reduce process variation using methodical problem solving techniques and statistical tools.

Integrated Business Planning (IBP) had begun in commercial affiliates and was later expanded to manufacturing sites. A critical part of IBP was that commercial affiliates and manufacturing sites were expected to obtain an IBP Certification from Abbott's Business Excellence Team. This certification required renewal every 2 years and was the result of a successful on-site assessment of key business processes and performance indicators.

By 2011, many Abbott manufacturing sites had renewed the IBP certification at least twice. Other sites completed successful recertification through the assessment process with as many as six recertifications over a 10 year timeframe. This led to new questions from Abbott's manufacturing sites about next steps and the value of ongoing re-assessments on essentially the same set of principles and processes.

In parallel, some manufacturing sites had started to apply Lean Assessments which were not linked to IBP. Lean Assessments did not lead to certification but rather positioned manufacturing sites on a scale from less mature to more mature by measuring progress on the continuous improvement journey.

Fig. 11.2 Three dimensions of a holistic system

In this context, the next step of Abbott's quest for Business Excellence became the creation of a new assessment for manufacturing sites called "Business Excellence Standard" which would include multiple starting points: IBP for the integration aspects, Lean Manufacturing for the continuous improvement aspects, internal and external benchmarking, and industry trends as described at many of the global manufacturing, supply chain, and business excellence professional conferences.

The Design of Abbott's New Business Excellence Standard

In May 2011, a team of four Business Excellence Managers accepted the challenge to develop a business excellence prototype within 5 months, followed by 5 months for testing, piloting, and refining the standard. The final test was executed in March 2012 and resulted in the company's current Business Excellence Standard.

Early in the process, the team agreed on a set of six design principles against which every design decision could be compared:

Completeness: Includes criteria for all three dimensions of sustainable, holistic continuous improvement programs. These dimensions are People & Leadership, Processes and Tools (see Fig. 11.2).

Integration: Focuses on value stream, integrating customers and suppliers.

Standardization: Involves objective evaluation of progress per site, clear description of the standard for excellence for an Abbott manufacturing site.

Ambition: Reflects world-class level based on benchmarking with competitors and non-pharmaceutical industry leaders.

Flexibility: Allows discretion for differences in environment, business type and priorities.

Rigor: Measures the results of successful implementation of Business Excellence Standard with key performance indicators.

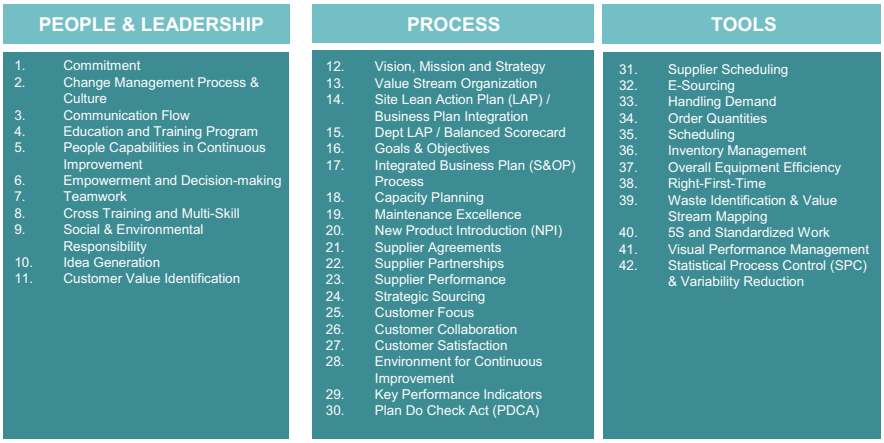


Fig. 11.3 Excellence criteria organized by holistic dimensions

Completeness and Integration

The roots of the new Business Excellence Standard were the existing Lean Assessments and the IBP Certification, each of which included a number of criteria. In addition, the team referenced many freely available assessments and literature to create a list of possible criteria against which the Business Excellence team could assess manufacturing sites.

The challenge was not obtaining a list of meaningful criteria but to limit it to those criteria which make the standard relevant without sacrificing the holistic view. After multiple iterations, the team defined a final set of 42 criteria (see Fig. 11.3).

To further emphasize integrated business management, supply chain integration and to effectively work with customers and suppliers, the same criteria were then re-organized into a framework of six categories: Organize, Plan, Source, Make, Deliver, and Improve (see Fig. 11.4).

In its very foundation, this framework acknowledges that business excellence in manufacturing sites is an end-to-end value stream competence and not only a site project. Manufacturing sites depend on the availability of accurate demand forecast and on a reliable, responsive supplier network.

Abbott's Business Excellence Standard drives continuous improvement in an integrated approach with the manufacturing sites as growth enablers.

Fig. 11.4 Excellence criteria re-organized by categories

Standardization and Ambition

Abbott's Business Excellence Standard describes four levels of maturity (as represented in Fig. 11.5) which are consistently used to perform the assessment of manufacturing sites.

Figure 11.6 describes an overall representation of how the Business Excellence Standard is visualized. As the site moves forward with its maturity journey, there is less focus on the manufacturing site and more strategic focus on the brand(s).

The Foundation and the Site Excellence levels emphasize improvements and integration between functions and value streams within the boundaries of the manufacturing site.

Foundation

- Evidence that there is stability within the operations
- Routine things happen routinely
- Improved labor and capacity utilization
- Continuous improvement focus

Site Excellence

- Evidence that performance excellence is not only within operations, but also within each support function in the plant (i.e. information technology, quality, human resources, finance, engineering, etc.)
- Strategy alignment within site and all the support functions
- Sustainable continuous improvement
- Improved decision making
- Reduced overhead costs and inventory

Fig. 11.5 Maturity journey

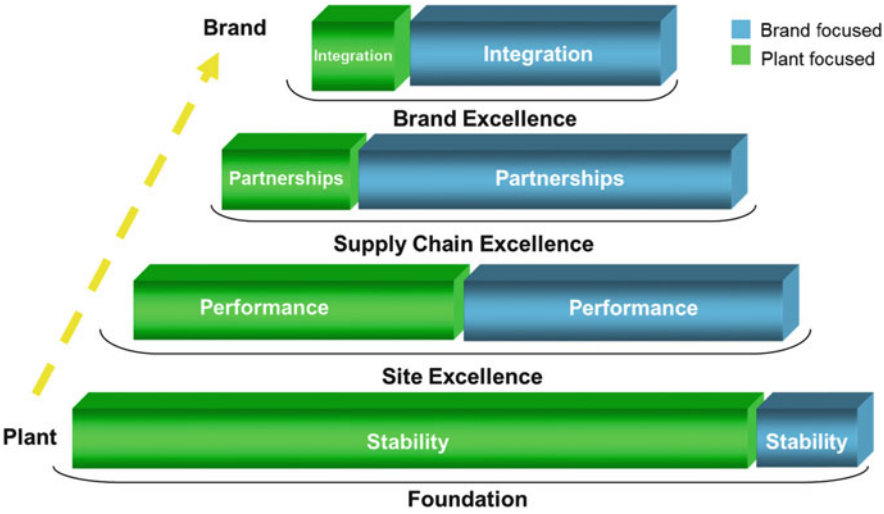


Fig. 11.6 Maturity journey towards brand focus

The Supply Chain Excellence and Brand Excellence levels emphasize win-win improvements and integration with partners outside the boundaries of the manufacturing site.

Supply Chain Excellence

- Focus on alignment of internal and external partnerships (i.e., internal manufacturing plant to manufacturing plant strategies are aligned, alignment of strategy with key third party manufacturers and suppliers, etc.)
- Improved flexibility, customer service, time to market
- Customer and supplier integration
- Robustness and reliability of the supply chain

5. DELIVER			FOUNDATIONS	SITE EXCELLENCE	SUPPLY CHAIN	BRAND
Function	Section	Item	Local processes and tools are in place and are being fully utilized. Pockets of excellence are observed	Local processes and tools are in place and are being fully utilized within the site. Highest expected level of results are achieved within the site.	Customers and Suppliers as well as division/corporate support groups become integral partners in the supply chain so decisions are made to improve the supply chain rather than individual nodes.	Completely harmonized operating platform, information shared widely across the network.
Supply Chain Planning Production	5.2	Customer Collaboration	☐ Roles and Responsibilities for the managing the customer relationship are defined.	☐ Communication and action plans have been identified with Internal/ external Customers in regards to improvements related to voice of customer concerns.	☐ Long-term mutually beneficial relationships with customers are being pursued to facilitate improvements in quality and cost.	☐ Customers actively participate in new product introduction meetings as a part of the value chain.
			☐ There is frequent information sharing with customers, including performance feedback.	☐ Collaborative planning is seen as a way of forming stronger strategic alliances with joint benefits, not only as a way of improving transactional effectiveness.	☐ Collaborative participation with customers exists in Kaizen and overall continuous improvement events.	
			☐ There is a process (agreed rules in place to manage changes to data) in place to ensure the two-way transfer of collaborative demand and supply data and other information between the organization and its customers.	☐ A formal strategy exists and some strategic partnerships exist with customers (e.g. distribution center) based on trust and long term plans which allow for predictability of demand and production leveling.	☐ A formal strategy and strategic partnerships exist with customers across the supply chain based on trust and long term plans which allow for predictability of demand and production leveling.	
			☐ Joint programs with customers are in place to identify and eliminate waste in the supply chain, using root-cause analysis and problem-solving tools.	☐ There is a formalized process to prevent reoccurrence of past due delivery issues.		

Fig. 11.7 Example of checklist criteria for the various level of maturity

Brand Excellence

- Brand strategy integration with all manufacturing sites, third party manufacturers, and suppliers
- Channel specific supply chain models
- Increase market share and improved margins
- Extended life cycle
- Transparency and trust throughout the value stream

For each of these maturity levels, the Business Excellence Standard provides detailed descriptions of what excellence means for the 42 criteria. Each criterion can be described in multiple sentences which can be rated individually during the assessment (Fig. 11.7).

This approach has several important advantages. First, it sets a standard for the manufacturing site and for the assessment team. A major drawback of many assessments is that they are heavy on vision but light on detail. This can introduce gage errors when assessment teams have different levels of experiences. In Abbott's Business Excellence Standard, there is a significantly reduced level of subjectivity for personal appreciation and gage errors.

Secondly, this level of detail provides an ambition level and a road map for the manufacturing sites. Because it is a shared ambition level for all the partners in the value stream, manufacturing sites can refer to it and demand compliance when needed.

	Section	Item	FOUNDATIONS	SITE EXCELLENCE	SUPPLY CHAIN	BRAND
1. ORGANIZE	1.1	Commitment	➔	➔	✘	✘
	1.2	Change Management Process & Culture	➔	➔	✘	✘
	1.3	Communication Flow	✓	✓	➔	✘
	1.4	Education and Training Program	➔	✘	✘	✘
	1.5	People Capabilities in Continuous Improvement	➔	➔	➔	✘
	1.6	Empowerment and Decision-making	✓	➔	✘	✘
	1.7	Teamwork	✓	➔	➔	✘
	1.8	Cross Training and Multi-Skill	✓	➔	✘	✘

Fig. 11.8 Example of scoring sheet summary

Assessments conducted previously applied a performance point rating system based on a numeric score from 0 (practices are required for this business, but they currently do not exist) to 5 (practices are excellent, fully effective, and exhibit internal best-in-class examples). The feedback of customers and manufacturing sites indicates there is essentially no difference on the rating when averaged between 3.5 and 3.6 from two distinctive participants on a 5 point scale.

This point scoring system was eliminated and replaced by a new system which standardizes the maturity assessment, maintains process transparency, and allows each manufacturing site to conduct self-assessments to visually see the current status towards the maturity journey. A green "check mark" in one of the sections means that all of the requirements are met with evidence of examples. A yellow "arrow" represents that at least one of the requirements in section is met. A red "x" represents no evidence of the practice exists in that specific category per the maturity level. It also provided the manufacturing sites a tool that they could use for internal discussions on specific practices in an effort to identify any potential gaps and improvement plans. The assessment sheet is programmed to automatically calculate the scoring once the box is checked. An example of a portion of the assessment sheet is shown in Fig. 11.8.

The overall objective of this program is to provide an improved roadmap on how to achieve higher levels of maturity and performance not only at the site level but for the overall supply chain.

Flexibility and Rigor

One cannot assume that all Business Excellence Standard categories and criteria are equally important at all times for all the company's manufacturing sites.

Key Performance Indicators (KPIs)	Definition
Supplier Performance	On-Time, In Full, No Quality Issues
Data Accuracy	Item Master, Bill of Materials, Routing, Inventory Accuracy, Supplier and Customer Master Data Accuracy
Days on hand	Inventory Levels Days On Hand
Internal Customer Service Level	Shipping Schedule Performance; On-Time In-Full
Master Production Schedule Conformance (weekly)	Manufacturing and Release Schedule Adherence
New Product Introduction Conformance	Milestone Adherence

Fig. 11.9 Key performance indicators included in the Business Excellence Standard

The local leadership must take into account the production type (e.g., continuous vs. batch), the environment (e.g., high-inflation vs. low-inflation, high vs. low regulatory complexity), the market (e.g., export vs. in-country-for-country) and the priorities (e.g., managing demand increase vs. reducing costs) to choose the best sequence of implementation for the continuous improvement program.

In some business cases, the site leadership may decide not to apply certain items of the Business Excellence Standard. The Business Excellence Standard allows for flexibility and it is sufficient to meet the expectations of 80 % of the line items to qualify for any given maturity level. On the other hand, the standard expects minimum performance improvements for Foundation and Site Excellence levels.

Figure 11.9 represents the minimum required Key Performance Indicators (KPIs) to be utilized at the manufacturing site. These KPIs serve two purposes. During an assessment, they are used for determining the maturity level. After an assessment, these KPIs will continue to be monitored to ensure they are meeting or exceeding established target levels.

If the KPIs show that the processes and behaviors of the Business Excellence Standard no longer deliver the desired results in a manufacturing site, then there will be a request to perform a re-assessment in order to determine the root-cause of the performance issues.

Change Management: Introducing a New Standard

Once the new Business Excellence Standards assessment criteria and tool was developed, more than 20 global senior leaders reviewed and approved it on concept. The business excellence team consulted an additional 22 internal global experts for

each of the subjects, including experts in customer service, manufacturing science and technology, distribution and logistics, supply chain, quality assurance, and demand management.

The next step was to pilot the new assessment with one of our European manufacturing sites. Upon completion, the Business Excellence Standard was updated to reflect the lessons learned and integrate the feedback of the site and the assessment team for improvements and modifications to the assessment criteria.

Only then, the updated program was launched with three new sites to be certified in 2012, two site certifications planned for 2013, and a number of additional re-certifications added to the strategic plan.

Standard for Executing Assessments

Like all other aspects of the Business Excellence Standard, the actual assessment process is standardized.

Manufacturing sites without prior Business Excellence Standard Certification will go through a process which prepares them for first time assessment. All other manufacturing sites go through on-demand re-assessments.

Preparing a Manufacturing Site for First Time Assessment

A typical manufacturing site with an existing Lean program will require approximately 12 months from kick-off to a successful assessment that achieves the minimum maturity level of Foundation. The average timeline for this process is represented in Fig. 11.10.

The *gap analysis* is initially performed by the manufacturing site and then validated with a global Business Excellence manager. The gap analysis will determine the scope of the Business Excellence Standard implementation and establish a rough timeline. It will also determine how many task teams the site should launch in order to close the gaps and implement a sustainability plan in the allocated time frame.

At *kick-off* the site leadership team, the program manager and representatives of the future task teams (*team formation*) will be trained in Business Excellence Standard processes and tools. For this purpose, the manufacturing site receives the most recent version of available good manufacturing practices. The use of these good practices significantly accelerates the implementation.

Change Management Training is provided as soon as the task teams have been nominated. All task team members, the program manager and the site leadership team participate in the training and become change agents for the rest of the organization. The change management training focuses on the theory behind change management, as well as hands-on practice creating the site's and team's

Fig. 11.10 High level planning for manufacturing site certifications (Note: M=Month)

"business case for change", developing stakeholder and communication plans, drafting action plans to close the assessment gaps (*process development*), and then successfully launching the program.

During the months following launch, the site gives periodic updates to the employees and Business Excellence network on current status of identified improvement opportunities as well as sharing current successes/benefits achieved. The global Business Excellence team gives direction on implementation, co-facilitates workshops, and performs up to two more visits before the assessment decision gate visit. This is the *Process Implementation* phase of the program.

During the *Assessment Decision Gate,* the manufacturing site and the global Business Excellence manager decide together to commit to the final assessment date. The decision depends on the progress towards gap closing and on the KPI performance.

Assessments

Assessments take 3 days and involve between two and four people who will visit the manufacturing site. The team generally consists of Business Excellence managers at the divisional level and from other manufacturing sites. Preparations begin 4–6 weeks before the final assessment.

Before the final assessment: To emphasize sharing and learning versus auditing, the Business Excellence Standard is reviewed well before the actual assessment with the manufacturing site team and with a divisional Business Excellence manager. The review includes finalizing an interview matrix which indicates who will be interviewed for each of the 42 criteria and which criteria will be discussed during the interviews. An example of the interview matrix is shown in Fig. 11.11.

The interview matrix emphasizes integration by requesting information on criteria which are often outside the person's day-to-day job responsibilities. During the preparation, current KPI performance is also reviewed with the manufacturing site team and the division Business Excellence manager.

	Count of Interviews	Plant Manager	Business Excellence Manager	Supply Chain Manager	Purchasing Manager	Engineering Manager	Production Manager	Quality Manager	HR Manager
Count of Questions:		10	11	11	8	10	10	10	9
Commitment	5	x	x					x	x
Change Management Process & Culture	4		x						x
Communication Flow	3					x			x
Education and Training Program	3							x	x
People Capabilities in Continuous Improvement	3		x				x		
Empowerment and Decision-making	4								x
Teamwork	3						x	x	
Cross Training and Multi-Skill	3								x
Value Stream Organization	3	x		x			x		

Fig. 11.11 Interview matrix example

During the assessment: Assessments work best when both teams (the assessment team and the assessed manufacturing site) envision the Business Excellence Standard as a learning opportunity.

For this reason, Business Excellence Standard assessments are typically completed with at least one Business Excellence Manager from another manufacturing site. This assessment team member will be able to learn and share good practices and benefits from his/her point of view and expertise based on holding the same job in another manufacturing site of the network.

Assessment teams assure that final reports are balanced and include good practices from the assessed site. In addition, good practices from other sites are shared. The final report out is delivered to the site leadership team and the task teams on Day 3 of the assessment. At this time, the report out includes the following information:

- Key Quotes/messages captured through interviews – see Fig. 11.12
- Good Practices Identified (including photos) – see Fig. 11.12
- Current Gaps and improvement opportunities (including the top five recommendations for improvement) as identified from the assessment
- Good Practices from other sites – see Fig. 11.13
- Maturity level indication

Because the entire assessment is interview and observation based, the majority of the work rests with the assessment team and not with the manufacturing site.

After the assessment: Upon completion of the site assessment, a confidential survey is sent by the division Business Excellence manager to the site leadership team and task teams to receive feedback regarding strengths and areas of improvement for the assessment program, the overall assessment process, as well as performance feedback regarding the team members who were involved in completing the assessment. Applicable feedback is then used to update/modify the assessment program on a continuous improvement basis, and feedback is given to team members for their continued learning and growth. Both elements are used to build a robust and integrated Business Maturity Model to continue to strengthen the program.

Good follow-up is critical to understand which of the recommendations the manufacturing site chooses to implement and if the site requests support from other manufacturing sites or from the global Business Excellence team. This is completed with follow-up conference calls and relevant future site support visits.

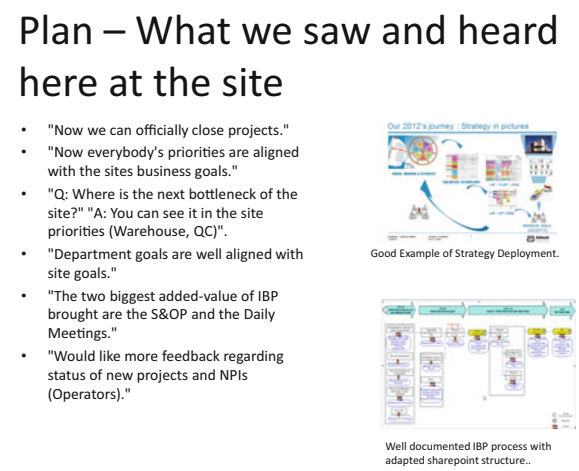


Fig. 11.12 Site example of key quotes and best practices

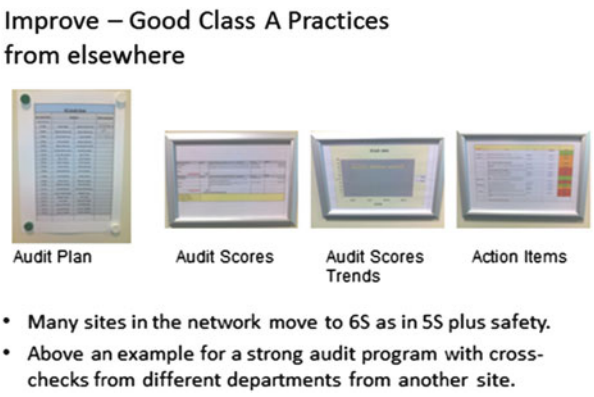


Fig. 11.13 Example of good practice shared from other sites

Steps Toward an End-to-End View

The Business Excellence Standard discussed in this article is a manufacturing site centric assessment. Commercial affiliates and planning centers use separate assessments due to differences in business needs. Third party manufacturers, however, are currently not assessed against a Business Excellence Standard. With the Foundation and Site Excellence levels of the Abbott Business Excellence maturity model, the emphasis is on vertical integration within the boundaries of the manufacturing site (see Fig. 11.14). With the Supply Chain Excellence and Brand Excellence levels of the maturity model, the emphasis is on horizontal integration with partners outside the boundaries of the manufacturing site (see Fig. 11.15). The planning center and the suppliers for the

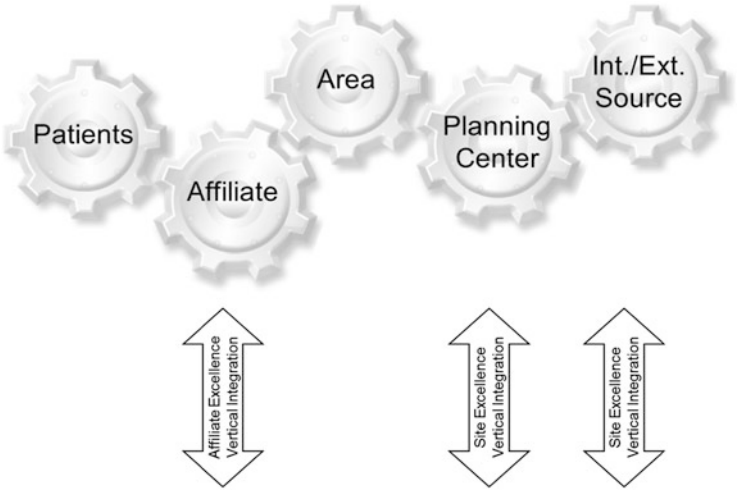


Fig. 11.14 Program emphasizing vertical integration on site level

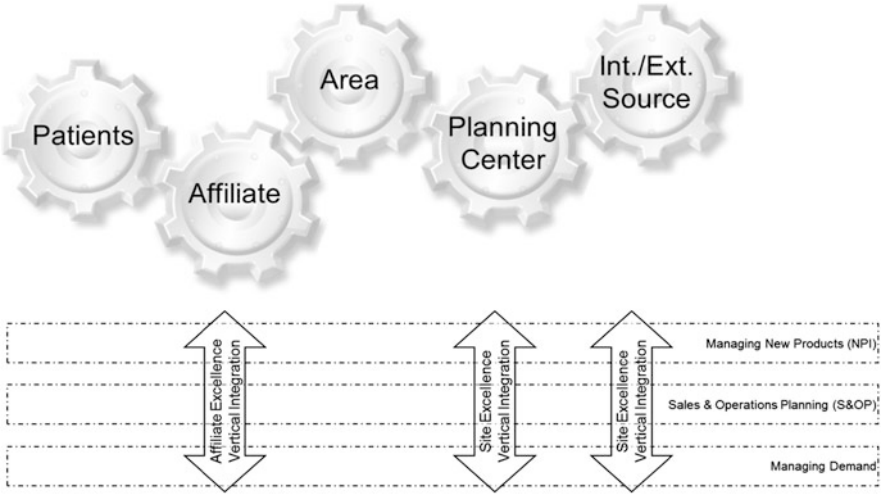


Fig. 11.15 Program emphasizing horizontal integration between partners in the value stream

manufacturing site are important partners which balance demand from the commercial affiliates with supply from the manufacturing sites and third party manufacturers.

This leads to an important question: "If every partner in the value stream worked according to Business Excellence Standards, vertically integrated and individually showing Site Excellence Performance Level performances, would this mean that the entire value stream would automatically reach the same performance levels?"

Abbott's experience has shown that bringing the partners in the value stream to the same Foundation Level is a necessary condition for sustained end-to-end performance of the value stream. It is, however, not a sufficient condition.

To reach sustained end-to-end performance, which can be experienced on a daily basis by our customers, Abbott has overlaid the existing assessments with "Integration Touch Points" to ensure that each assessment connects seamlessly into the others, reinforcing the horizontal integration between the partners in the value stream as represented in Fig. 11.15.

The mission critical processes to be integrated are:

- Managing New Product Introduction (NPI): The ability to quickly develop, register, manufacture and market incremental innovations. This requires a sustainable NPI process integrated with the Sales & Operations Planning (S&OP) processes to provide timely status updates, manage priorities and resources. This ensures that all changes to products are handled effectively and consistently.
- Sales & Operations Planning: This monthly S&OP balances supply and demand and helps to anticipate and address business challenges. This requires an S&OP process designed to focus management attention on the big picture and on what has changed since the previous month. S&OP includes new products, commercial (demand) and operations (supply).
- Managing demand: Being able to plan and forecast accurately is key to offering excellent customer service to all of our customers across the world. This requires establishing a sustainable process for updating forecasts each month, covering a 24–36 month rolling horizon to maintain a complete and accurate statement of demand.

For each of the processes, Abbott's Business Excellence team has created quick launch kits which can be deployed with little or no adaptation by every partner in the value stream. Using the same standards has helped drive compliance, integration, and end-to-end performance.

The standards are based on global policies as well as good practices identified over the years in affiliates, the supply chain organization and, as seen above, in manufacturing sites.

Each of the three processes can have both policies and good practices. In the case of Sales and Operations Planning (S&OP), a policy is used for establishing a global planning calendar which makes sure that the division S&OP process can be executed with information from all affiliates and all manufacturing sites. Good practices are used to improve the actual process which culminates in an effective S&OP meeting at local management level.

Summary

Abbott's Pharmaceuticals maturity journey of Business Excellence Standards has been evolving to give us the opportunity to drive the IBP, Lean, and Six Sigma programs to a new and improved level going into the twenty-first century. This has been accomplished through our Business Excellence Standards program that incorporates our senior leader's vision, support organization's input, current industry trends, good practices, knowledge sharing, and lessons learned in all of our

organizations. The program has been developed to define the specific aspects of what is important to our business and give our sites and support organizations a clearer roadmap to drive our leadership/people, processes, and tools from current foundation/site excellence to a journey of supply chain and brand excellence. Benefits of the program include:

- Alignment and consistency of programs and processes
- Reduction in working capital
- Agile IBP process that can supplement demand at a shorter notice
- More flexibility in the site's capability to deliver NPIs and quicker turn-around time
- Improved coordination, communications, and expectations from customers and stakeholders

In the case of Abbott's Business Excellence Standards, it is clear that continuous improvement is indeed a journey. With every iteration, with every certification and re-certification, the knowledge in the network increases and find its way back into the Business Excellence Standards.

Chapter 12
Structuring and Implementing an Operational Excellence Program from Scratch in the Biotech Industry

Wright Troy

Introduction to Amgen

Amgen discovers, develops, manufactures, and delivers innovative human therapeutics. A leader in biotechnology since 1980, Amgen was one of the first companies to realize the new science's promise by bringing safe, effective medicines from lab, to manufacturing plant, to patient. Amgen therapeutics have changed the practice of medicine, helping millions of people around the world in the fight against cancer, kidney disease, rheumatoid arthritis, bone disease, and other serious illnesses.

Amgen pioneered the development of novel products based on advances in recombinant DNA and molecular biology, and launched the biotechnology industry's first blockbuster medicines. Today, as a *Fortune 500* company serving millions of patients, Amgen continues to be an entrepreneurial, science-driven enterprise dedicated to helping people fight serious illness.

At Amgen, one of the many important ways we fulfill our mission to serve patients is by producing vital medicines in sufficient quantity to meet patient demand, while following good manufacturing practices to ensure that our products meet our high standards for safety and potency.

Manufacturing biotechnological medicines is a highly specialized activity, and Amgen is a leader in the field. The company's state-of-the-art biotechnology manufacturing and process development capabilities help us to realize the potential of our pipeline for patients around the world.

Scalable, flexible, and committed to safety and reliability, our capabilities in process development, manufacturing, quality, and supply chain management are continually growing. Amgen is continually monitoring capabilities in those areas to meet future needs.

W. Troy (✉)
Amgen, Longmont, Colorado, USA
e-mail: troy@amgen.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_12, © Springer-Verlag Berlin Heidelberg 2013

Pioneering Biotechnology Manufacturing

Manufacturing therapies based on proteins found in the human body is a complex process. In the biotechnology industry, therapeutics are manufactured using living organisms that contain the genetic code for the specific molecule being produced. Precisely controlling the manufacturing process and environment is necessary to obtain consistent results and to ensure efficacy and safety.

As one of the industry's original innovators, Amgen has extensive knowledge and first-hand expertise in clinical and commercial manufacturing of biotechnology-based medicines. We have an outstanding track record of regulatory compliance, thanks to stringent controls and a superior quality system. We have world-class capabilities in process development and continually innovate newer and more efficient ways to produce therapies using biotechnology. Most importantly, we have a track record of safely and reliably delivering medicines to patients who need them.

Amgen Operations Locations

California

Amgen has long had protein manufacturing capabilities at our Thousand Oaks headquarters. The site has a proud history as Amgen's first manufacturing location. Going forward, Thousand Oaks will increasingly focus on clinical operations.

Colorado

Amgen has two manufacturing facilities near Boulder, Colorado: Longmont and LakeCentre. Longmont is responsible for bulk manufacture of EPOGEN® (Epoetin alfa). LakeCentre manufactures XGEVA®/Prolia® (denosumab) and Nplate® (romiplostim).

Puerto Rico

Amgen has developed a state-of-the-art biotechnology campus for bulk manufacturing in Juncos, Puerto Rico, with biologics manufacturing capability, expanded full-testing quality analytical labs, formulation, fill, and finish capability, warehouses, process development facilities, administrative and training buildings, a cafeteria and a child care center. Amgen Puerto Rico's bulk manufacturing facility

produces a variety of medicines available to patients today, including NEUPOGEN® (Filgrastim), Neulasta® (pegfilgrastim), and Aranesp® (darbepoetin alfa).

Rhode Island

Amgen's facility in West Greenwich, Rhode Island, manufactures Enbrel® (etanercept) in bulk substance form. The first Amgen plant in West Greenwich received FDA approval in December 2002, and a new plant received FDA approval in September 2005. The new plant houses one of the world's largest mammalian protein manufacturing facilities as well as administrative, utilities, and quality analytical laboratory buildings.

Kentucky

Ensuring that Amgen medicines rapidly, reliably, and safely reach patients in hospitals, clinics, and doctors' offices is a critical part of the company's operations. Amgen's distribution center in Louisville, Kentucky, plays a key role in meeting that objective. The company's manufacturing facilities ship finished products to the center, which complies with the most stringent and protective handling and storage requirements. As soon as orders arrive, the Kentucky staff quickly loads and ships them where they are needed.

Breda, The Netherlands

Amgen Breda, the company's European distribution center, is located in The Netherlands between the ports of Rotterdam and Antwerp and close to airports in The Netherlands, Belgium, and Germany. The site houses commercial operations that assemble devices, label, package, and distribute product to Europe, North Africa, and the Middle East.

Dun Laoghaire, Ireland

The Amgen facility in Dun Laoghaire was purchased from Pfizer in May 2011. It is a world-class, 37,000 square-meter aseptic operations manufacturing facility with freeze dry product and liquid vial filling operations. The site also includes laboratories, a warehouse, packaging capabilities, and a bioprocessing suite.

The Dun Laoghaire site will build on the capabilities of other Amgen global manufacturing sites, helping to ensure continuity of supply of our medicines. Amgen will develop the capability to produce all of its medicines here and expects to expand the site's manufacturing capabilities over time.

Strategic Intent of Operational Excellence Program

Amgen Operations launched an Operational Excellence program in 2007. Figure 12.1 summarizes how the focus of the program has evolved over time.

To date, the program has progressed through four distinct phases. These phases are:

Launch With Cost Reduction Imperative

Initial focus of the program was on reducing operating costs. Industrial Engineers defined the Amgen Process Excellence methodology for process improvement. A large number of leaders and staff were trained on continuous improvement tools and methods.

Developing Infrastructure and Planting Seeds of Change

The infrastructure for the Operational Excellence program was developed through the implementation of corporate projects that were focused on addressing current needs.

Stabilization

The best practices from pilots that had been conducted at sites were integrated into the Manufacturing Lean Transformation. A formal Lean Six Sigma certification program was launched and provided to sites and functions based on demand.

Transformation

Plants progress along the Lean Transformation Roadmap towards the end goal of achieving fully integrated product value streams. The program is beginning to expand into other parts of Amgen beyond Operations.

The focus of the program will continue to evolve in order to maintain alignment with Operations strategy and future direction. The program is currently focused on enabling the following elements of the strategy:

- Drive High Reliability Performance
- Learn from success and failures to eliminate repeat errors
- Optimize cycle times and inventories
- Increase reciprocity in Knowledge Management

Launch with Cost Reduction Imperative

The OE program was launched at a time when the organization was focused on reducing operating costs in response to changes in the business. The program was structured to provide the framework to drive year over year performance

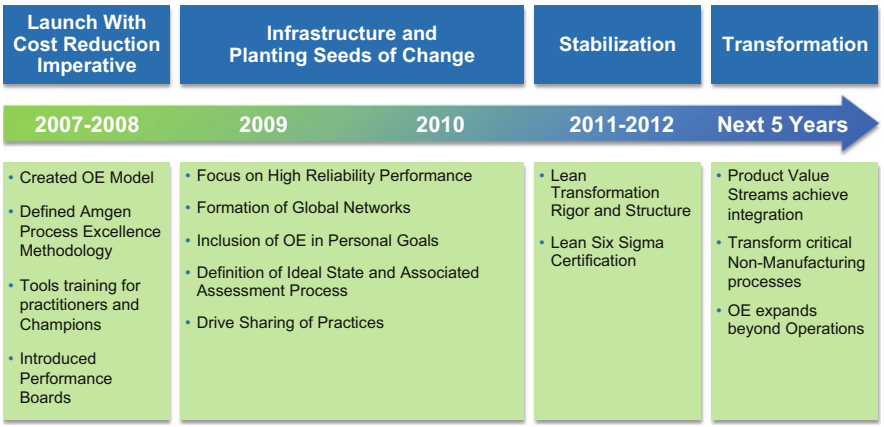


Fig. 12.1 Phases of Operational Excellence program evolution

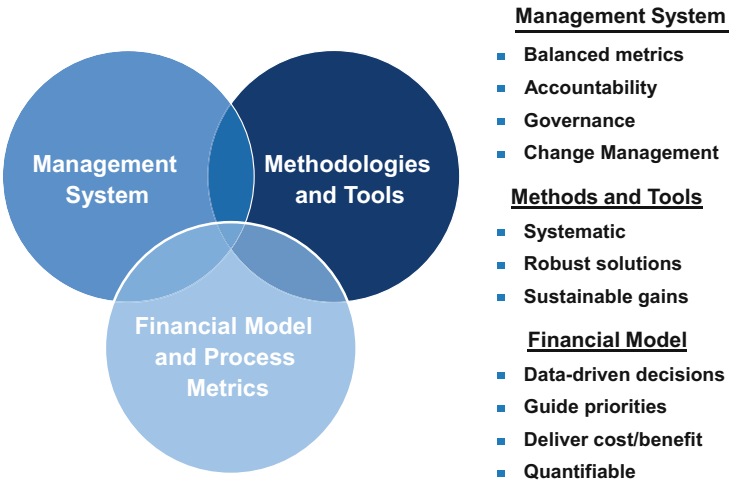


Fig. 12.2 Operational Excellence Model

improvement in alignment with Operations strategy. A simple Operational Excellence Model was developed to drive action and improvements in metrics over time were used to measure progress (Fig. 12.2).

A process improvement methodology was developed and provided to practitioners. The methodology is called Amgen Process Excellence and is based on the best of standard methodologies while recognizing Amgen's need to remain innovative and nimble. It is a phased approach to improving overall process performance (Fig. 12.3).

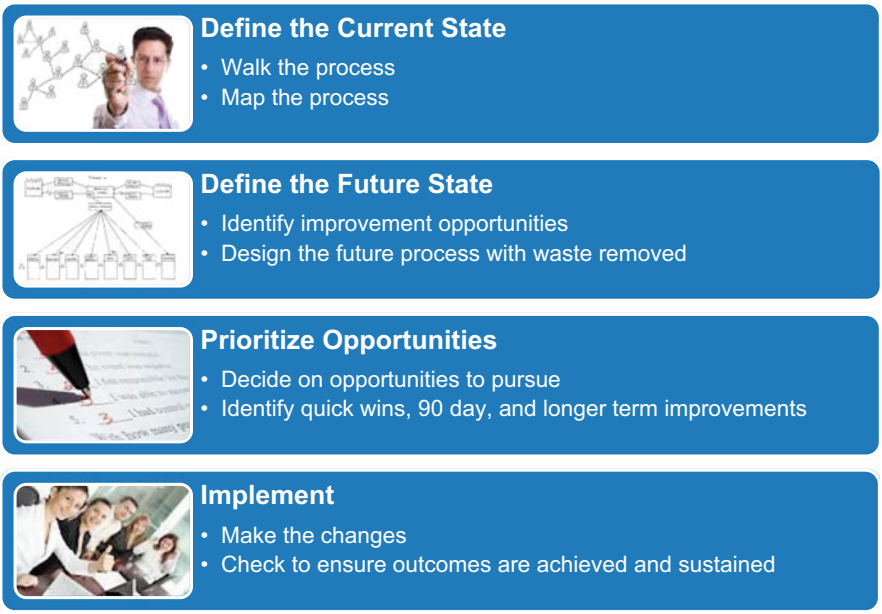


Fig. 12.3 Amgen Process Excellence process phases

Instruction on the process was included as part of a larger Operational Excellence Boot Camp training. This was a one week course that introduced practitioners to the tools needed for each phase of the process. The training was conducted by site Industrial Engineering organizations with support from a corporate Industrial Engineering organization. Leadership received a half day version of the training.

Organizational Structure

During this phase, there was a small centralized organization that developed and owned the Operational Excellence Program. This organization chaired the Operational Excellence Core Team that included a representative from each site. These site representatives gave input on the development of the program and provided monthly performance metrics.

Sites were at various stages of developing their OE Professional and Practitioner capabilities. Some sites had been working on developing Industrial Engineering capabilities for several years while others had not yet started. Some were regularly conducting OE Boot Camp trainings for staff while others were conducting them at a much lower frequency.

Outcomes

During this phase, the foundation for Operational Excellence was established and strengthened. Key outcomes for this phase included the following:

Tools and Methods

A large population of staff was introduced to continuous improvement tools and methods. They used what they learned to identify "low hanging fruit" and make associated improvements.

First steps were taken to introduce the organization to visual management. This was accomplished by broadly introducing Performance Boards across the organization.

Awareness

Staff became aware that the business was changing and that they were going to be involved in making the necessary changes. They were not only expected to do their job, but also to improve how they did their job in order to get better results.

Results

Business results improved during this phase. The most notable improvements associated with the Operational Excellence program were in the area of economic performance.

Lessons Learned

Several lessons that were learned during this phase were used to guide the further development of the Operational Excellence program in later phases. Key lessons learned included the following:

OE Seen as Cost Cutting

Because the Operational Excellence program was launched during a time when the organization was focused on reducing costs, some staff viewed operational excellence as the implementation of projects focused on cost cutting.

Early on, this may have had an impact on the rate of adoption. Over time, it has been clarified that Operational Excellence is a mindset in day-to-day operations to continuously improve in order to deliver better results. This is important because improved results are necessary to enable the strategy and to better serve patients.

Middle Management Engagement

There were pockets of middle management that were slow to embrace the program as a way to improve their organizations performance and to make life better. Even though there was broad acceptance and support for Operational Excellence at the executive level, the organization was figuring out how to translate this into action. Boot Camp training provided guidance and a call to

action for Practitioners at all levels of the organization. Middle Management relied on receiving a similar call to action and guidance from line management. This messaging was variable both across and within sites and functions.

Tools

Tools were broadly rolled out to a large number of staff. Although there was an expectation that staff should have a project when attending Boot Camp, this wasn't always the case. As a result, staff attended training and did not always convert what was learned into actions that led to the creation of value.

Infrastructure and Planting Seeds of Change

In 2009, the program transitioned into a phase where infrastructure started to be added to the foundation. This infrastructure was developed through corporate led project based initiatives aimed at improving performance.

One such initiative focused on improving reliability. To be reliable is to deliver an outcome in a predictable and expected manner. To be highly reliable is to not only deliver a desired outcome consistently but also have robust systems that provide greater assurance of repeatability. The initiative created a system of systems that have interdependencies that must be well understood and connected to ensure high reliability. The system connects equipment and operator performance on the floor with their foundational requirements and ensures reliability through effective response to variations in performance. Elements of the system include the following:

Defense in Depth

Defense in Depth outlines the integrated application of three equally rigorous and significant layers of defense: equipment, procedures and well-trained staff. Successful implementation of these linked concepts ensures robust and comprehensive design, control and understanding of critical process and operating parameters.

Standard Root Cause Analysis

Standard Root Cause Analysis establishes a standardized process with a consistent set of tools and guidance for conducting root cause analysis. The process ensures appropriate rigor is applied to identify and address immediate causal factors and their underlying root causes.

Purposeful Presence

Purposeful Presence is designed to help front-line managers and their staff to be successful by removing barriers, responding to feedback, fixing problems and ensuring equipment and systems are working reliably. It is through active presence on the floor that staff become more engaged and interested in their work because the manager acknowledges and recognizes the work's importance and complexity.

Knowledge Management

Knowledge Management is dedicated to getting the right knowledge to the right people at the right time. It helps people share and capture knowledge and act on what they have learned to improve organizational performance.

Organizational Design and Capabilities

Organizational Design and Capabilities guides organizations in translating business strategy into key capabilities and success factors to help them reach a desired future state and achieve their strategy. It defines key processes, critical roles, and provides a method to complete a skills gap assessment and create mitigation plans.

Identify, Track and Control Variation (ITCV)

ITCV establishes processes and roles to identify and monitor critical attributes across raw materials, manufacturing processes, finished goods and complaints and to take action when appropriate.

Another action that was taken during this phase was to create a common vision of an ideal state Operational Excellence culture. This was done by developing a framework that consists of seven dimensions with each dimension having multiple supporting elements. The seven dimensions are shown in Table 12.1.

A process was developed that allowed a team to assess where a site or function is at in terms of progressing towards the ideal state. Additional outputs of the assessment included identifying best practices that should be shared with the rest of the network as well as feedback on what to focus on in order to improve prior to the next assessment. The team conducting the assessment consisted of members from the corporate group, other sites and functions, and the organization being assessed. Every site and function received a baseline assessment during this phase.

During this phase, the decision was made to formalize Global Networks. A Global Network is a multi-site/cross-functional team that monitors the health and drives improvement of a business process through collaboration and knowledge sharing. The Global Networks take actions to improve performance in alignment with Operations strategy. Formal lifecycle management of the networks is facilitated by the Global Network Office. This includes annually assessing the maturity of each network against clearly defined criteria. The scoring framework that is used is summarized in Table 12.2.

With the creation of Global Networks came a renewed emphasis on sharing practices across the organization. Initial emphasis was placed on having individuals enter practices that had proven to add value into a database that was regularly reviewed by Global Network Leaders. The Network Leader would review select practices with the rest of the Network to ensure there was proper awareness and that applicable practices were being adopted by other sites or functions. Over time, this practice changed to including success stories in an enhanced knowledge management repository. This allowed a broader population to learn from the successes of others.

One of the networks that formed was the Operational Excellence Global Network. This network took action to develop a lean transformation roadmap for the

Table 12.1 Operational Excellence culture ideal state

Dimension	Examples of supporting elements
Leadership behaviors	Leaders model behaviors that support culture of Operational Excellence
	Leaders actively engaged in problem solving and efforts to improve performance
Continuous improvement	Staff have the mindset that processes can and should be improved
	Improvement ideas flow seamlessly through evaluation and implementation
Systems thinking	Customers and suppliers are involved in continuous improvement
	Staff understand how their work is part of a larger process
Problem solving	Staff appropriately match tools and methods with the complexity of the problem
	Counter measures effectively address root causes
OE principles	Visual controls exist that clearly indicate current status and the proper condition
	There is a clear understanding of value and waste
Goal alignment	Staff know the organization's strategy and what they need to do to support it
	Site, plant, functional, and individual goals are all aligned
Metrics and results	Metrics drive the right behaviors
	Metrics have performance targets that support the organization achieving its goals

Table 12.2 Global network maturity assessment scoring

Score	Criteria
Informal	Sponsor and Global Network Leader are identified
	Business case for having the network has been approved
Forming	Additional members and stakeholders are identified
	Roles and responsibilities have been defined
Formal	Members are engaging on a more regular basis
	Network has defined operating norms and formalized processes
Effective	Members engage on a regular basis
	Network is established and adding value on a regular basis
Best in class	Network is demonstrating optimal value

plants to follow with the intent of creating fully integrated product value streams. At this point in time, the NEUPOGEN® and Neulasta® plant in Puerto Rico was focused on implementing lean principles. This plant and the network partnered together to create the roadmap. This strong partnership continues to this day and, as shown later, was critical to creating the necessary rigor and structure around the manufacturing lean transformation program.

Organizational Structure

During this phase, the decision was made to reorganize the centralized organization. This resulted in the Global Network Lead responsibilities being added to one of the Directors responsible for Operational Excellence at a site. Also, the roles and responsibilities of the OE Core Team were modified to align with the standard that was established for all Global Networks.

Sites continued to improve their OE Professional and Practitioner capabilities. Some of the sites that had been lagging in terms of OE Professional capacity made significant progress during this phase by hiring staff with the right skill set.

Outcomes

During this phase, the Operational Excellence Global Network and the organization partnered to create a significant amount of the programs infrastructure. This was done by piloting different improvement methods in parts of the business where they were appropriate for solving specific problems and driving improvement. The key outcomes for this phase include the following:

Tools and Methods

At the beginning of the phase, improvement methodologies were almost competing against one another. Time was spent discussing theory and pontificating on why one method or tool should become the standard over another. By the end of the phase, there was a better understanding of which methods should be used in certain situations.

Awareness

Operational Excellence awareness significantly increased. By the end of this phase, over 3,000 staff members had received some sort of formal training focused on the use of methods and tools. The OE Assessments also contributed to this awareness. All sites and functions received at least one assessment. This meant a significant number of staff at all levels within the organization had been involved in discussions with OE Professionals about ideal state culture and how their site or function measured up to it. Another factor that contributed to this increase in awareness was the publishing of Operations wide articles on improvements that were made.

Results

Cultures at the sites and within the functions started to progress towards the ideal state. The amount and rate of change that was seen varied. The following factors contributed to this variance:

- All sites and functions were starting at different points
- Leaders had varying degrees of experience with Operational Excellence

- Amount of effort put into driving cultural change depended on overall workload for each site and function
- Variance in experience and capabilities of OE Professionals that supported the sites and functions

High Reliability Performance significantly reduced operating risks and had a positive impact on quality, economics, and supply reliability.

Global Networks started sharing practices and solving problems across the network versus each site and function determining unique solutions to the same problem.

Lessons Learned

Conducting pilots based on business needs was a great way to develop and prove methodologies while ensuring continuous alignment with what the business needed. The approach allowed for innovation and exposure to new approaches that would not have been ratified by the whole organization at that point in time. Networks helped to share and implement the practices that worked best.

There can never be enough communication and change management in terms of how an Operational Excellence program will enable better outcomes that are necessary to achieve the strategy. Early on in the development of a program, it is typical to have a heavy focus on tools and developing staff capability. This makes it easy for staff to confuse Operational Excellence as being the use of specific tools versus as improving behaviors and performance in order to achieve better outcomes and results. This can lead to a disconnect between different levels in the organization and result in middle management being slow to engage and adopt the program.

Broad training on tools alone will most likely not have the intended impact on performance. A more focused, just-in-time training approach that provides knowledge and coaching at the point-of-use may be more effective in impacting performance.

Stabilization

After investing in the creation of the program infrastructure, it was important to ensure it was sustained and further developed over time. To this end, the decision was made to invest in a small, centralized organization under the leadership of the Vice President of Operations Performance Excellence. This new organization was responsible for developing and owning the programs necessary to accomplish the following:

- Accelerate Lean Transformation
- Promote collaboration and instill network thinking
- Champion being a Learning Organization
- Drive error reduction
- Improve human performance
- Influence culture & behavior

Based on these responsibilities, it was decided that the Operational Excellence Global Network Leader role become a full-time position reporting into this organization. A small, centralized Operational Excellence organization reports into the Network Leader and supports the development and execution of the overall program. This team has Industrial Engineering capabilities and supports improvements of both manufacturing and non-manufacturing processes.

Other groups that joined the Operations Performance Excellence organization included Learning and Performance, Knowledge Management, and Business Performance and Analytics. Creating this new organization was a critical move that allowed Operations to experience an accelerated rate of progress during this phase. This is because the organization created a healthy tension to improve while, at the same time, providing the programs that were known to enable the necessary improvements.

This phase of the program focused on stabilizing the infrastructure to prepare for further and sustainable transformation of the business. This was done by formalizing the Operational Excellence Principles that the pilots had been based on as well as providing a meaningful sequencing for the transformation. This included defining key performance measures that would be used to gauge progress along the way as well as defining the required practices that were known to enable the necessary performance.

The Operational Excellence Global Network defined the principles. These principles were the basis for the pilots that had been conducted to date in different parts of the organization. They had been validated by actual improvements in performance over this time period. This was important because it meant that, rather than being based on theory, the principles were based on the actual experiences of the organization. The principles are summarized in Table 12.3.

Another action that was taken was to simplify expectations for plants associated with Operational Excellence. The risk was that the organization would be confused by the different methods that were being used to improve performance, view the program as being unnecessarily complex, and disengage. The counter measure to this was to take the best from all of the pilots and combine them into a single approach to drive improvement. This approach was branded as the Manufacturing Lean Transformation.

The goal of the Manufacturing Lean Transformation is for product value streams to achieve an integrated state. A value stream in an integrated state is defined by the following characteristics:

- Product is consistently supplied in adherence to the supply plan
- Waste is continuously reduced

Table 12.3 Operational Excellence Principles

Principle	Definition
Take personal responsibility to work in a safe manner and ensure colleagues do the same	Know the hazards associated with your work and demonstrate safe behavior
	Operate and maintain facilities to prevent injuries and incidents
Embrace continuous improvement	Leaders are champions for continuous improvement
	Leaders are purposefully present in the work area
	Establish performance measures and targets to drive improvements
	Participate in regular reviews of performance, generate improvement ideas, and take action
	Develop a deep ownership and understanding of one's work area
Find root causes of problems and take appropriate actions to prevent recurrence	Use visual management so no problems are hidden
	Build a culture of finding the root cause
	Increase right first time performance by designing quality into all products and services
Perform right the first time	Design and maintain equipment to reliably produce the product
	Provide people with the best instructions and training to perform reliably
	Retain key talent in critical job roles
Apply appropriate tools to reduce waste and remove variability in processes	Know the value stream for the product or service you are providing to your customers
	Remove non-value added activities to improve operational efficiency
Become a high performing organization through a commitment to learning	Learn from successes and failures and share knowledge across the network
	Become the expert of your area or process
	Take initiative to capture knowledge so others can benefit
Understand the cost structures and take action to address variances	Use actual results to identify waste, reduce variation, and improve productivity

- Able to operate with reduced inventory
- Collaboration with suppliers and customers in the value stream occurs and benefits are shared with them

At the core of the Manufacturing Lean Transformation is the roadmap that had been developed in an earlier phase. The roadmap consists of four interdependent phases. Each phase focuses on creating specific capabilities. Elements of High Reliability Performance were added to this core to create the holistic approach that is necessary for Operations to achieve its long term strategy. The Manufacturing Lean Transformation Roadmap is shown in Fig. 12.4.

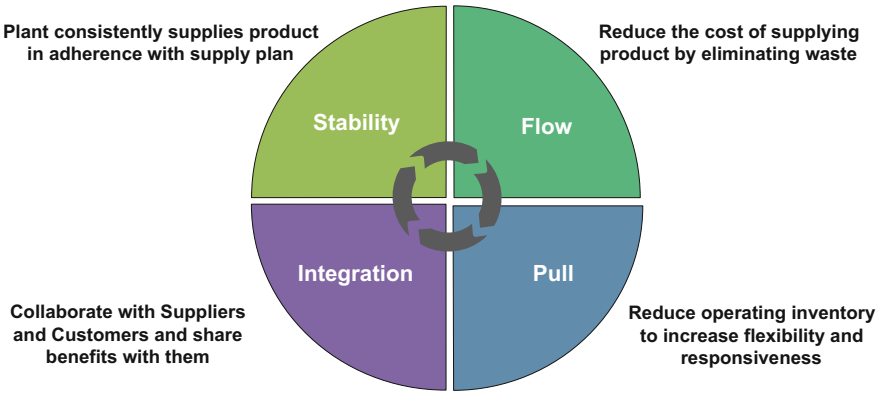


Fig. 12.4 Manufacturing lean transformation roadmap

The arrows in the center of Fig. 12.4 depict the fact that a plant can move between phases of the transformation. For example, a plant that has attained the standard for Pull may need to re-establish Stability if its product mix changes. The different phases of the transformation are defined as follows:

Stability

A plant is considered Stable when it consistently supplies product in adherence with the supply plan. This is achieved by reducing performance variance in manpower, machines, materials, and methods.

Flow

A plant has achieved Flow when it is capable of reducing the cost of supplying products. This is achieved by continuously removing waste from the process.

Pull

A value stream has achieved Pull when operating inventory is reduced to increase flexibility and responsiveness. This is achieved by producing only on receipt of a signal from the customer.

Integration

A value stream has achieved integration when there is collaboration with suppliers and customers and benefits from improvements are shared with them.

The rigor and structure of the program is documented in a playbook that contains the following elements for each of the four phases:

- Performance results necessary to complete the phase
- Practices that must be implemented
- Examples from across the network of what a good implementation of each practice looks like
- Process used to assess the plant against the standard

The playbook provides meaningful sequencing for the implementation of the required practices. The practices in a phase are meant to be implemented as a

Table 12.4 Examples of required performance for stability and flow

Measure	Definition
Supply plan	Hourly schedule consistently met
	Supply plan is consistently met
Non-Conformances (NCs)	NCs per lot consistently being reduced
Disposition	Cycle time is reduced
Safety	Recordable injury rate improves
Economics	Cost is removed from the operation

Table 12.5 Examples of required practices for stability and flow

Practice	Definition
Visual management	Use to communicate status and performance
Purposeful presence	Leaders regularly spend time on the floor
Work center teams	Areas are cross functionally managed as a plant within a plant
Problem solving	Standard methods are used to identify root causes and reduce performance variability
Learning organization	Knowledge is effectively shared across shifts and plants
	Learning groups are established and effective
Replenishment	Consumables and raw materials are replenished based on usage
Standard work	Standard Work exists for appropriate tasks
Event response	Immediate cross-functional management attention on the floor when a significant event occurs
Error proofing	Reduce errors through human performance and engineering controls
Metrics	Clear cascade of metrics from shop floor to site dashboard

system that is used to attain the required performance results. In this way, the practices have been directly linked to the results they enable.

The content of the playbook was created by a team consisting of the Corporate Operational Excellence group, the Operational Excellence Global Network, the Manufacturing Leadership Team, and the NEUPOGEN® and Neulasta® plant in Puerto Rico. The Manufacturing Leadership Teams membership includes all plant managers and their key business partners.

Examples of results that are assessed to determine if a plant has attained Stability or Flow can be found in Table 12.4

Examples of practices that are assessed to determine if a plant has attained Stability or Flow can be found in Table 12.5.

A key component of the transformation is the confirmation process. Confirmations occur for each phase at the request of the Plant Manager once the associated performance results are attained and the practices have been implemented. Confirmations are done for individual plants early in the transformation as they achieve Stability and Flow. At Pull, confirmations shift in focus from individual plants to an entire product value stream. The team performing the confirmation has the following membership:

- Vice President of Operations Performance Excellence
- Operational Excellence Global Network Lead
- Members of the Operational Excellence Global Network

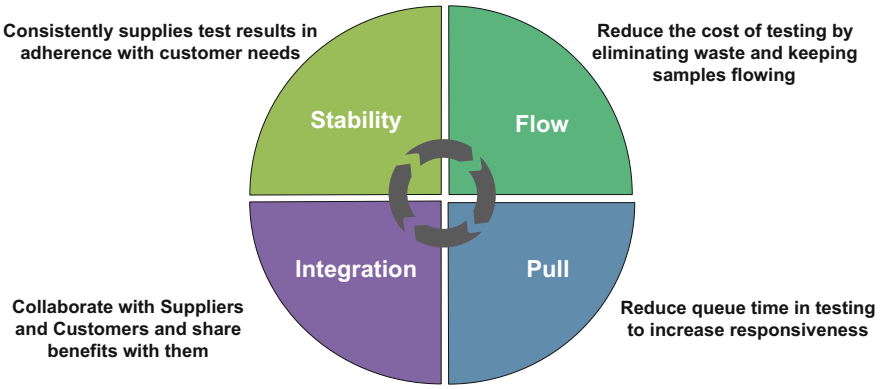


Fig. 12.5 QC Laboratory Lean Transformation Roadmap

Table 12.6 Examples of non-manufacturing practices

Practice	Definition
Process ownership	Business processes have owners, are documented, and have customer focused metrics
	Changes to processes are documented
	Customer/client requirements are documented
Performance management	Performance and results are reviewed as a part of a formalized management review cycle
	Use visual management to communicate status and performance
Purposeful presence	Leaders regularly spend time where the work is happening
Learning organization	Knowledge is effectively shared across process work teams
	Learning groups are established and effective
Global Networks	Global Networks drive process improvements

Based on the success of the Manufacturing Lean Transformation, a similar approach is being implemented for Quality Control (QC) laboratories. The roadmap for this transformation is shown in Fig. 12.5.

While phases, performance requirements, and practices for the Laboratory Lean Transformation are similar to those for the Manufacturing Lean Transformation, they have all been customized to meet the needs of a laboratory environment. This was done to help manage the change with the intention of accelerating adoption and application.

Work has also been done to define practices necessary to transform non-manufacturing processes. At the time of publishing, the approach to a lean transformation of these processes does not have the same amount of rigor and structure as the Manufacturing Lean Transformation. Table 12.6 shows examples of practices that have been piloted to date. These practices are intended to enable the consistent delivery of a service or product in adherence with customer expectations.

During this phase of the Operational Excellence journey, the Puerto Rico site launched a Lean Six Sigma certification program. Based on its success, the Operational Excellence Global Network expanded the practice and made the program

available on demand to all sites and functions. The program's focus is to support the implementation of critical, high impact projects using the DMAIC methodology. Staff received training and regular coaching over the course of the project. If they are successful in implementing the project and also complete case studies and a written examination, they are certified as Green Belts. Staff can then advance to Black Belt certification if they do the following:

- Execute additional projects
- Attend Black Belt training
- Mentor Green Belt candidates
- Teach Green Belt training
- Complete an additional exam

Outcomes

The rigor and structure added to the Lean Transformation during this phase simplified expectations for the plants and, in terms of practices, accelerated the rate of adoption. This contributed to the improved performance in terms of quality, speed, economics, and culture that was seen across all plants during this period of time.

Lessons Learned

Clarifying and simplifying expectations was critical. It is hard for plants to take action if they don't know exactly what they are to do and how the action is intended to help them improve performance. Once expectations were clear, leadership engagement increased. This increased engagement combined with support on the floor from Operational Excellence professionals resulted in an accelerated rate of change.

Progress was accelerated when three elements were present: having a burning platform for change, having engaged leaders who act as owners of their part of the business, and having Operational Excellence professionals providing coaching and support.

The same principles can be applied to improve manufacturing and non-manufacturing processes. However, the application of the principles is different and needs to be customized to meet the needs of the organization.

Transformation

The program is just entering the transformation phase. During this phase, the rate of improvement is expected to accelerate while the magnitude of the benefits is expected to increase. The program will continue to adapt and evolve to meet the

ever changing needs of the business. Future phases will be defined based on these needs.

Focus of the Manufacturing Lean Transformation will be to advance all plants through Stability and Flow and critical value streams all the way to Integration. This will require critical non-manufacturing processes to improve performance in order to enable the transformation.

Another area of focus will be expanding Operational Excellence into other parts of Amgen beyond Operations. This will enable improved performance at touch points with Research and Commercial Operations with the potential to result in enterprise wide transformation.

Key Recommendations

Several lessons have been learned over the years as Amgen's Operational Excellence program progressed through the various stages. Key recommendations for others embarking on a similar journey are summarized below.

Executive Support

Support for the program needs to originate at the very top of the organization. This will ensure the program remains a priority for the organization. This is important because the journey will require persistence.

Link With Strategy

It is necessary for the program to be focused on enabling the organization to achieve a desired future state. If this future state is not defined or accepted, put your effort there first.

Focus on Results

The program is not about methodologies or tools. It is about improving performance and outcomes in order to achieve better results. Make sure results are the cornerstone of any messaging about the program. Otherwise, the program will be seen as something that is additional work. It is hard for anyone to say that getting better results is not part of their job.

Pilot Methods

Build the program based on the experiences of your organization while learning from the successes and failures of others. Pilot methods to prove their value where they are best suited to meet the needs of the business. Broadly transfer them across the manufacturing network when they prove to be impactful.

The Success Formula

You will find success when you have a burning platform for change, engaged leaders who act as owners of their part of the business, and coaching and support from Operational Excellence professionals.

Chapter 13
Implementing an OE Strategy on Plant Level

Jürgen Werani, Volker Pfahlert, Kai Reimers, and Gert Diederich

Starting Situation

Hameln Pharma is a well-established contract manufacturer for sterile drug products. The aim was to develop Hameln Pharma into a modern, market-oriented, flexible and high-performing company which intends to be the first choice for its customers in the market for filling sterile liquids and related services. Hameln Pharma's mission is to be a strategic business partner for its customers, to supply them in a fast, safe and flexible way and offer them FDA-level quality products at fair market prices. The company maintains its competitive edge by

- Delivering products at the quality level required by the customers and government agencies;
- Using the Operational Excellence Strategy to further improve costs and process efficiency;
- Supplying products with the high degree of reliability expected by its business partners; and by
- Establishing a fast-acting and flexible organization which anticipates changes in the marketplace, realizes opportunities and takes advantage of them.

In order to meet these needs in the long-term, the company has made two important decisions. In the first phase, it invested in the building of a new plant for the production and packaging of sterile drug products. In the second phase, the existing organization was adapted to the new technological conditions.

The present case study will describe how this strategy was implemented.

J. Werani (✉) • V. Pfahlert
Schuh & Co. Complexity Management AG, St. Gallen, Switzerland
e-mail: juergen.werani@schuh-group.com; volker.pfahlert@schuh-group.com

K. Reimers • G. Diederich
Hameln Group GmbH, Hameln, Germany
e-mail: K.Reimers@hameln-group.com; G.Diederich@hameln-group.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_13, © Springer-Verlag Berlin Heidelberg 2013

Building a New Plant: Technical Conditions

The activities to implement an Operational Excellence (OE) strategy in an integral manner within the company took place on both a strategic and operational level. The concept of integrated efficiency became the guiding principle for the Operational Excellence strategy and for the overall project which spanned several years. The new plant was inaugurated in 2008.

The OE concept focuses on the optimization of technological and administrative processes in accordance with Lean principles, meaning the avoidance of all types of waste and the loss of both material and human resources by optimizing the design of the plant itself. To achieve this, optimum conditions must be created for the infrastructure of the production facility: the manufacturing environment needs to be designed in such a way that it perfectly fits the requirements of the manufacturing processes. Such requirements can only be met by a building which is explicitly conceived for a specific manufacturing process in order to attain maximum integrated efficiency.

The new plant was designed on the principles of Lean Management. This means that plant layout and the configuration of machines and equipment ideally match the flow the manufacturing process. Reduced interim storage facilities as well as optimized personnel and material movements over short distances are a characteristic feature. The arrangement of the work areas is logically based on the sequence of the individual production steps – from the receipt of raw materials, weighing, compounding to the filling process and ultimate shipment of vials and ampoules, thus considerably enhancing process efficiency. The cleanrooms and the layout of the production line are absolutely functional. In the new plant layout the configuration of the new filling systems is no longer linear but U-shaped. As a result, they integrate logically into the production process. Systematic standardization of rooms, systems, equipment, tools and processes boosts the productivity of employees and hence the efficiency of the production process as a whole. Generous use of glazing throughout the plant helps employees to provide a flexible response to different situation. It enables them, on the one hand, to keep track of the production sequence, monitor it and make it efficient and economical. On the other hand, employees can consult colleagues during the production process without having to leave their own work area. In spring 2009, the plant received the internationally renowned Facility of the Year Award of the American ISPE (International Society for Pharmaceutical Engineering) in the Operational Excellence category. Winning this award meant the first official acknowledgment of the company's OE strategy.

In the second phase which started in 2011 the focus was switched to adapting organizational and cultural factors to optimized technological conditions. Ways had to be found how to make the entire organization gradually adopt new modes of thinking and working and a new leadership behavior.

Redesigning the Organization: Cultural Environment

Before starting to redesign the organization, an assessment was made of the corporate culture which prevailed at the time. These were the results:

- The organizational structure was characterized by functional silos.
- There was little readiness to change. Employees tended to be backward looking, and change was associated with a high level of insecurity.
- Daily routines were marked by discontinuity, due to reactive action instead of proactive thinking.
- The organizational structure was highly hierarchical, with many interfaces and levels of decision-making.
- Managers at operative level were not 'visible' enough; they did not sufficiently engage in a dialogue with shop floor members.
- Employees were aware that the company was engaged in a change process. However, they did not fully understand the company's vision and what benefits they might derive from it.
- Employees generally felt that, due to reactive action, too many projects were being pushed forward, but they could not to see a meaningful link between them. To them, it seemed like "sheer activism".
- In a highly hierarchical culture, the employees' voices were hardly heard. As a result, their motivation to contribute to the improvement of processes and to enhance self-organization was rather low. Target definition, target control and target agreement were not consistently used as a management tool.
- The demands made on the employees and their skills were not in balance. The plant was built in accordance with state-of-the-art principles of Lean Manufacturing, but employees were not trained in Lean methods and tools.

The patterns of thinking and modes of behavior identified in the assessment did not meet the requirements of the envisaged integral Operational Excellence strategy. A new corporate culture had to be established marked by the following core characteristics:

- The new organization is customer and process oriented, with flat hierarchies to ensure short decision-making paths.
- Thinking and acting embrace the philosophy of continuous improvement while involving those concerned.
- Employees assume greater responsibility for plant, equipment and processes.
- Employees are encouraged to make active contributions, question existing ways of doing things, present and implement improvement proposals.
- The new organization increases the company's efficiency and effectiveness.

Development of the Organization in Three Phases

Phase 1: Design (Development of the Organizational Design)

The task for the project team was to transform the company from a functional organization, i.e. an organization which delivers what it is able to deliver (internal optimization), into a process-oriented organization which delivers what the customer wants (external optimization): This implies improving the company's efficiency and effectiveness by means of five levers, i.e. employee productivity, plant productivity, capital productivity, leadership performance and business performance.

A project team consisting of Sales, Product Life Cycle Management, Production, Personnel Management and Corporate Communications, led by the Process and Organizational Development Manager and supported by external consultants, was set up to develop a new, radically changed organization featuring the three following design elements (Fig. 13.1):

- **New ways of working** in a process-oriented organization focusing on the decisive core processes in a matrix organization (technical as well as operative responsibility).
- **New ways of thinking,** based on an equilibrium between demanding performance from employees and enhancing their skills, encouraging them to take on self-responsibility and embrace the idea of continuously striving for improvement.
- **New leadership behavior** by empowering people and delegating tasks, leading by objectives, and expecting that leaders will act as captains, trainers and coaches.

Structural changes were also aimed at developing and strengthening the sense of commitment, urgency and responsibility of each individual within the organization in order to achieve a sustainable increase of performance and significantly improved efficiency and effectiveness. The new corporate culture is based on the definition of the company's vision and mission which address four key elements: Quality, costs, customer service level and flexibility. In addition to this, seven values were identified which will jointly make up the new corporate culture – customer orientation, quality, appreciation, team spirit, performance, leadership skills, and reliability. These values constitute the social competences required from future leaders in anticipation of their new leadership role. Apart from that, four leadership qualities were described which will be needed for bringing the corporate culture of the future to life:

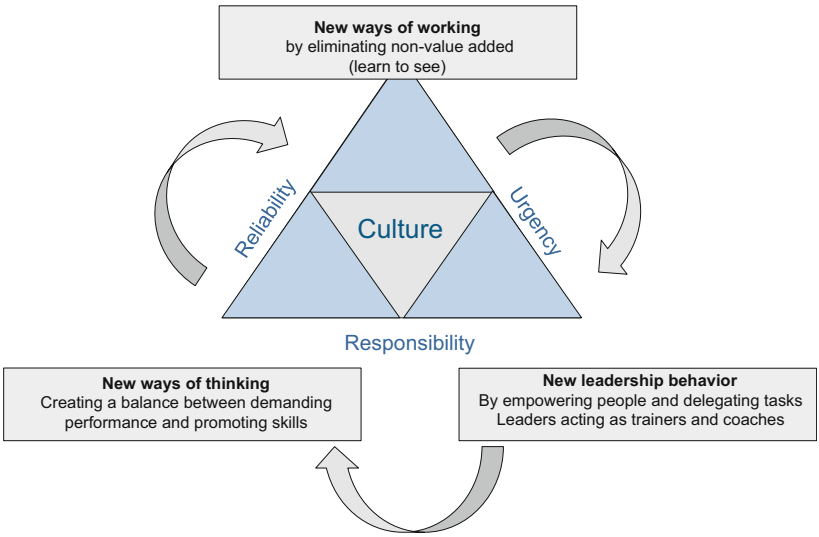


Fig. 13.1 Design elements of the organization

- **Responsibility for results:** Leaders will define clear goals and actively contribute towards achieving these goals. They make sure that sound decisions are made and set the right priorities within the timeline available to them. They encourage all those concerned and affected by such decisions to play a part in reaching these goals and involve them in the process.
- **Transparency and open communication:** Leaders recognize the needs, feelings and motivations of others and take them into account. They communicate in a transparent and honest manner, are open for new ideas and foster mutual feedback. They address problems and conflicts and deal with their own weaknesses in a constructive way.
- **Customer orientation:** Leaders are aware of the needs of their internal and external customers and actively respond to them. They react to customers' wishes in an appropriate way, anticipate new needs their customers may have, listen actively and think holistically.
- **Encouraging and demanding change:** Leaders challenge existing and established processes and structures. They are open for new ideas and support their implementation. They foster the exchange of knowledge and experience and respond appropriately to emotional reactions of those concerned. They adopt a solution-oriented approach when dealing with problems and uncertainties.

The Design Phase was mainly concerned with preparing the change process, performing analyses of the most important processes, establishing products, the creation of Master Batch Records (MBRs), changes to MBRs, Order Generation, Order Fulfillment and the derivation of goals. A rough design sketch was made of a Process House to visualize the core and support processes identified in this phase.

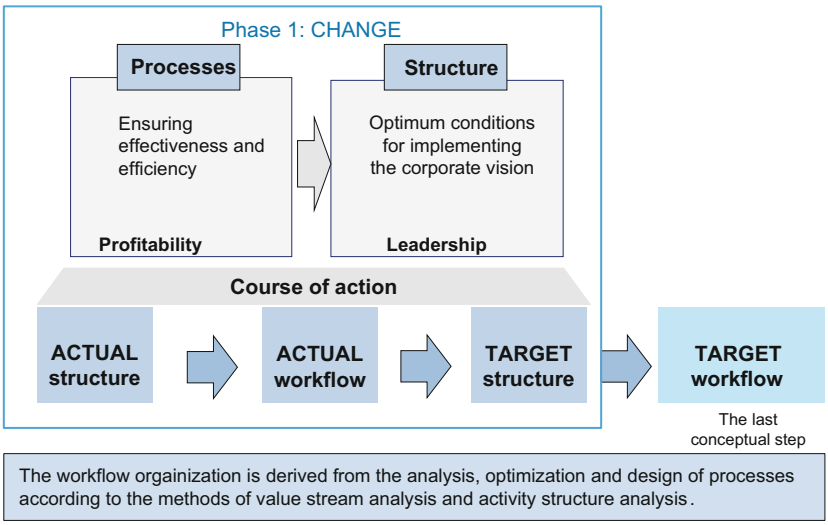


Fig. 13.2 Deriving the workflow organization

The design phase was divided into four steps:

Step 1: Selection of the business units which were to become the object of a detailed analysis and setting up teams to perform the analysis.

Step 2: Recording of the ACTUAL structure based on the method of activity structure analysis with a focus on the three value drivers, i.e. costs, time and quality, by conducting interviews with the process owners.

Step 3: Analysis of the ACTUAL workflow based on the method of value stream analysis by means of the given ACTUAL structure.

Step 4: Definition of the core processes and development of a TARGET structure, presentation of a first workflow organization diagram in a Process House in moderated workshops together with the process owners (Fig. 13.2).

As a result of the design phase, business units for the four core processes were defined:

- **Order Generation**
  The **Order Generation** business unit develops and implements the sales strategy and identifies target markets, target customers and target products. It is responsible for acquiring new customers and products and for building and maintaining the relationship with existing customers in line with the corporate strategy.
- **Product Life Cycle Management**
  This business unit establishes new products and provides support for existing products. This includes the validation of manufacturing procedures for new formulations and analytical procedures, scale-up, optimization of existing

products with a view to increasing profitability and efficiency, and product-related services in general.

- **Order Fulfillment**
  This business unit secures a competitive advantage by ensuring that top-quality products are manufactured and delivered on time and to the fullest satisfaction of customers. Apart from that, the Order Fullfillment business unit is in charge of Environmental, Health and Safety (EH&S).
- **Quality Management**
  The role of this unit is to ensure that all products (raw materials, intermediate and finished products) are manufactured in compliance with the official regulations and standards, and that they have been released for the market. It also warrants that all regulatory requirements as specified in the manufacturing license have been implemented and are being adhered to.

Phase 2: Change (Development of the Organizational Structure)

During the change phase, the main task was to fine-tune the concepts and work them out in greater detail. The details of implementation with regard to the five levers, i.e. employee productivity, plant productivity, capital productivity, leadership performance and business performance, were laid down in a Master Plan with a view to increasing performance (Fig. 13.3).

This phase consisted of six steps:

Step 1: Formulation of the **job profiles** in preparation of the Employee Development Assessment Center (ACs) and filling positions in the organizational structure.
Step 2: Development of a **Key Performance Indicator (KPI) system** for the job profiles, the target agreement process and for the Master Plan.
Step 3: Development of the workflow organization for the four core processes.
Step 4: Working on the **organizational structure** in greater detail and completion of the Process House.
Step 5: Development of **supporting measures** to encourage cultural change and improve technical competences.
Step 6: Deriving a Master Plan to implement all productivity-increasing activities.

Development of Job Profiles

The job profiles were written in a deliberately concise manner. They followed a scheme which was later used as the basis for the target agreement concept by forming a link with the KPI system. The first – general information – part contains

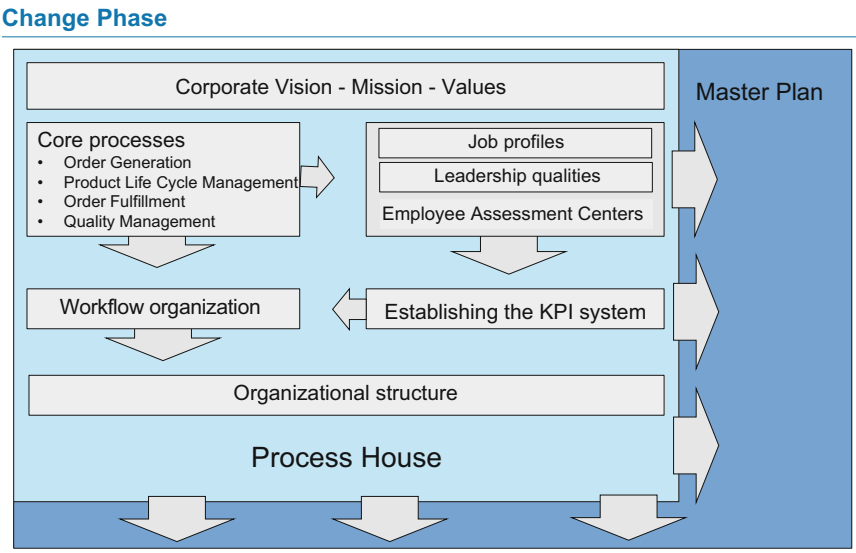


Fig. 13.3 Course of action in phase 2

all data referring to the job description, its ranking in the evaluation scheme and its position within the organizational structure. The second part describes the mission. The third part sets out the responsibilities, subdivided into the strategic implementation of the mission, monitoring to see whether the mission is actually being implemented, and leadership. The leadership part deals, among others, with the development of talent and promoting skills, but also with the commitment to corporate values. The third part is thus associated with the development and skills-promoting activities envisaged for the holder of the position concerned. The fourth part defines the KPIs which are vital for the strategic implementation of the mission and the reporting of these KPIs. The fifth and last part outlines the requirements with regard to education, training and professional experience the holder of the position is expected to fulfill (Fig. 13.4).

Employee Development Assessment Centers

As a preparation for job assignments in the organizational structure to be defined later, the majority of managers took part in Employee Development Assessment Centers. The objective was to draw up an individual learning and development plan to increase their capabilities and competences. Monitoring criteria were their leadership qualities observed at the beginning of the project.

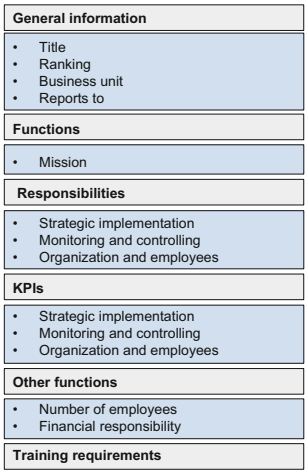


Fig. 13.4 Job profile scheme

These assessment centers addressed three key competences:

- Methodological competence, consisting of problem-solving abilities, decision-making abilities, organizational and planning abilities, as well as result-oriented and holistic thinking.
- Social competence, including flexibility, employee orientation, the ability to convince others, and communication skills.
- Personality, consisting of the readiness to assume leadership, emotional stability and empathy.

Development of the Workflow Organization

Once the core processes had been defined, they were charted in the workflow organization diagram and visualized in a Process House. The Process House served as a model for planning and operating the four core processes and had the following objectives:

- To achieve optimized work flows according to OE principles;
- To measure the results with a view to continuously improving the processes;
- Look for similarities between the four core process to achieve standardization;
- To speak the same "language" and communicate on a common level;
- To optimize cost and quality.

By proceeding this way, the processes to be developed could be continuously harmonized and improved. Attention focused on the close interrelationship between the way how processes should be operated within the company, and how they were

to be steered in terms of process performance. Based on the design of the job profiles, consistent job descriptions were drawn up according to process functions.

Later on, the Process House helped employees understand the "big picture" and identify the interfaces with the other core processes and their impact on their day-to-day work. The presentation of the processes in a Process House compels them to think and act in a process-oriented way and to apply this mode of thinking and acting to the development of the detailed workflow organization. The consistent descriptions of responsibilities in the job profiles for each function of the individual core processes facilitate a high level of transparency in their cooperation.

The core process Order Fulfillment serves as an example for the development of the workflow organization. It covers the entire range of activities from the procurement of all raw materials and supplies to the final delivery of the product to the customer:

The process flow begins with PLANNING as the first sub-step with the sub-process of Value Stream Management/Production Planning and the Sales and Operation Planning (S&OP) interface, followed by the sub-step MATERIAL PROCUREMENT with the sub-process Operative Procurement and Supplier Management and the Strategic Purchasing interface.

The next step in the process flow is PRODUCTION with the sub-processes Filling, Visual Control and Packaging, Process Control and Internal Logistics, followed by the sub-step QUALITY CONTROL with the sub-processes Analytics, Microbiology and Environmental Monitoring and the Batch Record Review interface.

The last step in the Order Fulfillment process chain is the sub-step STORAGE and SHIPMENT. Support processes such as IT, Personnel Management, Compliance, Technical Services and Finance support the Order Fulfillment processes flow in a matrix organization.

The following descriptions of the roles and responsibilities in the organizational structure of PRODUCTION give an example of the requirements and goals to be achieved by the new organization: customer and process orientation, flat hierarchies, involving employees in decision-making processes and fostering the continuous improvement process (Fig. 13.5).

The **Production Manager** is responsible for all activities in the manufacturing of ampoules and vials, their visual control and packaging in accordance with current production programs. Through all stages of production, he ensures that the products are manufactured in the desired quality and quantity by the agreed date and with the optimum and efficient utilization of production facilities and personnel resources. The production manager supports shift supervisors in their activities in the operative environment by acting as a leader, coach and trainer.

Shift supervisors play a central role in production. They ensure that the day-to-day business runs smoothly and in compliance with cGMP and EH&S regulations. To provide optimum assistance to operators at the production line, shift supervisors closely cooperate with production managers and process facilitators. All teams are supported by their colleagues in Operational Excellence (OE) and the Quality and Audit team, especially in transferring knowledge about methods. Shift supervisors

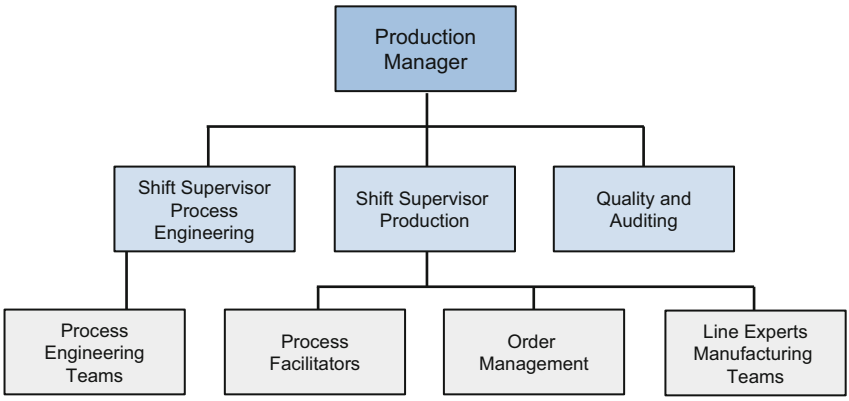


Fig. 13.5 Organizational chart production

are leaders, trainers and coaches. An important aspect of their job is to develop and support their staff.

Process facilitators ensure a smooth process flow and support shift supervisors in fulfilling their responsibilities**.** Their role is to:

- Support the line experts and their line teams in maintaining a high cGMP and EH&S standard, thus fostering the continuous improvement of the employees' quality and safety awareness;
- Coach and train employees in the development and implementation of improvement projects and optimization measures, and act as multipliers for OE; and
- Cooperate with the line experts in supporting the line teams to avoid waste (MUDA), deviations from standards (MURA) and overburden (MURI) by the consistent use of OE methods and tools.

Every line team has a **line expert.** The line expert works within the teams and has an additional coordinating function. He coordinates all activities of a line team whose members work different shifts, and supports them in dealing with their day-to-day business. With his expertise, he acts as a trainer and coach for his colleagues and shares his knowledge and skills with them.

Order Management is responsible for preparing the production orders for the system, the provision of starting materials for production, and, upon completion of the production process, for the timely control, accounting and recording of production orders in the system. This function aims to steer the documentation flow according to OE principles.

Conception and Implementation of Employee Development Activities

Training and development activities for employees were mainly about the cultural change of the company and about leadership skills. In fact, these leadership skills were an important point of reference for the participants of the Employee Development Assessment Centers. For this reason, training measures put great emphasis on real-life scenarios, a high level of interaction between the participants who were requested to deliver results upon completion of the training activities.

The company certainly did not want to offer classic seminars with tightly defined limits and a predictable result, or artificial seminar settings completely out of touch with the challenges of day-to-day business. Participants were not allowed to withdraw or play a passive role. On the other hand, participants were not to be left to themselves when having to apply the lessons learned in a hands-on situation.

Such criteria represent a great challenge for the company: first, because all development activities had to be specifically developed for the company, and second, because the demands of providing support and guidance to the trainees, once the training has been completed, is usually rather cost-intensive.

The concept of a learning journey with the aim of developing social leadership competences is exemplified in the training program for shift supervisors. The learning process is designed as a continuous training and development process and comprises two learning levels and four modules. It aims at:

- Making the transition into the new organization as effective as possible and fill it with life;
- Getting middle managers such as shift supervisors fit for their new roles within the organization while at the same time developing and strengthening them as a group;
- Ensuring that the new principles and learning philosophy become firmly anchored within the organization in order to bring about new modes of thinking and acting and a new leadership style; and
- Effectively interconnecting the various hierarchical levels to foster a culture of open dialogue and feedback.

With this concept, learning is to be encouraged on different levels. On the first level, learning is to increase team development competence within the framework of group-dynamic learning processes of an existing group. (Due to the three-shift model practiced in the company, it was essential to have shift supervisors acting as a leadership team.) On a second level, personal learning entails the reflection of the participants' own behavior, their leadership profile and their own personal development.

The four modules covered the entire range from understanding one's personal role, the development of individual and group competences of the shift supervisors to steering manufacturing activities.

The objective of the first module was to attune participants to the logics of the new process organization and make them reflect on their own future roles. This

implied finding a new definition of the type of entrepreneurial thinking and acting required from middle management. It also meant raising their awareness for the principles of the change process (Change Management) and developing their own competences as Change agents.

The second module was designed to improve leadership competences of the shift supervisors while trying to reconcile various expectations put forward by the corporate vision, by management and colleagues, with the demands participants pose on themselves. This module was about heralding the transition into a new understanding of leadership where shift supervisors act as captains and coaches and lead by objectives and Controlling instead of merely exerting control.

The third module was intended to teach team competences with a special focus on team building, team development and group dynamics, cooperation, communication skills, feedback culture and conflict management.

The fourth module dealt with the management of steering principles in complex organizations, i.e. complexity management, self-responsibility and self-steering in hierarchical systems. Even in flat organizations, there are, after all, a number of managers in a sandwich position. For this reason, particular attention was paid to shift supervisors whose position is right in the middle between the Production Manager, Process Facilitators and the manufacturing teams at shop floor level, a position which needs to be actively shaped.

The concept of a learning journey to develop technical expertise is exemplified in the Lean methods training program for process facilitators and shift supervisors. In analogy to the training program for social competences, the emphasis was also on "learning by doing". The program mainly focused on learning the methods, the practical application of methods in a simulation game, using the methods in real projects and reflections of the lessons learned through benchmarking with other companies in different industries. The program spanned several weeks. After passing a written examination at the end of the program and having successfully completed a project, participants received a certificate from the RWTH International Academy of Aachen University.

The most important methods and tools were presented in impulse lectures. Managers and trainers of the company itself were also among the lecturers. The entire training program was designed on the principles of a train-the-trainer concept.

Methods such as 5S, visual management, types of waste, set-up time optimization (SMED), Kanban, Poka Yoke, ergonomics and Layout Planning (Cell Design) were immediately applied in a simulation game on the subject of value-stream design by means of impulse lectures and practical exercises. Another group of topics dealing with problem-solving tools (PDCA/Kaizen tool), standardization and project management formed the practical part, requiring participants to work independently on a continuous improvement project in a manufacturing environment. During this stage, participants received guidance from managers (production manager and shift supervisors) who were supported by external experts and internal OE trainers. Over time, the OE trainers should be in a position to gradually take over the role of the external experts.

At the end of this learning journey, participants paid a benchmark visit to a different production environment where they could put their newly gained expertise to the test.

Phase 3: Supporting the Implementation (Training und Coaching)

The goal of the third phase was to get the new organization up and running, to get it firmly established and consolidated within an integral OE strategy. The platform for the implementation of the Master Plan had thus been created. Supporting activities were the training programs developed in phase 2 and the coaching and mentoring concepts.

Consolidation of the OE Program

To implement and support the OE activities, the position of an OE Champion was created. He is a member of the Site Leadership Team and reports to the Order Fulfillment Manager.

The OE Champion coordinates the implementation of all Operational Excellence activities throughout the plant and is responsible for establishing an appropriate infrastructure (definition of processes, KPIs, criteria of success, goals, system support and reporting). By raising the awareness among employees, he will help to build a sustainable culture of continuous improvement. The OE Champion encourages employees to actively use OE methods and tools and provides guidance to colleagues, project managers and leaders in the development, approval and execution of change projects and optimization activities.

In analogy to the concept of integrated efficiency which was applied to the building of the new plant, the development of the organization was determined by the concept of integrated effectiveness. This means that the technological infrastructure was linked to the organizational infrastructure, thus achieving a holistic OE approach. The terms of reference for OE were laid down in the company's vision, mission and its elements, as well as in its values and leadership qualities. The concept was backed by cultural change which again is founded on the principle of the continuous improvement process. The OE concept itself is based on five pillars: Competence management, asset management, quality management, value stream management and Environmental, Health and Safety (EH&S) Management.

Competence management, the first pillar, focuses on all activities pertaining to the development of skills of operational and management staff. All concepts and activities are carried out in close cooperation with the Process and Organizational Development and Personnel Management units. The holder of the OE position is a

member of the Site Leadership Team and has a driving and motivating role rather than executing projects himself.

Asset management, the second pillar, addresses the optimization of plant and equipment. There had been some successful activities in the past, but they were mainly due to volume growth. Here, it was particularly important to view Continuous Improvement as the underlying principle of the Operational Excellence strategy. It was vital to maintain the improvements achieved, and at the same time to keep raising the standard. In order to further exceed the initial accomplishments, it was necessary to capture the benefits of the new organization. The methods and tools used here were based on TPM (Total Productive Maintenance) principles.

Quality Management, the third pillar, deals with all types of quality problems and deviation. The standard tool for the analysis of problems was a PDCA/Kaizen-type tool, comprising four systematic steps: (1) presentation of the problem, (2) identifying the cause of the problem, (3) proposals for solutions, cost-effect analysis and implementation of the selected solution, and (4) checking the effectiveness. The company has explicitly refrained from using statistical methods such as Six Sigma, because the critical mass for the organization of Green Belts, Black Belts and Master Black Belts was not given, and it was expected that the majority of projects could be carried out without statistical tools. In their respective functions, the Quality Management and Product Life Cycle Management units are responsible for all GMP aspects and for product and process optimization. It is important to note that all activities in this area should be governed by the Right First Time philosophy. The methods and tools used here were based on TQM (Total Quality Maintenance) principles.

Value Stream Management, the fourth pillar, aims at process optimization by means of the value stream design method and is based on Just-in-Time principles. The conceptual preconditions were created with the plant layout. Production planning was based on combined Push-Pull manufacturing along the value stream chain from Receipt of Goods to Shipment. Having recorded the ACTUAL situation by means of a value-stream analysis, the second step consisted of categorizing the entire product portfolio into product families according to product similarity and similar take times. In the TARGET process, the product families were allocated to firmly assigned value streams. The OE Champion and the Value Stream Manager were to gradually and continuously improve the TARGET process in such a way that the new TARGET process would eventually become the ACTUAL process. This approach was aimed at shortening cycle times for both the product flow and the flow of documentation, reducing inventories (starting materials, semi-finished and finished products), increasing customer service level and improving process and product quality. The methods and tools used here were based on Value Stream Management principles.

The fifth pillar is Environmental, Health and Safety Management. It focuses on the avoidance of accidents, the ergonomic design of workplaces, prevention of environmental interventions as well as on energy and environmental policy. The OE Champion is supported by the Technical Services unit which is also responsible for EH&S concerns and Plant Utilities.

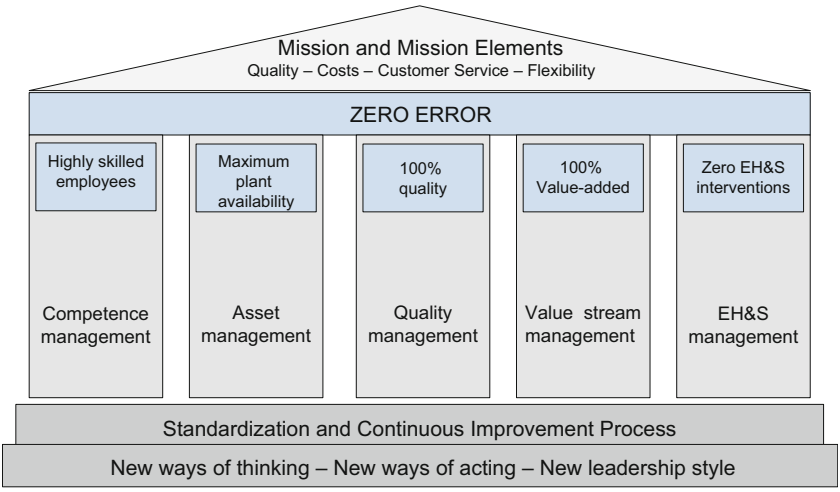


Fig. 13.6 OE from an integral perspective

These five pillars have one common goal: to achieve 100 % value added by ZERO error (Right First Time). This goal can be attained through optimum employee development, maximum availability of plant and equipment, 100 % RFT quality, 100 % waste minimization and ZERO EH&S interventions.

The technological and organizational conditions were to create the basis for standardization and a Continuous Improvement culture (Fig. 13.6).

Facilitating the Learning Process

Many managers and employees were reluctant to embrace the new role concept. They failed to fill it with life and tended to relapse in their old role behavior.

However, OE needs to be endorsed by leaders and workforce alike. To achieve this, executive managers, unit heads and shift supervisors need to change their leader behavior and act as captains, trainers and coaches. At the beginning, the role of trainer and coach was assumed by external experts. When the program was kicked off, this was fine. Training and coaching pursued two goals: First, to transfer OE experience into the organization, and second, to use OE methods and tools in the day-to-day business.

In this context, training did not mean formal training but rather the passing on of experience and know-how. This requires that managers themselves are able to understand and master the methods and tools if they are to teach them to others. By applying OE methods themselves, managers will make a strong point as to how important OE is for the entire organization.

Besides training, coaching is important as it helps employees to make practical use of OE methods and tools (learning by doing), which again will result in

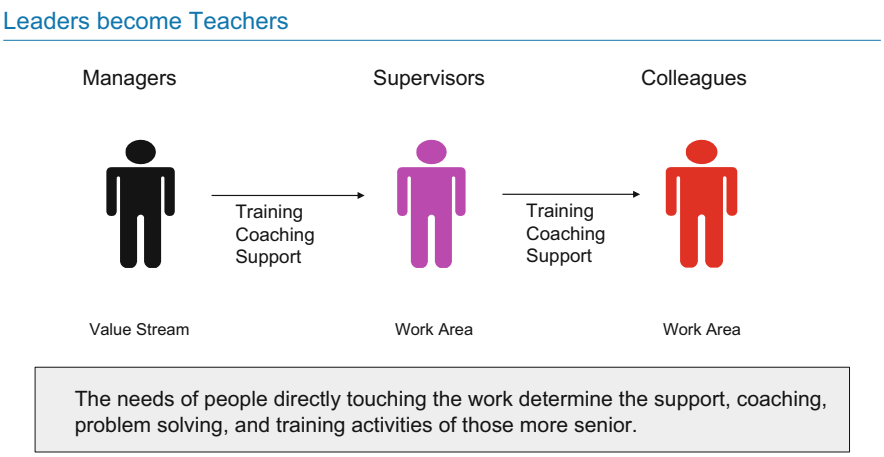


Fig. 13.7 Paradigm change in leader behavior

changing their ways of thinking and acting. Coaching implies making people gradually aware of changes and allowing them to see things from an OE perspective of value added (learn to see). Here, the biggest challenge was for people that they had to constantly question their own assumptions and ask themselves what improvements could be made (Fig. 13.7).

Apart from training and coaching, there is a third aspect, that of support. Managers need to anticipate where employees require support and help them find appropriate solutions.

This approach works in a top-down direction. Unit heads serve as trainers and coaches for shift supervisors, while shift supervisors cooperate with process facilitators to train and coach colleagues at shop floor level.

However, this concept represented certain challenges. Not everybody saw himself as a coach or wanted to act as a coach. At the beginning of the change processes, managers needed to have support so that they were able to develop into good coaches.

Mentoring is an approach to facilitate the learning process for managers and unit heads. Hence this program was applied for the management level above shift supervisors.

In mentoring, the mentor passes on knowledge or advice to another person (mentee) without being in a hierarchical relationship with this person. This in itself presents a challenge to medium-sized companies as the number of managers at top level is often limited. The mentoring program was set up to accelerate the development of talent through mentoring partnerships and personal development. Talents were to gain a better understanding of their career opportunities and receive support in career planning as well as in their every-day tasks. The mentoring program also contributed to intensifying the communication between different parts of the organization and gaining a better understanding of the corporate culture.

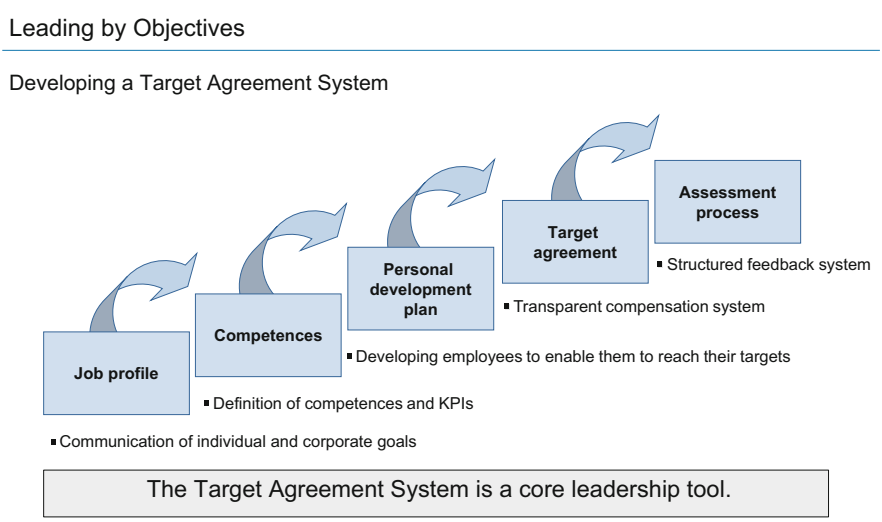


Fig. 13.8 Target agreement process

Introduction of a Target Agreement Process

The concept of the target agreement process had been developed, but it had not been introduced during the first year after the establishment of the new organization. Its launch was postponed until the following year because the process of cultural change was still in its early phase. The deliverables due according to the Master Plan had now to be regularly tracked by a strict project management. This was not an optimum solution at this particular phase of the change process. To introduce the target agreement process at any cost without sufficient preparation is, however, not in line with the integral approach to cultural change, the underlying OE philosophy and the understanding of the company's management.

The introduction of the target agreement process had therefore to be supported by appropriate education with the following objectives:

- To focus on the binding agreement between the leader (in his new role as coach and captain) and the employee (managers as well as shop floor members);
- To create an understanding of corporate goals, project goals as well as the individual and personal development goals of those concerned;
- To achieve this understanding by mutually agreeing on the deliverables, both on the part of the team and of the individual, to meet customer requirements;
- To define what each individual can do to achieve better results, and to point out how such results are interrelated with target agreement and with the activities of the new culture, the new ways of thinking and acting and leadership (Fig. 13.8).

Summary and Conclusion

After the new manufacturing plant had been built and started up in 2008, organizational development activities were initiated in 2011 and are still ongoing. This case study describes the results, success factors in pursuing an OE strategy, but also the obstacles to its implementation, and how they were overcome.

Critical success factors certainly included the uncompromising financial commitment on the part of corporate management to invest in the future, the consistent benchmarking against excellence with other companies in the pharmaceutical industry and the dialogue with companies which had undergone a similar process, the willingness to make the necessary changes in personnel and invest in the development of new leaders. The company was strongly committed to pursuing the formulated strategy in a turbulent, continuously changing market environment with limited opportunities. It succeeded in learning from setbacks and in regaining the courage and energy to further pursue its goal.

Obstacles and setbacks were caused by several factors which can be summarized as follows:

- The negative impact of an inherited and obsolete corporate culture cannot be eliminated without radical cuts in existing structures and internal networks. Socially compatible solutions need time.
- Radical changes pose a challenge in a phase of strong growth. They may initially result in instability which conflicts with the required growth of volume. Anticipated results did not materialize and led to deviations from the Master Plan.
- Due to the lack of a consistent, strong leadership structure, it was difficult to convey the credibility of the change process to employees.
- The need for "change communication" was underrated and not sufficiently met during the change process.
- Cultural change should be a result of activities, it cannot be prescribed.

Despite all obstacles and challenges encountered in the process, the dual strategy of investing in a new infrastructure and a new organizational structure has proved successful: in achieving short decision-making paths through flat hierarchies, by creating a transparent flow of information, and in allowing greater freedom of action and self-responsibility through greater competences and self-determination. Employee training and development programs made jobs more diversified, and employees had a greater say in how they would do them. As employees gained a more profound understanding and saw the benefits of the new organization, the efficiency and effectiveness of processes and workflows could be increased by gradually implementing a Continuous Improvement culture.

Chapter 14
Winning the "Facility of the Year" - Award with an Indian Plant

Eisai Knowledge Centre

Sanjit Singh Lamba

ISPE Judgment Criteria 2012 The judges have chosen the project as winner of the *Project Execution Category* for the following reasons:

- Outstanding safety record of no reportable safety incidents with more than five million hours worked.
- The completion of the entire complex that includes construction activities for all 14 facilities was accomplished in just 17 months.
- The ability of the project team to overcome the challenges of delivering a project of this size given the complexities of doing so in India.
- Good Japanese style and quality with a high degree of automation
- The capital efficiency of the project is commendable given such a high quality, fully integrated R&D and manufacturing complex was delivered for an investment of under US $50 million

Manufacturing in India

The Development of the Indian Manufacturing Sector

The Indian economy has undergone several structural changes in the last decades. Beginning with the 1950s, India faced excessive regulation that characterized its industrial development policy for the next four decades. These regulations, set up to govern manufacturing capacity, products, technology etc. had the objective to prevent the developing and capital-scarce economy from costly over capacity. With the opening of India's economy in the late 1980s inflows of knowledge, foreign technology, and capital has started. Local manufacturers expanded their

S.S. Lamba (✉)
Eisai Pharmatechnology & Mfg. Pvt. Ltd,, Plot # 96, 97, 98, 124 & 126, Ramky Pharma City (SEZ), Parawada, Visakhapatnam, Andhra Pradesh, India
e-mail: s-lamba@epm.eisai.co.in

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_14,

production and the country became a center of interest for foreign competitors. Moreover, a lack of sufficient import regulations evoked the structural change of the Indian economy. In 1991, India introduced a new set of reforms that substantially reshaped the competitive environment for both domestic and foreign companies. Due to the abolition of India's license regime, protectionism and control measures came to an end and brought the manufacturing sector at a critical juncture (Dangayachy and Deshmukh 2001). However, although the perception of manufacturing in India as a support activity for marketing and finance rather than the vital value creation of a company is gradually changing, today's manufacturing still lacks attention of senior management (Chandra and Sastry 1998). Therefore, it's no wonder, that most companies in India are still far from practices summarized under the umbrella of world class manufacturing (Dangayachy and Deshmukh 2001). Meanwhile, international competitors improve their manufacturing functions continuously, market new products in the country, and thus increase the flexibility and responsiveness of the entire Indian manufacturing sector. As such, the domestic Indian economy experiences rising competition from both multinationals entering the market and from imported goods. This new competition is characterized by the simultaneous combination of a wider range of products – mostly coming with higher performance, reduced cost, improved quality, and better services (Chandra and Sastry 1998; Dangayachy and Deshmukh 2001).

Challenges Faced by Manufacturing in India

Although the Indian economy in general has seen numerous changes in recent years, the pharmaceutical industry, as one of the most important pillars of the industrial sector, faces several hard challenges. Many of these challenges can be traced back to the legacy of the Indian culture and traditions that have evolved over thousands of years. As such, the Indian culture – as many cultures in other emerging markets – is characterized by strong hierarchical structures (Schwartz and Shalom 2004) that carry forward into Indian organizations and thus influence behavioral patterns and thinking.

India pursues the ambitious target to rank among the major players in the global knowledge economy and higher education is seen to be a critical factor to this success. In order to remain competitive beyond the provision of low cost manufacturing, the Indian industry is heavily dependent on well-trained and skilled personnel. But recent studies reveal that the Indian higher education is currently not keeping up with developed nations and thus is severely constraining the supply of qualified manpower (Agarwal 2006). This, however, not only hampers the search and employment of people in pharmaceutical manufacturing, but also in retaining them, once they are well-trained and experienced. Scarcity of experts and plenty of emerging pharmaceutical companies, provide especially young professionals that are often willing to move across the country with rich opportunities for work. Such high turnover rate is likely to negatively impact the organization's cultures. Several

shortcomings in legal systems abet young professionals to constantly try to get the best payment fostering the "company-hopping" across the country.

In addition, the manufacturing sector in India is influenced by the existence of strong labor unions. These unions enforce to tie in workers' payment with the current productivity level i.e. an increase in productivity entails the same payment rather than resulting in an extra bonus for exceeding initially set productivity levels. Thus, there are very few incentives for employees to increase productivity.

An often deemphasized aspect that has yet to be taken seriously lies in the integrity of the management and the underlying failure culture. Recent quality issues having their roots in India might be an unfortunate result of such behavior. Emerging markets like India often emphasize cultural embeddedness; such culture views people as entities of collective groups that highly emphasize maintenance of a group's status quo and discourage any behavior that might disrupt in-group solidarity. Moreover, decision making in such cultures is rather autocratic and willingness to share decision making is scarce (Burgess and Steenkamp 2006). This however might lead to the non-admittance of failures rather than an open communication and bearing the consequences, e.g. scrapping bad batches. When it comes to quality, literature of a decade ago testified the Indian manufacturing sector a modest situation. Quite often, Indian companies have pursued an opportunistic approach to spur growth, lacking a consideration of their true capabilities. Consequently, Indian shop floors and their improvement have seldom been in the focus of operations managers (Chandra and Sastry 1998). Thus, Dangayach and Deshmukh (2003, p. 279) argue that such behavior has resulted "in poor quality of products, little awareness of competitiveness, [and] little integration of various functions such as marketing, sales, production". This perception currently seems to change (IBEF 2012). Despite, many studies discussing latest quality advancements of the Indian manufacturing sector neglect the fact that for many Indian companies, the reason for competing for quality prizes is image and advertisement rather than a true "excellence" philosophy.

However, especially within the pharmaceutical sector, India has seen a lot of progress in recent years. No longer are shop floors characterized by outdated technology – in fact, the industry has taken its improvement potential to heart. Today, the Indian biopharmaceutical sector has set several examples of state-of-the-art plants that provide high quality products with latest technology.

The subsequent parts of this article describe such a success story providing insights in the establishment of an award winning pharmaceutical manufacturing site.

Eisai: A Global Company

Eisai in General

Eisai Co., Ltd. is a research-based human health care (hhc) company that discovers, develops and markets products throughout the world. Eisai focuses its efforts in

three areas: Integrative neuroscience including neurology and psychiatric medicines; gastrointestinal disorders; and integrative oncology including onco therapy and supportive-care treatments. Through a global network of research facilities, manufacturing sites and marketing subsidiaries, Eisai actively participates in all aspects of the worldwide health care system. Eisai had employed 10,495 people worldwide. As such, Eisai is a human health care company seeking innovative solutions in disease prevention, cure, and care for the health and well-being of people worldwide. As a reflection of that commitment, the Company's "hhc" mission symbol is derived from the letters in Florence Nightingale's signature. Following the example set by the famed health care pioneer who devoted her life to caring for others, yet never lost sight of the importance of listening to her patients, Eisai marshals its talents to explore new therapeutic approaches that address two key goals: to meet the medical needs of patients and their families and to improve quality of life.

The traditions of genuine concern for people, dedication to excellence, and contributions to society have become hallmarks of the Company. Eisai regards patients and their families as the most important "participants" in the health care process and expects all of its employees to consider – and be responsive to – the patient perspective.

Eisai strives to promote the well-being of the patient, family and our community by discovering and developing innovative drugs in areas of unmet medical need, by raising awareness of vital issues through educational and fundraising events, and by encouraging volunteer involvement. We are determined to make a difference locally and globally.

Eisai is a responsible, focused, efficient, innovative Pharmaceutical company. This vision is designed to provide the overall direction for our company. It describes what we need to continue to succeed in the future, based on changes in the marketplace and our capabilities. Our vision helps us set goals based on the potential of our organization and what we hope it will become. Most importantly, it forms the basis for our work and business strategies.

Eisai in India

Eisai Knowledge Centre, a state-of-the-art 50-acre complex that covers the complete production cycle from research to product development, to pilot plant, to clinical manufacturing and manufacturing of drug substances and, ultimately, the final drug product in solid dosage form. The complex incorporates India's most advanced chemical synthesis technology. The Centre is located off the southeast coast of India in Visakhapatnam, the second largest city in the state of Andhra Pradesh and the third largest city on the east coast of India. Eisai made a significant investment of around more than 4 billion JPY to locate the Centre within the Ramky

Pharmacity, Special Economy Zone (SEZ) in Andhra Pradesh. The research and manufacturing complex currently occupies 33 acres with the remaining 17 acres available for future expansion.

The complex is a major part of the company’s strategy to transfer a portion of primary operation functions to areas with high technology standards aiming for reinforcement of global flexibility and realizing its strategic plan. Production at the site will also support global logistic infrastructure and supplement Eisai’s production plants in Japan and other countries.

This is the first time that a major Japanese pharmaceutical company has established a major production facility in India. The Eisai Knowledge Centre ensures a stable supply of high quality pharmaceutical products and supports the company’s hhc philosophy to supply high quality pharmaceutical products to meet the various needs of patients around the world. Eisai aims to benefit millions more patients around the world by entering all of the world’s top 20 markets and transforming itself into a global top-tier, high performing company by adapting to changing market conditions.

The Eisai Knowledge Centre was designed to be a global comprehensive pharmaceutical complex for the manufacturing of drug substances (Active Pharmaceutical Ingredients – API) and drug products (Oral Solid Dosage – OSD forms), as well as for process research and development of APIs. The center, Eisai’s fourth knowledge creation base, was established to generate higher efficiency and productivity by integrating production, research, global procurement and administrative functions into one site to ensure a stable supply of high quality pharmaceutical products.

This is a unique complex where all technical buildings are *integrated* from a business and production standpoint. The *Drug Substance* facility is *designed* to *produce all API* required for the *Drug Product* facility. The production capacities, operating schedules, storage capacities, etc. of the Drug Substance facility are *matched* and *integrated* with the *production capacities* of the Drug Product facility.

This flexible, fully integrated site offers Active Pharmaceutical Ingredients (API), formulation manufacturing and API process research functions, and enables advanced preparations such as technical transfer, process validation and stability testing towards full scale operations. The new complex consists of 14 buildings, including locker rooms, cafeteria, critical utilities, laboratories, administration, warehousing, research and development and both Pilot and Manufacturing Blocks.

The Drug Product facility, with an annual capacity to produce two billion tablets, and the Drug Substance facility, with an annual capacity of 30 t, will supply products to the United States, Europe, Japan and other global markets.

Eisai's innovative chemical manufacturing capabilities for cGMP API production and formulation offers greater speed, flexibility, safety and security of the supply chain and outstanding quality, meeting strategic drug development/manufacturing needs with flexibility for expansion. The facility has reserved sufficient place for expansion.

The integration of API research, support and manufacturing facilities into one flexible, state-of-the-art complex has increased the capacity and capability to research, scale-up and manufacture multiple API products simultaneously for the benefit of the patients throughout the world.

The Eisai Knowledge Centre was able to successfully manufacture cGMP commercial product immediately 7 months after facility completion. The facility is scheduled to reach full annual production capacity of two billion tablets in fiscal year 2014–2015.

The Drug Substance and Drug Product facilities were fully validated to Japanese, US and European regulations. Construction activities, involving one project team, have been run simultaneously and in parallel, successfully completed within 17 months and were below the released budget of around more than 4 billion JPY.

Establishment of the Site

Construction Type

The project to establish the multi-functional complex followed a greenfield approach that combined a unique design, seamless quality, innovation, and facility integration. During the peak of construction the project team counted nearly 2,000 people working on site. Moreover, about 70 different vendors, contractors and subcontractors had been coordinated on simultaneous and paralleled construction project that altogether contributed to complete the entire complex within 17 months.

Building structures and ceilings are made of reinforced cement concrete and walls have been built of a brick masonry that is plastered with cement. Additionally, the walls are coated with polyurethane paint to provide a hard, smooth finish. All floor, wall and ceiling joints in the manufacturing area are coved with epoxy to avoid dust accumulation and to facilitate ease of cleaning. Also from a cleaning aspect and to support housekeeping, all manufacturing area floors have an easy-to-clean self-leveling epoxy that provides a smooth, impervious, hard surface. Double glass view panels (free of joints and crevices) have been installed at doors and walls to facilitate viewing and supervision of activities on either side. Since finishing requirements were different in each building, manufacturing areas were finished according to cGMP requirements whereas at administration and offices attention has been paid to aesthetics and modern finishing requirements. Thus, friendly and pleasing offices are located in beautifully landscaped open areas. Besides, the complex offers night catering and company vehicle transportation to support the three shift production schedule.

Construction Safety Statistics

From the very beginning, safety during the construction period was seen as mandatory by Eisai's management. Everybody agreed that it is not only to establish a new state-of-the-art facility complex that in the future will supply millions of people with high quality medicine and helping them to enjoy a healthier life but also to treat and value high every single individual that contributes to this ambitious vision. These safety aspects were also requested from and enforced at all vendors that supplied the construction site at an initial vendor meeting through the finalization of the contract. Therefore, all workers and supervisors were conscientiously trained in several safety aspects like tool box talks and electrical and grounding safety. Beyond training safety techniques on site like barricading, staging, edge protection, safety belts and nets have been employed. Supervisors additionally trained in project management skills ensured safety for on-site personnel and substantially

contributed to the construction site's record of zero accidents at the total construction time of more than five million man-hours.

Environmental Impact and Sustainability

The Eisai Knowledge Center was established as a place for all employees to share knowledge and information in modern and aesthetic biopharmaceutical complex. Therefore, the center on the one hand provides a bright staff cafeteria, a fitness center, a reading area and other cozy spaces for employees to relax and collaborate. On the other hand the center has no constraints for employees with disabilities as all buildings are accessible via ramps, upper floors via lift, and every building has disabled friendly restrooms.

Cafeteria

The entire complex features environmentally responsible technologies. A natural ventilation system is used for office acclimatization and brings in fresh outside air. Besides, the air handling system is equipped with a heat recovery wheel for efficient energy use. High intensity incident solar radiation is damped by high-insulation, double glazing, light shielding screens and skylights. Inside the office spaces high-efficiency lighting with presence sensors foster a comfortable atmosphere.

Cafeteria

Corporate Environmental Protection Policy was extended to the site that entails the minimization of environmental impact through protection measures for water, air and effluent. Overall energy usage reduction results in lower CO_2 emissions. The reduction and gradually removal of chemical substances that cause pollutant emission is promoted. All data that give information about environmental impact such as energy, water, paper consumption, waste volume, discharge, contamination, vehicle exhaust and atmospheric emissions are measured and assessed routinely.

The Facilities

Drug Substance (API)

The building was sized to allow the production of up to 30 t of API per annum that is used for on-site formulation as well as exported to the West and Japan. The design involves the vertical configuration of the drug product facility. Hence, process operations maintain a vertical flow in clean areas for the product to follow progression from final crystallization process to finished product. Dispensing of raw materials occurs within contained dispensing booths under laminar air flow to avoid cross-contamination. Three segregated booths facilitate dispensing of powders, liquids and corrosive powders and liquids. Powder Transfer Systems (PTS) are applied to avoid cross-contamination and minimize oxygen content in the reactors by creating nitrogen blanketing. Dispensing of solvents through a distributed control system minimizes manual errors and avoids direct exposure to the solvents. The integrated Powder Handling System (PHS) facilitates contamination free manufacturing of final operations e.g. milling, sifting, metal detection and predefined weighing with online sampling. For the first time in India a drug substance building used clean classifications similar to drug product operations.

API Pilot Plant

The API pilot plant enables verification of process improvement studies of all intermediates performed in the API laboratory through scale up, it serves as a multi-purpose plant to produce intermediates.

Bulk Product Storage/HazMat Storage

Raw materials for production and products from drug substances are stored within a controlled environment. The effective use of space and insect/pest control measures was incorporated into the design of the storage building.

Administration Buildings

The design offers Japanese open-style layout in administration and cafeteria to support better a communication while considering unique Indian customs. Open courtyards provide with natural lighting creating a comfortable atmosphere.

Drug Product (Formulation)

With a capacity to produce approx. Two billion tablets the OSD formulation facility supplies the global market. At the two-floor building the ground floor is used for warehousing, manufacturing and packing operations. The second floor is the technical area, including air handling and purified water systems. In order to ease and

facilitate a smooth material handling, storages for raw and packaging materials are adjacent to the production area. Also designed to encourage lean operations, warehousing and shipping is located next to formulation and thus improve traffic direction of the finished products and their shipping processes.


Drug Product (Formulation)

The innovative design of the facility involves a “one room – one unit operation” concept that clearly separates various unit operations to avoid cross-contamination. Furthermore, closed loop granulation and drying equipment is applied to prevent any contamination and exposure to operators in the drug product building. For an effective prevention of cross-contamination either by personnel or by material a pressure cascade system with H13 high efficiency particulate air (HEPA) filtration and various airlocks for both personnel and material to avoid dust circulation between rooms has been installed.

The facility is provided with full automatic granulation, compression and coating equipment. A state-of-the-art laser based tablet inspection equipment is used to check any defects to the level of 40 μm – a valuable device when it comes to the supply of the challenging Japanese market.

R&D/Laboratories/QA

The building houses R&D and Laboratories for API producing processes on the ground floor. The architecture incorporates key concepts like the possibility for future expansion and common facilities for both API and formulation laboratories. Chemical R&D is focused on complex synthetic and organic chemical compounds, including process research at kilo lab level and scale up to pilot scale. In contrast, analytical R&D delivers feasible, cost effective, eco-friendly & commercially viable analytical and validation methods for identified products.

R&D / Laboratories / QA

Quality Assurance (QA) and Quality Control (QC) for the entire complex are located in the upper floor. The Quality Control lab has in-house testing facility for incoming materials, raw and packaging, in-process materials and finished product. Besides, the lab is self-contained and has separate labs to cater to the needs of various kinds of analysis.

Energy Centre/Pump House

External electric power is transformed in the energy center and supplied to each zone throughout the campus. In order to cope with unstable power supply, emergency generators for each zone have been installed to provide 100 % power back up. Moreover, each zone is supplied with WHO standard drinking water and medium pressure steam that is generated in the Utility Zone.

Energy Centre

The site’s waste water plan segregates the effluent on site in low total dissolved solids (TDS) and high TDS streams. Both streams are sent out for final treatment. The ISO 14644 conform HVAC system is equipped with H13 HEPA filters in the supply air stream to remove contaminants and prevent cross-contamination in the process areas. The motors for supply and return air blowers have variable frequency drives to maintain the desired air flow and help in energy conservation.

On site infrastructure also comes with access roads around each building. However, material and vehicle movement is restricted to one gate only. Flows of people, material and equipment have been optimized from scratch. As mentioned earlier already, the process flow for the drug product is designed to maintain linear whereas drug substance flows are arranged vertically, such that the product follows a natural progression from incoming starting material to finished product. The campus master plan has provision for expansion for each building adjacent to the existing building. To also meet future requirements and developments of the complex, critical utilities are located within the Energy Centre in the middle of the complex and effectively fulfill the utility requirements of the R&D, API and Formulation buildings. Latest fiber optics-based communication links enable data integration between all building operations.

Advances in Design, Commissioning/Validation Technology

At the planning phase, a validation master plan has been developed. The defined approach and methodology was applied for commissioning and qualification of all technical buildings, equipment, systems, utilities and processes. A risk-based approach was adopted for equipment and facility at the design stage to look at the possible risks and their mitigation built into the design. The risk analysis also comprised systems and processes that establish and maintain environmental control and provide a harmonized environmental standard. Based on the ISPE baseline guide, impact assessments were carried out by evaluating the impact of operating, controlling, alarming and failure conditions of a system on the quality of a product. Direct impact systems were subjected to installation, operational and performance qualification (IQ/OQ/PQ) testing; indirect impact systems were subjected to IQ/OQ (only functional testing) and periodic calibrations and no impact systems were installed as per Good Engineering Practices (GEP). For immediate corrective actions on-site vendor support during IQ/OQ execution was guaranteed. Only validated methods were transferred to the site and revalidated to ensure comparable results.

Pollution Control

As mentioned above, liquid effluent is segregated at each facility level as low TDS and high TDS. The Low TDS effluents are collected and transferred into a common collection pit where it is neutralized prior to disposal for further treatment. In case of high TDS, apart from separating low TDS, the streams are further segregated as acidic, solvent, and aqueous & solvent. These streams are separately collected in above ground tanks and disposed of through a common effluent treatment plant.

All corrosive gaseous emissions are scrubbed prior to venting into atmosphere. A point exhaust system is provided for fugitive emissions, which are separately collected and scrubbed. Besides, all vacuum pump exhaust that is connected to the scrubber, also exhaust from the reverse laminar air flow (RLAF) charging booth is connected to the scrubber. Hydrogenator exhaust is processed through a specialized exhaust tower, then scrubbed with low pressure steam. In order to control fugitive emissions, all solvent storage tanks are kept under nitrogen blanketing and solvent transfer pumps are provided with mechanical seals.

Success Factors

The project planning and execution was centered on the need for "total backward integration", as India is a key Eisai location for supplying all global markets at affordable price, as well as for developing new processes. This, however, put considerable pressure on the entire project that was condemned to success from the start.

The main reasons this project was successful and accomplished its intended goals can be summarized as follow:

- Senior management oversight of project with a close monitoring
- Excellent project management and communication with the teams
- Use of risk assessment and mitigation strategy right in the design stage to look at the possible failure probabilities and its solutions
- Elaborate commissioning and qualification activities through an experienced team
- Small close knit team for enhanced decision making and choosing alternate course of actions
- Blank dry runs in the beginning of the trials to prevent any wastages
- Good training both for operational and regulatory compliance
- Sound procurement practices and negotiation to keep costs in control
- Vendor development activities started before the construction started to give sufficient trials for search, evaluation, audit and certifications
- Culture of safety and compliance throughout the whole project including regular training and inspiring the teams to follow a compliance driven decision making.

Project Management

A decisive success factor was indeed a sound project management. Influenced by several observed projects of launching global manufacturing facilities in the US and UK, along with the following concepts of existing formulation facilities in Japan, lessons learned were derived, optimized, adapted, and implemented into the complex.

To start very early with all planning procedures was key to coordinating a project of this magnitude and not to waste time while get bogged down in details or needless micro-management. The construction activities for all 14 facilities began simultaneously and were run in parallel and constituted a daily challenge for the project management team. The entire project was based on an aggressive timeline that at the end was exceeded as the facility complex was constructed in 17 months only and its inauguration date was scheduled earlier as intended at project onset.

An integrated project team was established at project inception and continually collaborated with all stakeholders. The entire project was handled by one project team whose members brought in sound knowledge of manufacturing operations along with execution of large projects. During project peak, the entire workforce counted nearly 2,000 people. Daily meetings with a highly effective project team communication offered a tight coordination; pre-planning and execution of several activities and "to dos" were discussed, and critical issues were addressed in a timely and proactive manner.

The tight team collaboration facilitated to continuously monitor and forecast deliverables and to address all potential issues in advance. Tracking of the project implementation, planning and execution was supported by several tools e.g. MS Projects, S-curve etc. Such outstanding teamwork with cohesive relationships, communication and the team's commitment to safety and quality resulted in increased efficiency and productivity.

Budget Control

Budget control of such a large project requires sensitive management skills. It is important to remain always consistent when it comes to business, but fair and friendly when it comes to people. This approach, however, was meaningful for successful negotiations with key vendors.

As there are worldwide many examples available of how the management team of large construction projects has lost control on cost, regular review meetings on how to leverage cost were held; unnecessary expenditures have been identified and if possible they have been removed.

Finally, speed in decision-making was the key to keep the project on its tough schedule which resulted in the project being under budget.

Eisai's Performance

After having won the Facility of the Year Award 2012 for Project execution and having run production successfully for more than 1 year, the leadership team of the site was looking for a meaningful industry comparison of the Visakhapatnam site with other successful industry practices. The leadership team was looking for a benchmarking not only based on single Key Performance Indicators (KPIs) but rather for a management cockpit like visualization of a broad summary of KPIs. The St.Gallen OPEX Benchmarking provides such a holistic consideration of a multitude of KPIs that need to be taken into account and continually measured. This goes with the leadership team's pursue of excellence and was considered as beneficial for a target setting, future tracking of the site's improvement progress, and beyond.

Eisai Knowledge Centre as part of Eisai's global manufacturing network is a corporate center for R&D and supplies several sites within the network with high quality OSD products. The site's manufacturing strategy is in line with corporate and is primarily focused on achieving highest quality. A balanced network approach allows the complex to focus on its existing product portfolio – there is no need to provide the company with a high manufacturing flexibility and a broad product mix.

Before the site's very first SOP, all employees attended several trainings. Especially for shop floor employees, Eisai Knowledge Centre run several maintenance and machine setup & cleaning workshops and trainings to get a proper machine handling and understanding of necessary maintenance work. Workshops on the mindset of continuous improvement (CI) laid the foundation for all value-creating processes and CI mindset is encouraged by management and evolves step by step ever since. These trainings, however, contributed to the site's TPM performance that is apparent in lower setup and cleaning times as well as a lower proportion of unplanned maintenance compared to other OSD manufacturers in the St.Gallen database.

One of the site's main markets is Japan, a highly demanding market when it comes to product quality. Several constraints of pharmaceutical manufacturing in India have been discusses in section "Manufacturing in India" of this article. However, corporate and the site leadership team are aware of the challenges but also of the rich opportunities of manufacturing in India. In order not to challenge luck, quality was handled with utmost care and is meticulously supervised. Such persistence on quality became evident while participating at the St.Gallen OPEX Benchmarking. The significantly higher proportion of the Visakhapatnam complex' indirect QC and QA compared with an industry average of approx. 100 pharmaceutical manufacturing sites underlines the focus on quality. Moreover it symbolizes the awareness of India's quality issues in the past and the efforts never to be mentioned with those in the same breath. Additionally, benchmarking certified the site to put above-averagely high emphasize on customer involvement, cross-functional product development, and supplier quality management in order to achieve its high quality products. High quality performance, however, is reflected

by less process deviations per batch, zero rejected batches, a significantly shorter release time, and zero customer complaints. On a quality cost perspective, the site utilizes its advantage of manufacturing in a low wage country and realizes a pleasant input–output ratio.

As mentioned above the Eisai Knowledge Centre was designed to facilitate smooth flow of people, material, and equipment at the entire area. Optimization of layout thus comprises both infrastructures like roads and material supply, and shop floor layout facilitating low inventories, fast throughput and highly synchronized process steps. High employee involvement and cross-functional teams support the site’s implementation of the Just-in-Time philosophy. A higher JIT performance than most of the sites in the St.Gallen database is demonstrated in e.g. high turns of finished goods, shorter cycle and lead times, and surpassingly short changeovers.

Although the St.Gallen OPEX Benchmarking testified the site an already high performance, based on the assessment of the St.Gallen Model’s technical system (Chap. 2) the benchmarking also revealed potential for further improvements. The potential and how to utilize it has been discussed by the site leadership team, and an agenda list with distinctive initiatives for future improvement has been drafted. In accordance with daily business management will work thorough the prioritized list of initiatives and start them little by little. A repeated participation at the St.Gallen Benchmarking will reveal the site’s progress not only based on Eisai’s own KPIs but also in comparison with the entire industry’s movement.

Outstanding pharmaceutical manufacturing is a tough challenge in India and many companies struggle to get their manufacturing function in line to cope with the country’s volatile environment. Against all criticism, the example described is evidence of the possibility to achieve very high performance from the start – even in a country that is yet in its development stage. But facing the challenge and taking the advantage of the situation will pay off in the future and strengthens the position in one of the world’s fastest growing markets.

Future Challenges for the Site

At present the facility acts as a supply hub for the Japanese market. The site is also approved by US FDA, MHRA, WHO and Korean FDA for supply of APIs and drug products. In the future a number of additional products for different markets will be supplied from this site making it more complex both from a stable supply and a regulatory compliance perspective. The number of SKUs will increase considerably leading to challenges in operational excellence. The process research and development needs will increase further having to deal with additional scale up requirements and the need for the development of new vendors and new materials. We will approach this situation with the following measures:

- Kaizen for continuous improvement.
- Quality by design approach for greater reliance on compliance by design and not relying on quality by testing.
- Six sigma approach for sustainability in supply to stringent pharmaceutical markets.
- Training of employees at various levels for their skill development.
- Building a culture of openness, transparency and professional conduct.
- Benchmarking of operational excellence parameters and improving them continuously.

References

Agarwal P (2006) Higher education in India – the need for change, Indian council for research on international economic relations. Working paper no. 180. http://www.icrier.org/pdf/icrier_wp180__higher_education_in_india_.pdf. Retrieved 26 May 2013

Burgess SM, Steenkamp J-BE (2006) Marketing renaissance: how research in emerging markets advances marketing science and practice. Int J Res Mark 23(4):337–356

Chandra P, Sastry T (1998) Competitiveness of Indian manufacturing findings of the 1997 manufacturing futures survey. Vikalpa 23(3):25–36

Dangayachy GS, Deshmukh SG (2001) Practice of manufacturing strategy: evidence from select Indian automobile companies. Int J Prod Res 39(11):2353–2393

Dangayach GS, Deshmukh SG (2003) Evidence of manufacturing strategies in indian industry: a survey. Int J Prod Econ 83:279–298. http://e-dergi.atauni.edu.tr/index.php/IIBD/article/viewFile/3687/3516

IBEF (2012) Operational excellence in Indian manufacturing. India Brand Equity Foundation. http://www.ibef.org/download/Operational-Excellence-in-Indian-Manufacturing-310512.pdf. Retrieved 27 May 2013

Schwartz SH (2004) Mapping and interpreting cultural differences around the world. In: Vinken H, Soeters J, Ester P (eds) Comparing cultures: dimensions of culture in a comparative perspective. Brill, Leiden, pp 43–73

Chapter 15
Succeeding at the 'Harder' Side of Change: The 'ABCs' of High-Performance Behavior

Ned Morse, Nick South, and Gideon Walter

It was an increasingly familiar story. A well-established and successful biopharma production site, accustomed to large, relatively stable production volumes for blockbuster products, was starting to see the effects of wider changes in the industry: products going off patent, fewer products coming through the R&D pipeline, and a shift from churning out blockbusters to ramping up new smaller products and supporting increasingly competitive post-loss of exclusivity products. These macro trends were creating new pressures for the manufacturing site such as reduced and more volatile demand, less certainty about future volumes, much more intense cost pressure, and an even greater need to deliver the highest possible levels of quality and safety.

The site's management team worried about whether employees fully understood the critical challenges the company faced and what those challenges meant for the site; after all, the site had been at critical turning points in the past and warnings of impending change had come and gone. In addition, there were concerns about leaders' and employees' levels of ownership and accountability, their focus and follow-through on plans, and whether or not they could think and act cross-functionally rather than just in their "silos."

The management team's underlying worry was that the organization might not be sufficiently ready, willing, or able to meet the site's goal of becoming operationally best-in-class in this brand-new environment. Without the "people" capabilities that could bring to fruition earlier investments in change, new performance

N. Morse (✉)
The Boston Consulting Group, Atlanta, GA, USA
e-mail: morse.ned@bcg.com

N. South
The Boston Consulting Group, London, UK
e-mail: south.nick@bcg.com

G. Walter
The Boston Consulting Group, Summit, NJ, USA
e-mail: walter.gideon@bcg.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_15,

initiatives would simply not pay off as planned. The site would be unable to advance from performance that met expectations to performance that exceeded them. Top management's worry – couched in language like "how on earth can we achieve such a step change in performance without our people fully on board?" – was typical of the concerns of biopharma executives everywhere.

Later in this chapter, we will describe how this biopharma manufacturing site tapped into the science of behavior – what we call the "ABCs" – to tackle those crucial people aspects and catalyze transformative change. More broadly, this chapter sets out to show that all organizations, including biopharma production plants, can leverage basic facets of behavioral science to substantially improve operational efficiency and effectiveness. The science brings behavioral data into the workplace, establishes and accelerates feedback loops, and deliberately shifts the balance of positive and negative consequences to reward the most appropriate actions. The result? Highly engaged employees who consistently behave in ways that lead to operational excellence.

The Boston Consulting Group's (BCG) longtime study of change management, and our wide-ranging empirical work across many industries and geographies, shows that successful transformation is not just about making technical changes to manufacturing and supply chain processes. It is about getting all employees to behave in ways that respond effectively to the dynamic state of the business – and that drive value across the business as a result. It is about getting people to use the new processes fully, quickly, and consistently.

In a nutshell: biopharma manufacturers have to change itself. They can do that by focusing on the "people" side of change.

The Need for a Holistic, Balanced Approach to Change

There is no question that it is incredibly hard to effect large-scale change across an enterprise or operating unit of any size. Yet it is still surprising that the failure rates remain so high when so many business leaders have been exposed to decades of conversation, coaching, and consulting on change management. At least half of all change initiatives fail to deliver their anticipated value.[1] Some academics and consultants cite even higher probabilities of failure.

Despite the statistics, there is often great enthusiasm for change among corporate leaders. What is commonly missing, however, is access to the change tools that are critical to enabling success. This is as true of biopharma as it is of industrial manufacturing or grocery retailing.

BCG's work has found that most organizations interpret change management to mean an unwavering focus on the *operational* side of change – in other words, creating *executional certainty* and ensuring delivery of results by applying clear, cross-functional governance and transparent progress-tracking mechanisms.

Those facets are essential, no doubt, but insufficient in most cases. If companies are to achieve real operational excellence through successful change programs, they must balance their operational emphasis with full attention to the people side of

change, all the way from the leadership ranks to the front lines (see sidebar 1). This calls for *enabled leaders* who build a case for change and whose behaviors accelerate adoption of the "new way" at every stage of the change journey. It also calls for an *engaged organization* in which the workforce is motivated and mobilized, and desired behaviors are "hardwired" into new habits so that employees become assets to, and champions of, the transformation effort.

BCG's "Change Delta"

BCG thinks in terms of what we call the "Change Delta." This approach to explicitly managing change across four dimensions helps organizations flip the odds toward success by strengthening executive sponsorship; coordinating and driving execution; aligning leaders around goals, initiatives, and decisions; and, finally, boosting employee engagement (see Exhibit A).

Exhibit A Change delta breaks down change management into four key dimensions covering "operational" and "people" change
Source: BCG experience

The framework element – *executional certainty* – is more operational in nature. It helps to ensure positive results by giving top managers a forward view of progress and the means to make course corrections early enough to make a difference. A second element, *enabled leaders*, positions the whole leadership team (middle managers as well as senior executives) to "own" the change and its connection to the vision and strategy of the company – enabled leaders speak with one voice and have the necessary training and tools to manage the change. Change happens in earnest only when accountability is made explicit through robust governance structures (the central element of the Change Delta) and when managers are armed with the information to facilitate timely decisions and actions.

However, attention to those three elements of the Change Delta won't lead to sustained change unless the final element – an *engaged organization* – is

(continued)

BCG's "Change Delta" (continued)
also activated and as focused as it can be. If a critical mass of the workforce does not buy into the change effort, then top management should reconsider trying to push it through. Why? Even if the change effort manages to get solidly off the ground from an operational perspective, the lack of support from the rank and file will begin to erode any early headway, causing the effort to falter before results materialize or can be sustained. Deploying all dimensions of the Change Delta helps to ensure that as many employees as possible experience and contribute to the change process in constructive ways, leading to a more positive trajectory for change and sustained business results.

The sponsor of a major change program at a leading global medical company explained it this way: "People face constant uncertainty in their lives. Given the stress they're under these days, you must be empathetic and flexible – yet resolute. You've got to address the uncertainty among all those affected if your change effort is to be successful."

From "Have to" to "Want to"

We have learned that there are two broad families of behaviors that enable a manufacturing site, or any other type of organization, to deliver expected results. There are *results-linked behaviors*: discrete behaviors undertaken by employees that produce very specific, and typically measurable, outcomes. For example, if an organization needs to change the order of the steps in a production process in order to drive out cost, then the employees whose job has been to follow those steps must now understand the new way of doing things, and begin behaving in this new way consistently and meticulously to streamline the process and maximize its efficiency. Being half-hearted about the new steps – or lapsing back into the old way of doing things believing that it "really is just the same as the new way, only easier" – will only undercut the results expected from the process improvement.

Then there are *values-linked behaviors*: the *ways* in which employees behave that demonstrate their individual values and that transcend any single outcome or result. Take the case of an employee who gets his own work done and then keeps very much to himself; if the organization requires his team to work more cross-functionally on a new production process, that worker will need to be more transparent about his work by proactively offering to be more open and collaborative with his team. This kind of values-based behavior will constitute his new "way of working"; as such, it will help his team to make big strides with the new production process.

The reality is that, currently, one or both of those types of behaviors is likely to be out of sync with the site's strategy for transformation and with the new operational realities required to implement that strategy. This should come as no surprise: by definition, change efforts require a shift from the status quo. At the outset of a

change effort, therefore, misaligned behaviors are not necessarily a cause for concern, in and of themselves. They must simply be realigned. The real issue is if, and how easily, employees can *change* those behaviors in order to adapt to their organizations' new circumstances.

Of course, no two employees are alike. There are employees whose current behaviors are aligned to support the status quo, but who have strong "muscle memory" for change: they are ready, willing, and able to change how they currently behave in order to support new requirements. In such cases, the trickle-down effects of more traditional, operational change tools such as PMO governance, detailed initiative tracking, etc., may be enough to spark the necessary behavior changes.

But there are other workers who, while exhibiting behaviors that are equally well aligned with the status quo, are resistant to change. It doesn't matter whether their resistance is due to cynicism about previous initiatives or fears about the initiative at hand, change simply is not going to happen fast or comprehensively enough as long as they remain resistant.

For these workers – the impact of traditional change management tools is blunted and increasingly limited. Yes, these traditional change management tools can cause employees to change behaviors, but only because they have to, so as to avoid negative consequences. This kind of top-down enforcement, when used in isolation, typically creates short-lived results and puts a site's workplace culture at risk. Management ends up with grudging compliance from employees, and "just enough to get by" performance. Worse: when the pressure is off, employees often revert to their previous behaviors because the new "enforced" behaviors (as distinct from "reinforced" behaviors, explained below) never gelled into new habits.

Therefore, when planning an organization's journey toward operational excellence, the executive team must consider how exactly to augment the use of the traditional "have to" tools like deadlines, checklists, and audits by applying managed behavioral change to tap as much "want to" behavior as possible. In other words, they must reinforce rather than enforce.

BCG has developed an approach that effectively shifts the change management bias from "have to" to "want to." Rapid and lasting change requires both modes, but BCG's approach calls for changing the conventional balance between them. It does this by methodically unpacking, analyzing, and altering the contextual factors that directly enable and motivate employees' behaviors. Let's take a closer look at the "ABCs" of this behavioral science-based approach.

The ABCs of Behavior Change

The "ABC" nomenclature refers to *antecedents* (the "As") and *consequences* (the "Cs"), which are the two forces that affect *behaviors* (the "Bs"). The ABC approach is a tool to enable and motivate high-leverage behaviors that will drive near- and long-term results; it helps to create the context for intrinsic reinforcement so that employees behave in the desired ways even without management supervision.

The foundation concept for our approach is rooted in a simple principle from behavioral science: antecedents lead to behaviors, which lead to consequences

(see sidebar A Close-up of the ABCs). The approach is anchored on two simple maxims that stem from behavioral psychology. First, the behaviors that a production site may be getting right now are perfectly aligned with the context (the antecedents and the consequences) surrounding the site's employees right now. If the site's executives like these behaviors, they don't need to change the context.

A Close-Up of the ABCs

The ABCs lie at the heart of BCG's fusion of process change with rapid and precise behavior change. By definition, antecedents precede behaviors; they trigger what people say or do. In a biopharma manufacturing setting, a typical antecedent ("A") might be training in certain technical or collaboration skills on production teams; these antecedents enable collaborative behaviors. However, As do not motivate behaviors ("Bs"). It is the consequences ("Cs") that reinforce – or discourage – behaviors.

BCG has identified three "enablement" categories of antecedents: skills, clarity, and resources. Most efforts to improve or change behavior use these levers, focusing on factors that range from better metrics to improved training (see Exhibit B).

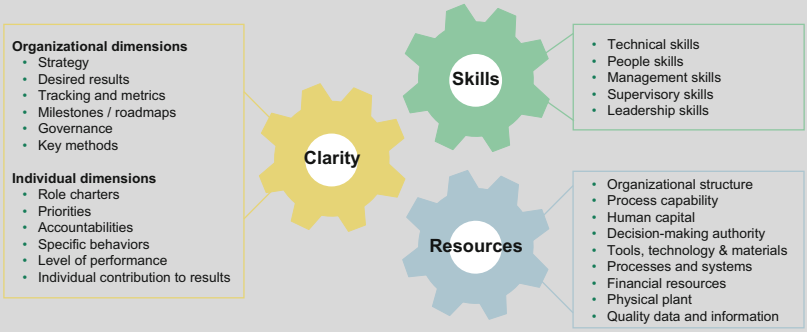


Exhibit B Critical antecedents enable employees with clarity, skills, and resources
Source: BCG Experience

Consequences determine whether desired or unwanted behaviors occur. These come from five sources:

- *Work and workplace consequences*: If a new process takes more time than the one it replaced, or if it is harder or slower to implement, these workplace consequences will discourage the behaviors needed. Conversely, if the process is easier or faster, the consequences reinforce the desired behaviors.
- *Intrinsic/self-consequences*: Pride and a sense of ownership are positive consequences; they reinforce the desired behaviors. Conversely, if employees feel foolish or embarrassed attempting to match the needed behavior, they likely won't continue trying.

(continued)

A Close-Up of the ABCs (continued)

- *Peer/group consequences*: The factors that peers celebrate or disparage are very powerful sources of consequences. Many organizations underutilize these sources, in part because many managers don't know how to align and activate them effectively. In some cases, efforts to do so backfire badly, making managers doubly shy of trying this route.
- *Individual/leader consequences*: These are consequences delivered directly by a key individual – often "the boss." Managers' habits, such as a small frown when they disagree with something or a short nod when they agree, are easily read by everyone on the team, and steer their behaviors accordingly.
- *Organizational consequences*: These are the consequences on which most managers and organizations rely to motivate employees – pay, promotion, titles, and so on. The problem is that these consequences have longer timelines and are typically not as effective.

So which consequences are most powerful? Of course, there are always competing consequences for any behavior. The more predictable, immediate, and meaningful the consequence is to the performer, the more powerful it becomes. This is what gives so much more impact to consequences coming from the work itself or from valued peers. Intrinsic consequences, such as pride or embarrassment, get their power because they usually occur as the person engages in the behavior – they are essentially immediate. Such consequences are more predictable, immediate, and meaningful than, say, getting a promotion someday or the boss perhaps noticing and commenting on some "good" behavior. This hierarchy of consequences is seen in the "power pyramid" (see Exhibit C).

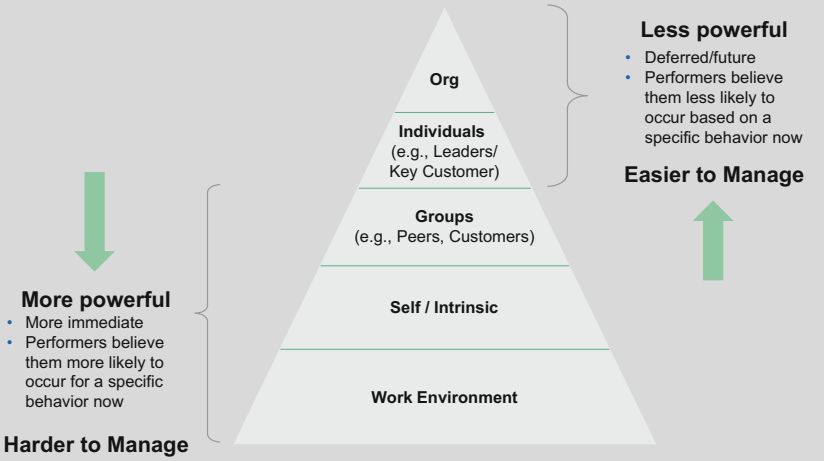


Exhibit C Five types of consequences at managers' disposal
Source: BCG Experience

(continued)

A Close-Up of the ABCs (continued)

Put simply, the Cs are the real motivators or demotivators. The As are just enablers. It is the ratio of positive to negative consequences from all sources (from peers, from the work itself, from inside the individual) that determines how sustainably high-performing the work environment is and how motivated or demotivated employees become.

Study after study show that peak performance is achieved at a 4:1 or 5:1 ratio of positives to negatives. Having more positives than this actually degrades performance, leading to insufficient accountability and learning. Ratios lower than this degrade performance; in such cases, the workplace becomes a slog where people work just for the paycheck and to avoid getting in trouble.[2]

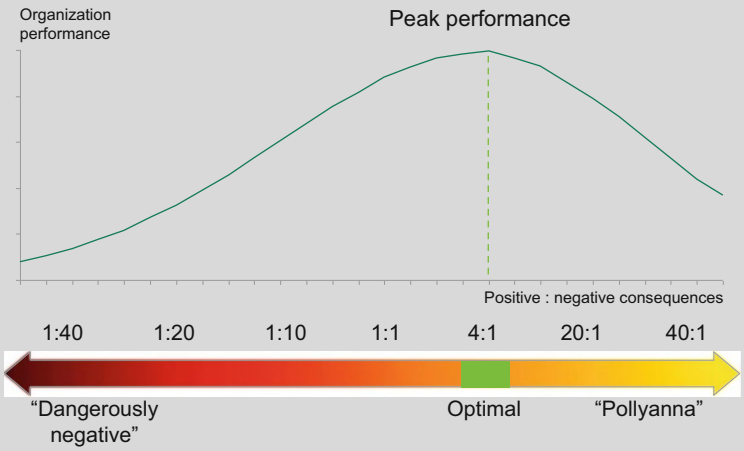


Exhibit D Consequences are most powerful when employees experience a 4:1 ratio of positive to negative
Source: Losada M and Heaphy E, "The Role of Positivity and Connectivity in the Performance of Business Teams: A Nonlinear Dynamics Model". *American Behavioral Scientist* 2004; 47; 740

Gaps in desired behavior can be traced to any of the three antecedent enablers or the five consequence motivators. Careful analysis of the performance context using these factors – their presence, alignment, and strength – will always reveal the root causes of any performance gaps, as well as the drivers of performance strengths. If these root causes can be understood, they can be managed.

The second maxim: if they don't like the behaviors, they must change the context. The "right" As and Cs are those that will create real alignment between behaviors and the change program's overall objectives; in other words, the right context will drive desired behaviors and by extension, the right results for the business.

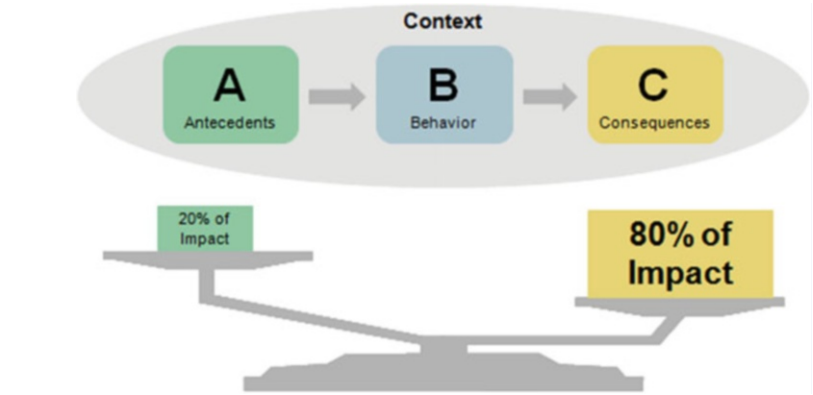


Fig. 15.1 Many organizations fail to fully leverage the power of consequences
Source: Braksick LW, "Unlock Behavior, Unleash Profits". McGraw-Hill, Inc., 1999/2007

Here's an example of how the ABC relationship usually plays out: effective collaboration within teams (a behavior) may shorten cycle times, generating positive consequences for the site and the company broadly. It may also mean that team members finally feel free of obstacles that historically caused frustration over wasted time – a positive personal consequence, to be sure. On the flip side, effective collaboration may also mean that the team works harder and experiences higher stress because cycle times are shorter – a C that team members may view as negative. Cs come in all shapes and sizes, and though they follow behaviors, they will compete to motivate or discourage desired behaviors in the future. As such, they should be viewed a critically important behavior management tool.

To improve collaboration, however, typical change management practice might say it is important to hold meetings to explain why collaboration is a good thing (an A), or to provide training in how to collaborate day-to-day (another A). The problem with such practices is that the Cs are four times more impactful in driving behaviors than the As[3] (see Fig. 15.1). Yet research, and our own experience, tell us that managers persist in spending 80 % or more of their time trying to manage by working on As, leaving Cs largely unmanaged.[4]

It's not uncommon to hear senior managers make enthusiastic declarations such as "Let's institute more team meetings to improve focus and discipline" or "Let's cascade better KPIs, and go a level deeper this time, to foster real accountability at all levels." Or perhaps they say they want to have a series of "town hall" meetings to help make communication more open. Declarations like these are typical of the strategies employed to motivate behavior change. Note, however, that all of these are antecedents; they are essential, yes, but they *enable* behavior rather than *motivate* it. Motivation comes entirely from consequences, as we will see in the example that follows.

An Example of the ABCs in Action

The ABC approach has helped to launch change in many contexts. One example comes from a site that produces large, high-precision machinery. Over a period of 3 years, the site had been operating at about four-fifths of its rated potential. The plant – one of the worlds' most sophisticated, dealing with machining tolerances within 5 microns – wanted to break through its "80 % efficiency" level while maintaining high quality. The plant's general manager had tried everything from new incentives for middle managers, to "come to Jesus" meetings with production workers. But over time, employees had learned that their production site would not come under scrutiny from upper management if they stayed just at or slightly above the 80 % line. Only when performance dropped below that line did they have to hustle because their company's bosses were displeased.

The challenge of change – getting employees to rapidly change ingrained habits – was not for the faint of heart. The plant manager pulled out every "traditional" change tool in the book, but without success. Efficiency went up for short periods of time while these tools were deployed, but performance inevitably returned to the mean as the impact of these traditional change efforts dissipated and old behaviors returned the site to the 80 % norm.

When the manager and his team were introduced to the ABCs approach, they began to see a way forward. The approach began with a detailed study of the "high-leverage" behaviors that needed to proliferate in the workplace and of the unwanted behaviors that had to decrease or disappear. Next came the actual behavioral analysis to understand *why* the current behaviors were so persistent. This analysis led to the plan for changing the ABC context – in particular, the Cs. The analysis showed very little "want to" among the employees; in the past, the only way management had worked to improve efficiency was via "have to" techniques – mostly by disciplining non-compliant employees.

After the plant's management team had been coached in how to apply the approach – placing far more emphasis on "want to" outcomes – they started to get the results they sought. Their shift to leveraging the science of behavior – managing both As and Cs with skill – yielded rapid and sustained improvement. The wins came fast. In less than 3 months, efficiency hit an all-time record and by the end of the first year it had soared from the long-term average level of 80 % to 107 % – that is, to levels above the rated maximum for the plant (see Fig. 15.2).

These changes came about with no material investments in new equipment and no major changes to business processes. Morale on the shop floor picked up significantly. The management team also learned what it takes to sustain the benefits of a plant-wide transformation: they discovered that managers have to be trained in how to effectively reinforce the right behaviors in their workforce, and to see how the celebration of success generates camaraderie, improves collaboration, and delivers results.

Biopharma manufacturing sites that are striving for operational excellence are prime candidates for a similar ABC approach. In the section that follows, we return to the story with which we opened this chapter: the production site that already had

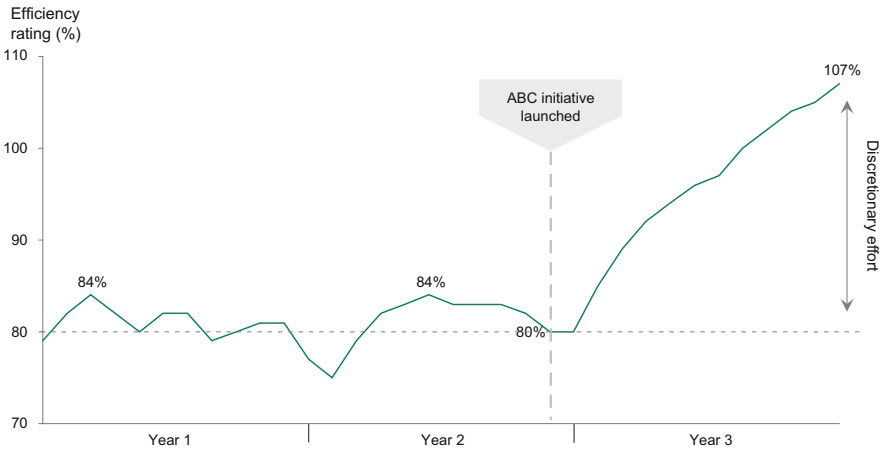


Fig. 15.2 Manufacturing company drove unprecedented workforce efficiency – up by more than 30 % above baseline (Source: BCG case experience and analysis)

high levels of operating efficiency but was yet to reach its targeted levels of best-in-class efficiency. Here is how the site's leadership team used the ABC method to achieve that breakthrough.

The ABCs in Action at a Leading Biopharma Production Site

The site's leadership team was under no illusions about the scope and scale of the challenge in front of them. The executives had worked hard to address it, responding with a battery of operational initiatives and cutting-edge techniques intended to propel production to new levels of efficiency. However, despite meaningful progress on many fronts, they were not convinced that they could effect the required change quickly or sufficiently enough to attain best-in-class efficiency levels and remain competitive in an increasingly challenging environment.

The management team decided to start transforming the workplace context by redesigning the site's organizational structure, making the "value stream" the organization's central design principle. Structuring around value streams would strengthen the levels of cross-functional working and set things up to enable greater end-to-end accountability for product quality and production efficiency. However, the senior managers saw that even this significant move, by itself, would not be enough to support lasting change. Simply put, there had to be a fundamental shift in the way things were done at the site. Employees and leaders alike needed to rethink day-to-day behaviors in order to meet the new expectations.

This led the site's senior executives to bolster their restructuring effort with a plan to identify, communicate, and embed the behaviors that would align with the site's new performance objectives. The executives assigned a behavioral change

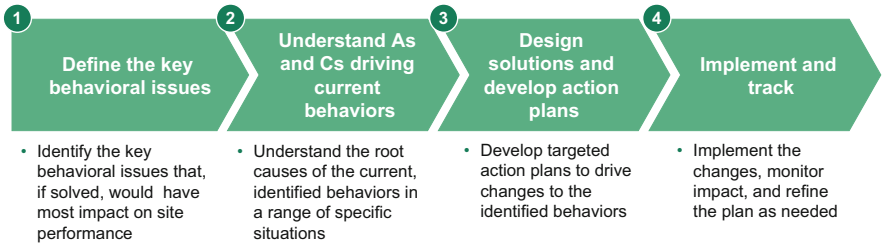


Fig. 15.3 Managed behavior change, in four phases
Source: BCG experience

team that, with BCG's support, would leverage the ABC approach to identify the root causes of employees' current behaviors, pinpoint the high-impact behaviors they wanted to optimize, and focus on making very practical changes to the As and Cs of those behaviors to do exactly that.

Essentially, the site combined the move to a new organization with a radical shift in behavioral culture and thereby positioned itself to rise to the performance challenges the site was facing. More broadly, the site added to its repertoire a new, analytical way of reviewing and addressing undesired behaviors – an approach that could be applied to any aspect of operational performance in the future, ranging from reinforcing the proper use of personal protective gear to increasing adherence to standard work plans.

The site implemented the ABC approach in four phases (see Fig. 15.3). Let's look more closely at each of those phases:

Phase 1: Define the key behavioral issues. The behavioral change team began its diagnosis by drawing on the output of previous workshops and other employee engagement activities conducted at the site over the previous 9 months – activities that hadn't yet been mined in much detail for behavioral insights. In many organizations, there is existing data like this to draw on (for example, from engagement surveys, town halls, feedback sessions, exit interviews, incident investigations, etc.). Where such data does not exist, it can be acquired relatively easily and quickly from a mix of well-structured interviews, focus groups, and workshops. The output is the same: candid insights into current workplace behaviors – and into which desired behaviors are missing or insufficient.

The team took this rich bottom-up information, complemented it with top-down insight from senior leader interviews, and captured it in a database of hundreds of comments. The database was then analyzed and organized into different behavioral themes. Four main current-state needs emerged from the discussion with the site's senior managers:

1. More ownership and accountability
2. Sharper focus and discipline in execution
3. Breakdown of siloed thinking and ways of working
4. Increase in employees' willingness to change

The executives all agreed that their site could not achieve best-in-class performance unless these four themes were addressed head-on. In order to do that, they needed to know what specific behaviors – as opposed to intangible behavioral issues – to address. The change team set out to uncover the behaviors driving these issues, with the outcome of this effort translating into specific behavioral "pinpoints." For example, the team discovered a pinpointed behavior contributing to a need for "more ownership and accountability;" if something was not going right, often individuals would not immediately flag this problem to others. This behavior was added to the list of specific undesired behaviors. Similarly, when employees hit barriers, they would at times wait for others to take action rather than trying to proactively work out solutions to make things right. That behavior was also added to the "undesirable" list.

This practical pinpointing exercise set the stage for the change team to contrast and define, again in very specific and understandable terms, the desired behaviors that they currently observed. This attention to explicitly contrasting the bad behaviors with the good behaviors was critical. Spelling out exemplary behaviors not only created buy-in by softening and balancing out the message (a potentially negative-sounding message that might cause defensiveness) but it also made the overall goal of optimizing behaviors seem attainable by showing employees where they had already reached specific targets.

The team members were now ready to investigate why the employees at the site acted the way they did – both behaviors that would and would not help drive the site toward success.

Phase 2: Understand the As and Cs driving current behaviors. The central question in this phase was: "What are the root causes of the behaviors we have now?"

Working closely with the site's managers and workers, the change team identified a set of specific practical situations in which unwanted behavioral issues were tangible and evident, as well as a few positive situations in which the desired behaviors were already the site's norm. Interviews and workshops with those closest to the workplace situations teased out the "why" behind both the unwanted and the desired behaviors. The goal was to make sure that all of the critical root-cause As and Cs were uncovered and to arrive at an understanding of exactly how they had been impacting behaviors.

To illustrate, let us take a closer look at the As, Bs, and Cs of "ownership and accountability" in two such circumstances – one with desired Bs and another with undesired Bs.

Process improvement projects. As is the case in many plants, the biopharma production site had a large number of projects underway to drive continuous improvement. However, the change team spotted several situations in which project teams experienced a negative cycle of behaviors. More than a few projects had been set up with insufficient commitment to follow through and deliver. Team leaders were saying yes to requests yet implicitly denying the reality of project difficulties. Employees would quit their project teams when the road got bumpy, meaning that those who stayed became overloaded with work.

After probing the situation, repeatedly asking "why," and encouraging honest dialogue about the As and Cs, the change team began to see powerful cause-effect relationships taking shape. For example, there was inadequate project prioritization at the site – an A – that inhibited project team leaders' ability to know which initiatives were truly important and therefore which projects to allocate time and resources accordingly. Team members, meanwhile, were stretched to the limit and lacked the time – an A – to dedicate to the project. And when they failed to attend a meeting, nothing happened. There were no negative consequences for this behavior, giving the employees more time to make meaningful contributions to other projects (that is, positive consequences).

New product introduction. By contrast, a recent new product introduction at the site had been very successful. The biopharma company's production executives had selected the site for production of a medicine with a complex manufacturing process. Despite challenges, the project's team leaders and production line operators rose to the occasion. Stronger-than-expected batch yield results were proof of how each individual took ownership of the challenge and took seriously his or her role in making the project a success.

So what made this situation different? The project team, knowing the risks they faced, took the initiative to conduct a "reverse brainstorming" exercise off-site to consider all the potential pitfalls that they might encounter in the production process – and then they began to systematically and proactively troubleshoot them, one by one. Why? For one thing, team leaders were clear about the importance and the complexity of the task at hand (an A), which helped them focus their energy and efforts. As one team member explained, "People were good at making time; the case was clear."

At the same time, the site's executives responded consistently and quickly (a very powerful C) to the regular email updates that they had asked team leaders to send. "We'd send daily updates to them during [batch] processing, and we would always get swift replies back. It motivated me," recalled one team leader. This kept reinforced the message that this project remained a top priority.

The operators who ran the new process behaved likewise. Morning meetings were standing room only; project outcomes such as yield results were communicated and each new milestone achieved was celebrated. By working on something of such clear importance, where their ideas were listened to and improvements were applauded, operators became proud of what they were achieving. A simple "Job well done – thank you!" comment from a senior executive was characterized by one team member as "one of the proudest moments" of his year. The employees' pride, coupled with the celebrations of milestones, spurred a virtuous cycle, generating even more sense of ownership and still better results.

Analyzing these successes, the change team committed to bringing these same ingredients to all of the changes facing the site: clear and consistent priorities, listening to and acting on employee suggestions, sharing data on progress as soon as it came in, encouraging and enabling operators and management to solve problems together, and genuinely celebrating improvements.

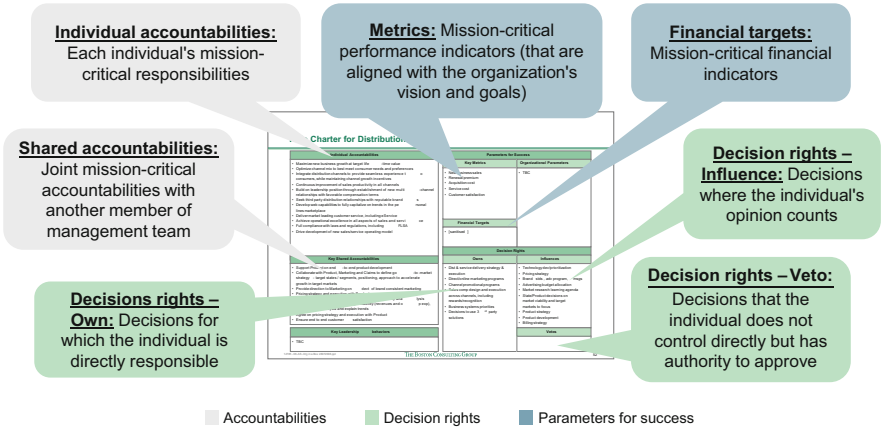


Fig. 15.4 Role charters capture accountabilities, performance metrics, targets, and decision rights *Source*: BCG experience

Phase 3: Design solutions and develop action plans. Next came the question of how to change the As and Cs to get the Bs to where they needed to be. This phase kicked off the actual behavioral change – the team designing practical changes to the behavioral context with a keen eye toward the key challenges facing the site at the time.

The team revisited the discrete operational areas for solution development that they had analyzed in Phase 2, and in a series of cross-functional workshops and interviews, they hosted discussions not only about what undesired behaviors existed but also about tactical ways to meaningfully influence them. These in-depth brainstorming exercises led to numerous great ideas about how to change As and Cs to improve discrete, results-linked Bs. Two examples of Cs that could easily be enacted: coaching managers to intervene confidently when workers did not wear proper personal protective equipment and scheduling a team dinner if everyone on the initiative team defined and submitted metrics for their area of the project on time and in full.

A challenge for the team at this point was to focus and prioritize the ABC effort itself. While there were plenty of potential opportunities to target discrete, results-linked behaviors, the bigger opportunity – with the new organizational model being finalized – was to ensure that the organization's structural change was accompanied by widespread, values-linked behavioral change to create an even stronger high-performance culture.

The change team determined that a priority focus area was strengthening ownership and accountability at the leadership level in order to eventually cascade the theme down through the rest of the organization. Key to achieving that objective was creating clarity around role expectations, so much effort was devoted to clearly defining some critical As. For instance, initiative prioritization was discussed, agreed to, and locked in, and individual accountabilities, performance metrics, and targets were captured in simple, one-page "role charters" (see Fig. 15.4).

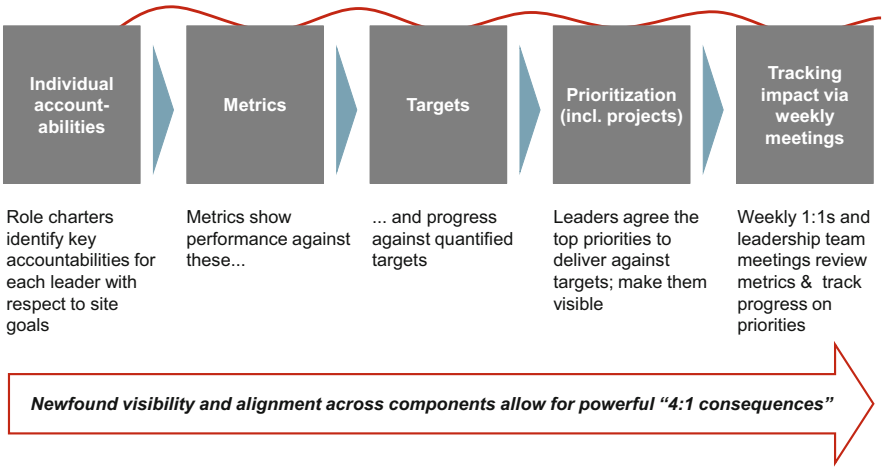


Fig. 15.5 The "red thread" unlocks powerful, largely positive, consequences
Source: BCG experience

With those behavioral *enablers* in place, the team then faced the task of creating the right Cs to *motivate* and *reinforce* leaders' ownership and accountability.

The team knew that in this case, the "right" Cs would be similar to what they'd seen having an impact during the new product introduction: peer recognition of performance improvement; and personal pride in seeing one's performance drive real value for the site; constructive feedback and pressure from peers – Cs that the science of behavior indicates are more powerful not only because they are more "immediate" and more "intrinsic" because they are collectively skewed toward the positive. To create those Cs, the team needed a way to facilitate real transparency and alignment within the leadership team.

Consequently, the solution developed by the change team was a strong "red thread" to create a *visible* and *coherent* connection across all clarified components of accountability (see Fig. 15.5). The red thread became a line of sight from the site's broadest strategic goals to:

- Each individual's key accountabilities for meeting them
- The specific metrics that would measure their individual performance against those role accountabilities
- The site's overall progress against quantified performance targets
- The site's operational performance priorities for delivering against those targets

A key element of the red thread was a weekly forum at which the leadership team reviewed and checked in, as a group, on progress against the various metrics and priorities. Out of this transparency and alignment, the consequences have begun to emerge both in this forum and outside it: encouragement, challenge, pride, recognition. The desired behaviors – focus, discipline, ownership, and accountability – follow and deepen.

Phase 4: Implement and track. In this phase, action plans were prepared and launched, progress was tracked and communicated, and successes were celebrated. Action plans were focused on strengthening accountability (as noted), improving prioritization and follow-through, and increasing collaboration as the site moved to a new organization structure and operating model.

All of these measures helped to change the site's As – by giving employees and leaders greater clarity on expectations and true priorities, and equipping them with the skills and tools to drive higher performance. But the real shift occurs because so many of the site's employees and managers learn the science of behavior and how to harness it more effectively to leverage the Cs. There are now more immediate and highly visible feedback loops on progress against key metrics and high-priority projects. Employees are actively engaged in discussions about how to solve problems and they begin to see that their ideas about how to achieve further gains are being acted on. Furthermore, the increased focus on what matters most generates pride and strengthens follow-through because employees know they are working on important site priorities that have high visibility with top management.

The last step in this journey will be to embed these desired behaviors as habits, so they become self-sustaining. Some of this is happening already; for instance, the language of ABCs is being used at the plant to create change in areas such as results-linked behaviors. Overall, though, the rollout at this production site is still in its early days. In time, a big push will be needed to further develop the capabilities of leaders and managers in key areas – for example, in prioritizing, delegating, and providing project teams with more effective challenge and support, all in order to continuously strengthen the As and Cs for the behaviors that the top management team wants to see more or less of. As this "embedding" initiative takes shape, the site will also see its managers become adept at leveraging the science of ABCs to start driving desired results-linked behaviors on a regular, day-to-day basis.

Finally, the site's ABCs initiative will be underpinned by a concerted effort to explain to the workforce the changes taking place across the wider biopharma industry and business environment and to make clear the implications of those changes for the plant – in effect, to "bring the outside in" and fortify the organization's commitment to change.

\+ \+ \+ \+

The changes being driven at this example production site are a powerful testament to what can be achieved not only at other production facilities within this biopharma company but more widely across the industry. Although many of the specific steps are obviously tailored to the plant we have described, the broad principles and practices of the ABC approach are relevant for and applicable to biopharma manufacturing sites large and small, regardless of geography.

The core conclusion remains universal and unassailable: changing behaviors is very challenging but it is absolutely essential to meaningful performance improvement. Behavioral change has been labeled the "soft" side of change to distinguish it from the operational, or "hard," side. But given the extent of the challenge, it would be appropriate to characterize it as the "harder" side of change, too.

The biopharma manufacturing sites that stick to the essentials of behavioral change – getting to the As and Cs behind the issues that cause gaps between current and required behaviors, engaging all pertinent parties in the change journey, and making plans that will change the A and C context around the behaviors that matter most to driving operational results – are the sites that will outperform their peers. They are set to become tomorrow's operational excellence exemplars.

Notes

1. Higgs M, Rowland D (2005) All changes great and small: exploring approaches to change and its leadership. Change Manag J 5(2): 121–151
2. Losada M, Heaphy E (2004) The role of positivity and connectivity in the performance of business teams: a nonlinear dynamics model. Am Behav Sci 2004; 47; 740
3. Braksick LW, "Unlock Behavior, Unleash Profits". McGraw-Hill, Inc., 1999/ 2007
4. "Performance Management Magazine", Daniels, 1989.

Chapter 16
Structures of Operational Excellence Initiatives

Thomas Friedli and Nikolaus Lembke

What Is a Structure for?

Operational Excellence (OPEX) as a continuous pursuit of improvements in all dimensions (see Chap. 2) leads to changes in existing working environments. Improvements in processes, set-up times or layout as well as adaptions in decision-making or work organization lead to productivity optimizations, but these improvements don't come without the adaption of the existing organization. As a consequence, the sustainable implementation of OPEX in organizations requires the consideration and selection of a suitable organizational support structure. But what is a structure exactly for?

According to Mintzberg (1979), one of the great scholars of organizational science, every organized human activity is based on two fundamental and opposing requirements: the division of labor into various tasks, and the coordination of these tasks to accomplish the activity. Thus, the structure of an organization can be defined as the sum of the ways in which it divides its labor into tasks and then achieves coordination among these tasks (Mintzberg 1979). Structures do not emerge out of nothing, but require a goal-orientated configuration influenced by amongst other factors – the external environment (Lawrence and Lorsch 1967; Rüegg-Stürm 2005). While an organization is reacting to environmental changes and fulfilling the company's strategy, the organizational structure provides the framework for the social-operational-control system and is influencing individual and group behavior. One scholar addressing this issue formally was Chandler with his famous hypothesis that structure follows strategy (Chandler 1962).

Taking a look at the research on organizations, a variety of ways to structure organizations can be found. Here, our focus will not be on the overall organization of a global pharmaceutical company, but on the OPEX support structure.

T. Friedli (✉) • N. Lembke
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; nikolaus.lembke@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_16, © Springer-Verlag Berlin Heidelberg 2013

Nevertheless, we will first have to take a look at the general aspects of organizational structures. We start with differentiation and integration; Differentiation refers to the way in which an organization is divided into divisions and functions, and integration to the way in which the divisions and functions are then combined (Müller-Stewens and Lechner 2005). Together, these two perspectives determine how an organizational structure will operate (Hill and Jones 2001). The basic forms of organizational structures are the result of horizontal differentiation. The horizontal differentiation takes place according to execution (functions) or objects (products, regions, projects, processes). A function-oriented structure leads to a functional organization; an object-oriented structure to a divisional organization. Divisions may themselves be product-, region-, project-or process-oriented (Osterloh and Frost 2006). A functional structure is often used by smaller- to medium-sized organizations with limited product ranges. In a divisional structure, units are guided by a corporate-level strategy which outlines the desired results. A matrix structure consists of functional departments on one axis, while the vertical counterpart is based on differentiation by a product group (Avdelidou-Fischer 2006). Over the last years, a development away from self-contained organization designs to more horizontal organizations with team- and process-based emphasis could be observed, and more and more organizational boundaries are opening up (Anand and Daft 2007). This can be the effect of a search for excellence, which usually emphasizes a stronger process orientation.

With regards to the OPEX support structure, we have to scrutinize some of the specific requirements such a structure has to fulfill. What is the right structure to support an OPEX initiative? What structure is necessary at the beginning of an OPEX implementation? How does this structure develop over time? Given that OPEX is a long-term initiative with continuous improvement as key objective, how can people be structurally empowered and supported to participate in this continuous improvement process? There is no "one size fits all" solution to these questions. Drucker (1999) states that there are only organizations, each of which has distinct strengths, distinct limitations and specific applications and any given organization structure fits for a certain time (Drucker 1999). Therefore, every company ultimately needs its own specific organizational model and only basic types of organizations, together with criteria for adapting and evaluating the most appropriate one at a certain point of time, can be specified (Ulrich and Krieg 1972).

Figure 16.1 illustrates the problem practitioners are often faced with when implementing and sustainably embedding OPEX in their organization. There are a lack of evidence about the right structure and the right amount of trained people to successfully launch and maintain an excellence initiative. To determine what level of specification of different organizational structure dimensions is needed in order to derive the optimal corresponding structure, it is necessary to take a look at the characteristics of OPEX.

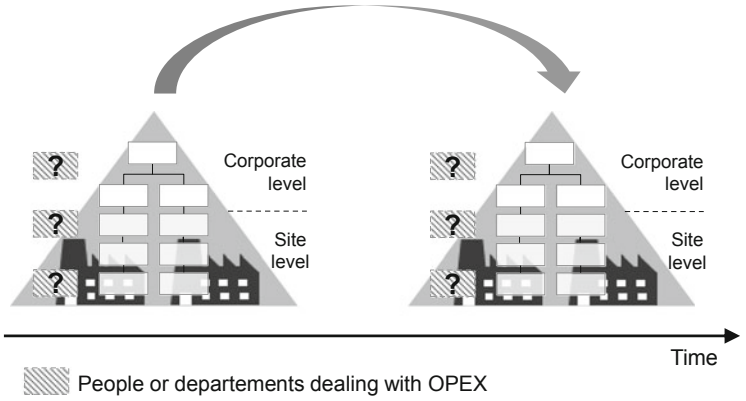


Fig. 16.1 Where to place OPEX in the organization?

What Are the Main Objectives an OPEX Structure Has to Fulfill?

Over the last years, a search for excellence could be observed in most industries. Besides the introduced excellence models in Chap. 2, Peters and Waterman (1982) identified eight attributes that characterize excellent, innovative companies. Peters and Austin (1985) condensed these findings into four critical success factors: (1) people who practice; (2) care of customers; (3) constant innovation; and (4) leadership which binds together the first three factors by the attendance of management at all levels of an organization (Dahlgaard-Park and Dahlgaard 2007). These factors provide us with a basis, but conclusions regarding the organizational structure are hard to derive from these success factors alone. Therefore, we describe the characteristics of OPEX which allows us to derive the main objectives an OPEX structure has to fulfill.

OPEX characteristics. Beside the well-known technical aspects of OPEX, like Preventive Maintenance in TPM or the Pull System in JIT, the holistic St.Gallen understanding with its Effective Management System (see Chap. 2) also provides a social aspect. Specific characteristics like employee involvement, continuous improvement or qualification make OPEX work and enable a sustainable implementation. Most characteristics, technical and social, are interconnected. Based on Pettersen (2009) and our understanding, we take team organization, cross-functional training, employee involvement, continuous improvement and high qualification as key elements of an OPEX-orientated organization (Pettersen 2009; Doppler and Lauterburg 2008).

Team organization. The percentage of employees working in multifunctional teams is much higher in OPEX initiatives than in traditional work organizations. A multifunctional team is a group of employees who is able to perform many different tasks (Karlsson and Åhlström 1996). Total Productive Maintenance (TPM), Total Quality Management (TQM) and Just-in-Time (JIT) all require a strong focus on

teamwork. TPM does not only focus on technical aspects like reliability, but also on engaging all employees in maintenance-related activities. Similar to TQM at which every employee, throughout different departments and hierarchical levels, should be concerned with quality thinking. In a JIT system, a worker cannot produce another unit until the worker at the next station signals that this other unit is needed. The output of each worker is therefore -both in terms of volume and quality – strictly linked to the output of the other workers in the section. Workers have to act as a team, rather than as individuals (Forza 1996).

Cross-functional training. Employees are usually cross-trained to increase their understanding of a process in its entirety, and make them flexible with regards to the changing needs of customers (Nahm et al. 2003). In JIT, for example, each worker must be cross-trained to perform several tasks so that employees can work wherever they are needed (Forza 1996). As a consequence, employees become more self-managing than in a command-and-control environment. Each team is given the responsibility of performing all the tasks along this part of the product flow. This means that the number of tasks in the group increases. At the same time, the use of multifunctional teams decreases the number of job classifications. Instead of having different employees performing only a limited number of tasks, the aim is to have employees who are able to perform multiple tasks within a team (Karlsson and Åhlström 1996). This is only possible with a high level of qualification.

Qualification. To achieve multi-functionality, employees need to receive training in a bigger number of tasks than in traditional work organizations. Tasks previously performed by indirect departments are now the responsibility of a team. Therefore, training in areas such as maintenance and quality control becomes essential (Karlsson and Åhlström 1996).

Employee involvement and *active participation* are perhaps the most important aspects to get closer to OPEX. Involvement is especially demonstrated by each worker's commitment to a continuous improvement philosophy (Bonazzi 1995; Forza 1996). In an OPEX environment, multifunctional teams are expected to perform supervisory tasks. In its most elaborate form, this is done through rotating team leadership among employees especially trained for the task (Karlsson and Åhlström 1996).

Continuous improvement. Involving everyone in improvement efforts is often accomplished through quality circles. These are activities where operators gather in groups to come up with suggestions on possible improvements. Tied to this is an elaborate scheme for implementing suggestions, rewarding employees, and feeding back information on the status of the suggestions. This can be contrasted with the traditional suggestion scheme, where individual employees are encouraged to leave suggestions in a suggestion-box (Karlsson and Åhlström 1996).

Based on these characteristics of OPEX, we can thus derive the objectives for an OPEX structure. At least, it should be supportive of the following requirements:

1. Makes the priority on continuous improvement transparent for all employees
2. Helps to control and sustain a long-term initiative
3. Comes with sufficient resources and capabilities

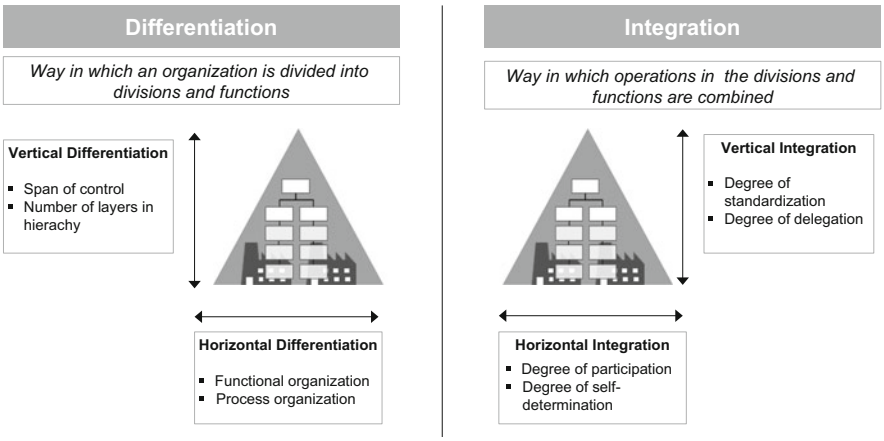


Fig. 16.2 Sub-dimensions of an organizational structure (Müller-Stewens and Lechner 2005, p. 446)

4. Supports the engagement of all management levels down to the shop floor
5. Fosters a direct and fast communication (important, for example, to create a sense of urgency for change)
6. Takes local adaptions into consideration
7. Helps to define and enforce standards also against resistance

Structural Variants for Operational Excellence

An organizational structure consists of different sub-dimensions (c.f. Fig. 16.2). Most relevant for the organizational structure of OPEX initiatives are in our opinion the following ones:

- Span of control and number of hierarchical levels
- Degree of standardization and delegation
- Degree of participation and self determination

Level of Horizontal and Vertical Differentiation

Horizontal differentiation refers to the way tasks are organized and distributed in an organization (Koufteros and Vonderembse 1998. Vertical differentiation refers to the number of hierarchical levels in organizations and separates work performance from its administration (Mintzberg 1979). As shown in Fig. 16.2, we take span of control and number of hierarchical layers as sub-dimensions to describe the vertical differentiation.

Level of span of control. Span of control refers to the number of subordinates reporting directly to a supervisor (Vickery et al. 1999). Fundamental to the span of control concept is a mathematical principle set forth by Graicunas (1933): as the number of positions reporting to a superior increases arithmetically, the number of possible interrelationships increases geometrically (Delbecq 1968). Proceeding from principle, the hypothesis has been generated that "No superior can supervise the work of more than five, or at most six, subordinates whose work interlocks" (Urwiek 1956, p. 34). The spans of control and levels in a chain of command (layers in hierarchy) may be visually ascertained from an organizational chart.

Number of layers in hierarchy. The "number of layers in hierarchy" is the degree to which an organization has many versus few levels of management. The greater the number of layers in the hierarchy of an organization the steeper the pyramid of an organization chart. There is a strong interdependence of hierarchical levels and communication channels and the degree to which vertical communication is slow, difficult, and limited versus fast, easy, and abundant (Nahm et al. 2003). It needs to be noted that span of control and layers of hierarchy are strongly connected and influence each other. The larger the span of control, the less hierarchical levels can be found in an organization.

Important for OPEX: Continuous improvement, the main philosophy of OPEX programs, requires shared tasks, empowerment, teamwork and a flat hierarchy with clear rules. As a consequence, the span of control should be higher and the number of layers in hierarchy should be less in an OPEX-supportive environment compared to traditional work organizations.

Level of Horizontal and Vertical Integration

The level of horizontal integration is the degree to which departments and workers are functionally specialized versus integrated in their work, skills, and training (Davenport and Nohria 1994; Nahm et al. 2003). As can be seen in Fig. 16.2, we use degree of standardization and delegation to describe the vertical integration. According to Müller-Stewens and Lechner (2005), horizontal integrations is described by the degree of participation and self-determination.

Degree of standardization. Standardization replaces occasional with general regulations in the form of a defined sequence of activities. Standards are important to achieve comparability of processes or areas. Further, standardization is a basis for the continuous improvement of processes. Standardization allows for a high degree of transparency, which enhances understanding among employees (VDI 2870). Standardization is strongly connected with formalization. The degree of formalization specifies the extent to which an organization uses rules and procedures to prescribe behavior (Hall 1977; Gupta et al. 1997). Thus, formalization specifies how, where and by whom tasks are to be performed. A high level of formalization eliminates dubiety, but it also limits organization

members' freedom of decision-making. To keep standards part of the daily work discipline is essential (Olivella et al. 2008).

Degree of delegation. Delegation stands for the process of transferring powers. It denotes the vertical transfer of powers and responsibilities to a subordinate hierarchical level or position (Osterloh and Frost 2006). The delegation of power enables people to make decisions, especially at lower organizational layers, and is therefore closely linked to empowerment (Malone 1997). Supervisors get relieved of workload and the professional competence of employees needs to be qualified because of rising performance requirements.

Degree of participation. Participation means the involvement of organizational members in decision-making. With an increasing degree of participation, employees are more involved in decision-making or might even make decisions jointly with supervisors. Direct employee participation can take place at different levels of an organization (Tonnessen 2005).

Degree of self-determination. To be self-determined means to experience a sense of choice in initiating and regulating one's own actions. The idea of managers supporting self-determination is conceptually and philosophically consistent with participative management and vertical job enlargement (Deci et al. 1989).

Important for OPEX: Standardization and formalization are crucial – especially for TQM. According to Kim (2007), a high level formalization is positively linked to good performance. Formalization enables an organization to use knowledge more efficient. This can be important for TQM as the analysis and evaluation of activities developed within the firm may generate a series of formal documents that lead to improved quality and to the avoidance of deviations from the established standards (Claver-Cortés et al. 2007). In addition, standards are important to achieve a high level of continuous improvement. Continuous improvement is based on active participation at all hierarchical levels, which requires delegation of power to employees(Olivella et al. 2008). The degree of delegation is closely linked to empowerment. Empowerment can be viewed as a comprehensive contemporary version of participation. It is a set of motivational techniques that is designed to improve employee performance through increased levels of employee participation and self-determination (Vecchio 1995).

Level of Centralization Versus Decentralization

Talking about global companies, the level of centralization has also to be taken into account. It reflects the degree to which decisions are made higher versus lower in the global organizational hierarchy. We call an organizational structure decentralized when decision-making has been disaggregated into a number of subunits, each making its own decisions. In contrast, an organizational structure is called centralized when decisions are made only at the corporate level of firms as a whole (Nahm et al. 2003). With the centralization of decision-making, it is important to distinguish between two kinds of decisions: work-related decisions and strategic decisions (Aiken and Hage 1968). The first refers to the amount of

participation and the autonomy workers have in making decisions about their environment, e.g., the speed of the assembly line. The second concerns "real" power or the responsibility for setting strategic direction (Koufteros and Vonderembse 1998). Decentralization allows for the interplay between a variety of perspectives and leads to a rich internal network of diverse knowledge resources (Claver-Cortés et al. 2007).

Important for OPEX: Teamwork and problem solving at a lower hierarchical level allow decision-making to be decentralized, and therefore variance and uncertainty can be managed more easily (Flynn et al. 1994). Thus, the more individuals become involved in the decision-making process, the more variety and more ideas will arise to improve differentiation strategies. As company size increases, however, decentralized structures may cause coordination problems (Avdelidou-Fischer 2006). Especially in an OPEX-driven organization that is active worldwide and therefore requiring global standards and global practices, there has to be a centralized part counterbalancing some of the local freedom.

In the following section we combine the content of the previous section – the characteristics of OPEX and the different sub-dimensions of an organizational structure – with the objective to derive an ideal OPEX support structure from the different specifications of each organizational sub-dimension.

The Ideal Operational Excellence Support Structure

Today, most pharmaceutical companies are organized according to a matrix structure. Especially big global pharmaceutical companies like GSK, Roche or Novartis are mostly following this kind of setting. Novartis' businesses, for example, are organized into six global operating divisions that report results in the five segments Pharmaceuticals, Alcon, Sandoz, Vaccines and Diagnostics, over-the-counter medicines and Animal Health (Novartis 2013). It has to be kept in mind that a given organization structure fits for a certain time and striving for OPEX, in the sense of continuous improvement, is an on-going process. Still, OPEX needs to be implemented in a structured manner and an OPEX support structure has to fulfill defined requirements. And yet, there is almost no available knowledge about meaningful sub-dimensions to discuss this support structure that has to have the right impact on the main structure of the organization. We take a look at the automotive (Mercedes-Benz) and engineering (TRUMPF) industry to learn from experiences in other industries.

What Can We Learn from Other Industries?

The Mercedes-Benz Production System (MPS) is a unified, company-wide production system that resulted from the merger of Daimler-Benz and Chrysler in 1998. Its basis is the TPS, but it has been heavily modified and structured to fit Mercedes-

Benz requirements (Clarke 2003). It has three main levels with three subsystems (work structures and workgroup, standardization, quality and robust principles, Just-in-Time, continuous improvement), 15 production principles (e.g., Participation and employee development, standardization methods and processes, pull production) and 92 methods (e.g., continuous improvement workshop, 5-S-method) (Oeltjenbruns 2000). A separate MPS organization has been established that deals with the methodologically basis of the implementation process, and supports and control it. This organization can be broken down into central, site and center levels (Clarke 2003). There is one central MPS office with an MPS office in production planning, and MPS offices in the production network on site level. All are supported by MPS experts and continuous improvement managers that are decentralized. The central MPS team on corporate level is responsible for a consistent, company-wide implementation of the MPS, as well as supporting and coordinating plants' activities. It is part of the planning department to report directly to the production board. Part of the MPS central team is responsible for the concept, the continuous evolution and the controlling of MPS. The other part of the team is composed of production system specialists in charge of training MPS trainers and preparing the implementation MPS elements. On plant level, individual MPS (project) plant teams are accountable for MPS implementation and give functional directives. Together with the central MPS team, they design work packages that cover methods and topics such as communication concepts. Individual plant level project teams are supported by the core team representing the main production centers and functioning as a facilitator for the information flow between the centrally organized MPS team and individual centers. MPS trainers also support the plant level teams; in 2003, for every 1,000 employee at each site-center, one MPS trainer with a high level of qualification (skilled worker or supervisor) was chosen. These trainers, who are accountable to the MPS center coordinator, received an intensive MPS training, including a visit to MPS best practice sites. MPS trainers have a dual function, supporting the implementation process at the shop floor level and contributing to the MPS plant team's daily work. On center level, implementation organization is broken down into three levels: the MPS steering committee at the management level, sub projects at interdepartmental levels and working groups within each department. The MPS steering committee adapts MPS standards to fit the center's particular production needs. Sub-projects refer to teams, each specializing in one of the five subsystems of the MPS. The center level implementation structure tries to assure that the MPS is adjusted to fit the context of each center (Clarke 2003).

What can we learn from Mercedes Benz? Mercedes Benz, as a global company, has full-time OPEX-responsible persons at both a corporate and site level, which together are in charge of a company-wide MPS implementation. This kind of structure shows that a central planning institution drives the institutionalization process and that the MPS central team functions as top management's extension in terms of authority and power. The central team is in charge of the company-wide implementation and together with production system specialists responsible for qualifying MPS trainers and preparing MPS implementation at site level. Training by well-experienced specialists is of high importance in the MPS, at both corporate

and site level. The local teams at site level are responsible for the local adaptability. Furthermore, we can find a high level of standardization and formalization to ensure a company-wide implementation and to control the initiatives.

TRUMPF is a German high-technology company focused on manufacturing, laser and medical technology. TRUMPF has taken a leading role in OPEX in the manufacturing industry and has been able to benefit greatly from the implementation of their production system, Synchro. According to Synchro, people in charge of the implementation first of all need committed people at all levels and in all areas. TRUMPF is involving people from all hierarchical levels. The production staff works together with "their" Synchro specialists on practical solutions. The Synchro Specialists are trained in the use of Synchro production system elements and methods. Together with managers, they appoint objectives for their production area and implement them together with the employees. The middle management is very important at this stage, as it takes on innovative solutions and makes them available across different locations. Basic teams take care of the further development of the Synchro system, and new topics are developed and provided to the staff and Synchro specialists. A supreme committee is the core team, which sets the Synchro guidelines, abuts new issues and coordinates the implementation of Synchro at the sites and reports to the production chief officer. Members are the site manager of the largest sites, the head of the Synchro Consult, the head of quality management, the purchasing manager and the works council chairman (Trumpf 2013).

What can we learn from TRUMPF? Like at the MPS, production staff and specialists are dedicated full-time to OPEX principles and tools. Further, we can find committed people at all levels and in all areas. Reporting systems with involvement of different departments, such as Synchro specialist, quality, and purchasing coming from a high hierarchical level, ensures the implementation and shows the commitment to Synchro. Cross-functional team work is empowered by authority and similar to the MPS, training has a high importance in the sustainable implementation of Synchro.

Is There Anything Like a Lifecycle Model for an OPEX Structure?

The described structures from Mercedes-Benz and TRUMPF have a high maturity level as these companies have been on their journey towards an excellence organization for many years. The organizational structure of MPS and Synchro, too, developed over time. References that structures adapt over time can also be found in previous literature. The contingency model proposed by Lawrence and Lorsch (1967) states that there is not a best way of organizing; instead, there are appropriate organizational structures for specific situations.

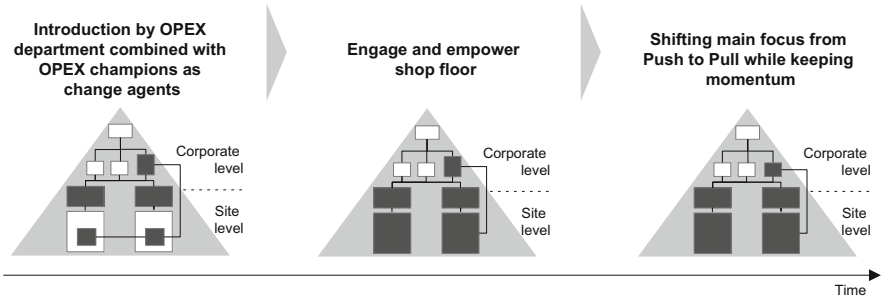


Fig. 16.3 Change of OPEX structures over time

When organizations first launch OPEX, they often start from a rather hierarchical structure, well suited for the conduction of routine operations. Such structures tend to have a high number of hierarchical levels with a low span of control. Furthermore, they show a high level of centralization and a large number of narrowly defined job classifications (high specialization). Forza(1996) showed the differences between such structures and lean organizations, and pointed out that lean production sites seem to make more use of teams when it comes to problem solving, and employees' suggestions are taken more seriously. In addition, lean organizations rely more heavily on quality feedback both from workers and supervisors, document production procedures more carefully and their employees are able to perform a greater variety of tasks including statistical process control (Forza 1996). However, launching OPEX, it is not possible to build on such an ideal organization right away. The changes from a traditional work organization to an OPEX environment require different roles for the OPEX support organization over time. That is, there is indeed something like a lifecycle model for OPEX structures. Figure 16.3 shows different variants of OPEX structures over time, which are described in the following section.

Organizational Structure for Operational Excellence

We first focus on the optimal launch phase of OPEX and then continue to describe the specifications of the introduced sub-dimensions over the lifecycle, from the introduction to a high maturity level of OPEX.

Introduction with OPEX Department Combined with Champions as Change Agents

At the beginning of each OPEX program, existing organizational structures are company-specific, with different specifications of each sub-dimension. This structure mostly will have historically grown. Wildemann and Baumgärtner (2006)

suggested different introduction variants of an integrated production system, depending on the maturity level of an organization. In addition, we segmented in corporate and site level, and derived an introduction variant that is a combination of their variants: The "Introduction with OPEX department combined with champions as change agents". Based on insights from other industries and our own experience in pharmaceutical OPEX, we suggest an implementation by a dedicated OPEX department. An independent organizational unit in charge of the OPEX introduction is established at the corporate level. The responsible person for OPEX at a global level should be a direct report to the head of global production. As OPEX should be launched as a long-term program, the unit remains permanently in the organization. OPEX is at global and at site level an interface function leading to a matrix form, which will be complemented by OPEX champions at site level. Champions are employees from the operative site level with a high technical qualification, good leadership skills and high acceptance among the employees, who are instructed by a central administrative staff unit. The OPEX champions remain in their respective reporting lines. The champion acts in his task as a change agent, consistently promoting the OPEX program and doing so in a socially responsible manner (Doppler and Lauterburg 2008). As an OPEX initiative's basic architecture must be constructed according to a company's specific initial situation and as the starting point usually is a rather strong hierarchy, the launch of OPEX should be supported by a convincing push from the corporate unit but also from the site leadership level. Therefore, the plant leaders are seen as crucial change agents, too, and have to be prepared for their role in the launch of the program.

All this results in the following specifications of the introduced sub-dimensions: As consequence of a push orientation, a vertically structured rather than centralized OPEX support structure is beneficial. Integration is reflected by a high degree of standardization and formalization. This enables a high level of control during the OPEX initiative. The involvement of more people is prepared for by establishing carefully selected change agents including the plant leaders.

Providing resources, capabilities and tools for continuous improvements is key to get closer to a continuous improvement philosophy in an organization. Furthermore, engaging and empowering employees at all management levels, down to the shop floor, is crucial. We focus on these objectives in the "Engage and empower the shopfloor" phase.

Engage and Empower the Shopfloor

According to Peters and Austin (1985), it is practicing people who are a critical success factor in achieving an excellent organization. Based on their research and the experience from other industries one can conclude that a further key factor of the OPEX journey is qualification. The qualification of employees, like the OPEX initiative in general, should take place at all levels of an organization: at the shopfloor and the organizational level, but also at the individual level. Our St.Gallen

OPEX benchmarking shows that the importance of training days as number of yearly training days per employee (all training off- and on the job) rose over the last 10 years in the pharmaceutical industry. Between 2003 and 2012, the score has more than doubled; from 3 days/year per employee in 2003 to 7.7 days/year in 2012 (c.f. Chap. 4).

To achieve more teamwork of multifunctionally qualified employees, the number of tasks in which employees receive training increases. The central OPEX department should therefore provide training, knowledge and information exchange, assessments and individual coaching, and establish a mechanism to constantly re-adjust invent the program by adding new priorities. OPEX uses a variety of improvement specialists to achieve its goals, often referred to as Black Belts, Master Black Belts, Green Belts, Project Champions or lean experts. Full-time Black Belts often lead improvement projects, while Master Black Belts generally serve as trainers and internal consultants. Green Belts are part-time improvement specialists who have received less training and take on supporting roles in improvement projects. Lean experts are specialized in value stream mapping and other typical lean tools (c.f. Chap. 18). Project champions identify strategically important projects to improve teams and provide resources. They typically receive an introduction about OPEX rather than detailed training. Intensive and differentiated training evidently is an integral part of the OPEX approach.

Adapting the organizational structure over time is necessary to provide the right resources and capabilities and to ensure lasting acceptance of the program. A higher level of qualification normally leads to a higher degree of delegation. With more qualification, the vertical transfer of powers and responsibilities to subordinate hierarchical levels or positions is possible. A higher qualification enables the delegation of power especially to the shopfloor, where decisions can be made directly. A rising degree of delegation in order to gradually empower people leads to a higher importance of horizontal integration with more participation and self-determination. To reach a high level of continuous improvement, this higher level of horizontal integration is crucial.

Shifting Main Focus from Push to Pull While Keeping Momentum

Up to this point, a high level of centralization and push from corporate level has been beneficial. With a rising empowerment and participation of employees a pull-orientated organization with a higher level of horizontal differentiation is desirable. A lower number of hierarchical levels and a higher span of control enables a more pull-orientated procedure and a more direct and faster communication. The flatter organization goes hand in hand with a higher vertical integration, described by standardization and degree of delegation. A high level of standards enables a company-wide controlling of the OPEX initiative and a high degree of delegation

empowers employees. The horizontal integration should also be higher as participation is the basis for continuous improvement in the daily work. But to develop an organizational structure towards this specifications, a high level of qualification is needed. All sub-dimension are strongly interrelated; they depend on and influence each other. For example, well-trained workers will be more productive when they are more directly involved in the decision-making process rather than being closely supervised by many layers of management. The shift from push to pull facilitates a higher degree of decentralization. This is necessary as more decentralization enables the consideration of local adaptions. The man-power at the corporate OPEX department should decrease and be partly shifted to site level where OPEX specialists concentrate on the work together with multifunctional teams. This leads to decentralized responsibilities and more easily allows for local adaptions. However, the central department will remain in place and will still be an important part of the further development of OPEX, as without a steady central push each program will lose speed and momentum over time.

Conclusions

It is reasonable to assume that the pharmaceutical industry is at its beginning to consider organizational structures as key success factor of OPEX, therefore increasingly putting emphasis on having the "right" structure in place. The term "organizational structure" refers to the way responsibility and power are allocated, and how work procedures are carried out among organizational members. As a systematic OPEX strategy leads to improvements in quality, cost, and delivery performance, an organization has to undergo changes in organizational structure. Based on the characteristics of OPEX we could derive the following focus points:

- Create structures to get the right information at the right time, and to provide the right information at the right time to the right people
- Choose the right level of standardization and formalization
- Choose the right level of participation
- Define centralized/decentralized roles and responsibilities
- Clarify decision-making responsibilities

Practitioners should consider the following sub-dimensions of an organizational structure when thinking about these challenges and implementing OPEX: Span of control, number of hierarchical levels, degree of standardization, degree of delegation, degree of participation, degree of self-determination and degree of centralization. Every company needs to define its own, specific organizational model and structures, which ensure a reasonable division of labor (differentiation) and to enable efficiency and productivity gains. In a divisional labor process, produced single solutions need to be coordinated and effectively brought back to an integrated whole. Differentiation thus serves primarily to establish cost-optimized production processes with the goal of efficiency. Integration, however, primarily is

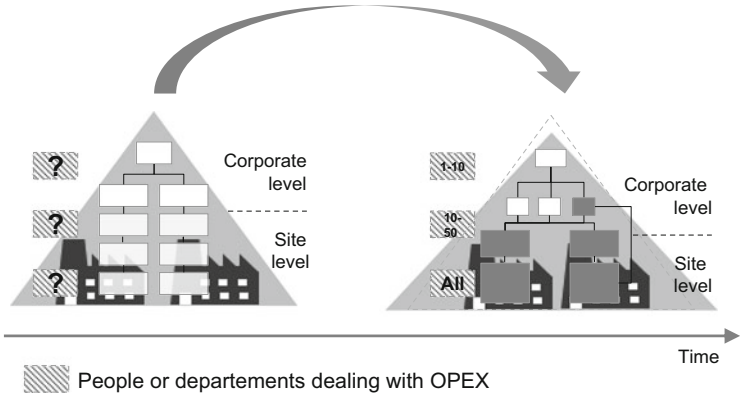


Fig 16.4 Thinking about an ideal OPEX structure

the generation of the greatest customer benefit with the aim of effectiveness. Structures are in this sense an expression of order and organization (Rüegg-Stürm 2005).

An OPEX organizational structure has to develop over time, adjust organizational sub-dimensions at the right time and accelerate the sustainable implementation of OPEX. During the whole journey of OPEX, qualification is of high importance. At a certain point in time, all employees at shopfloor level should be trained in basic OPEX methods and tools (see Chap. 18). As middle management is highly represented in the pharmaceutical industry, the involvement and qualification of this hierarchical level is necessary. Houborg (2010) analyzed Lundbeck's success in launching an OPEX program and mentions: "...the success of the program was due to all leaders from all levels participating in it together; sharing views, sharing knowledge and learning together"(Houborg 2010. Figure 16.4 illustrates the effects of adapting an organizational structure over time.

While a company's organizational structure provides the "hardware", the design of the "software" is just as important. While Chandler's (1962) principle "structure follows strategy" is omnipresent in management literature, the concept of "culture follows strategy" is still often neglected. Organizational culture is the pattern of basic assumptions that a given group has invented, discovered, or developed in learning to cope with its problems of external adaption and internal integration, and that have worked well enough to be considered valid, and, therefore, to be taught to new members as the correct way to perceive, think, and feel in relation to those problems (Schein 1984). Further, the role of leaders is substantially different in organizations on their way to OPEX than it is in traditional ones, as leaders at corporate and site level have to act as facilitators. In addition to their functions of control, they also have to create a climate that encourages participation and improvement.

References

Aiken M, Hage J (1968) Organizational interdependence and intra-organizational structure. Am Sociol Rev 33:912–930

Anand N, Daft RL (2007) What is the right organization design? Organ Dyn 36(4):329–344

Avdelidou-Fischer N (2006) The relationship between organizational structures and performance: the case of the fortune 500. Int Financ Rev 7:169–206

Bonazzi G (1995) A gentler way to total quality?: the case of the "integrated factory" at Fiat Auto; background: is there a western way to lean production? In: Cross cultural perspectives of automation: the impact on organizational and workforce management practices. Edition Sigma, Berlin, pp 125–168

Chandler AD (1962) Strategy and structure: chapters in the history of the American industrial enterprise. MIT Press, Cambridge, MA

Clarke C (2003) Forms and functions of standardization in production systems of the automotive industry: the case of Mercedes-Benz. Doctoral dissertation, FreieUniversität, Berlin. http://www.diss.fu-berlin.de/diss/receive/FUDISS_thesis_000000001108. Retrieved 23 Nov 2012

Claver-Cortés E, Zaragoza-Sáez P, Pertusa-Ortega E (2007) Organizational structure features supporting knowledge management processes. J Knowl Manag 11(4):45–57

Dahlgaard-Park S-M, Dahlgaard J (2007) Excellence – 25 years evolution. J Manag 13 (4):371–393

Davenport TH, Nohria N (1994) Case management and the integration of labor. Sloan Manage Rev (Winter) 11–23

Deci EL, Connell JE, Ryan RM (1989) Self-determination in a work organization. J Appl Psychol 74(4):580–590, American Psychological Association, Inc

Delbecq AL (1968) The world within the span of control. Bus Horiz 11(4):47–56

Doppler K, Lauterburg C (2008) Change Management. Campus Verlag, Frankfurt

Drucker PF (1999) Management challenges for 21st century. HarperBusiness, New York

Flynn BB, Schroeder RG, Sakakibara S (1994) A framework for quality management research and associated measurement instrument. J Oper Manag 11(4):339–366

Forza C (1996) Work organization in lean production and traditional plants: what are the differences? Int J Oper Prod Manag 16(2):42–62

Graicunas VA (1933) Relationship in organization. Bull Int Manag Inst 7:39–42

Gupta A, Chen IJ, Chiang D (1997) Determining organizational structure choices in advanced manufacturing technology management. Omega 25(5):511–521

Hall RH (1977) Organizations: structure and process. Prentice-Hall, Englewood Cliffs

Hill CWL, Jones GR (2001) Strategic management theory: an integrated approach, 5th edn. Houghton Mifflin, Boston

Houborg C (2010) Implementing a successful lean program: where do you begin? Pharmaceut Tech Eur 22 (9). http://www.pharmtech.com/pharmtech/article/articleDetail.jsp?id=685046&pageID=1&sk=&date=. Retrieved 3 Nov 2012

Karlsson C, Ahlström P (1996) Assessing changes towards lean production. Int J Oper Prod Manag 16(2):24–41

Kim SW (2007) Organizational structures and the performance of supply chain management. Int J Prod Econ 106(2):323–345

Koufteros X, Vonderembse M (1998) The impact of organizational structure on the level of JIT attainment: towards theory development. Int J Prod Res 36(10):2863–2878

Lawrence PL, Lorsch JW (1967) Organization and environment: managing differentiation and integration. Harvard University, Graduate School of Business Administration, Boston

Malone TW (1997) Is "empowerment" just a Fad? Control, decision-making, and information technology. Sloan Manage Rev 38(2):23–35

Mintzberg H (1979) The structuring of organizations. Prentice-Hall, London

Müller-Stewens G, Lechner C (2005) Strategisches Management: Wie strategische Initiativen zum wandel führen, vol 3. Schäffer-Poeschel, Auflage, Stuttgart

Nahm AY, Vonderembse MA, Koufteros XA (2003) The impact of organizational structure on time-based manufacturing and plant performance. J Oper Manag 21:281–306
Novartis (2013) Novartis organizational structure. http://www.novartis.com/downloads/about-novartis/people/novartis-org-chart.pdf. Retrieved 3 Mar 2013
Oeltjenbruns H (2000) Organisation der Produktion nach dem Vorbild Toyota, Dissertation TU Clausthal
Olivella J, Cuatrecasas L, Gavilan N (2008) Work organisation practices for lean production. J Manuf Technol Manag 19(7):798–811
Osterloh M, Frost J (2006) Prozessmanagement als Kernkompetenz: Wie Sie Business Reengineering strategisch nutzen können. GablerVerlag; Auflage: 5.,überarb. Aufl
Peters TJ, Austin N (1985) A passion for excellence – the leadership difference. HarperCollins, London
Peters TJ, Waterman RH (1982) In search of excellence – lessons from America's best-run companies. HarperCollins, London
Pettersen J (2009) Defining lean production: some conceptual and practical issues. TQM J 21 (2):127–142
Rüegg-Stürm J (2005) Das neue St.Gallen Management and Model. Haupt, Berne
Schein EH (1984) Coming to a new awareness of organizational culture. Sloan Manage Rev 25 (2):3–16
Tonnessen T (2005) Continuous innovation through company wide employee participation. TQM Mag 17(2):195–208
TRUMPF (2013) SYNCHRO – innovative in Prozessen. http://www.trumpf.com/innovation/synchro.html. Retrieved 11 Mar 2013
Ulrich H, Krieg WK (1972) Das St.Gallen Management Model. Haupt, Bern
Urwiek LF (1956) The manager's span of control. Harv Bus Rev 39–47
VDI 2870 Part 1 (2012) Lean production systems. Basic principles, introduction, and review
Vecchio RP (1995) Organizational behaviour, 3rd edn. The Dryden Press, Forth Worth
Vickery S, Dröge C, Germain R (1999) The relationship between product customization and organizational structure. J Oper Manag 17:377–391
Wildemann H, Baumgärtner G (2006) Suche nach dem eigenen Weg: individuelle einführungskonzepte für schlanke produktionssysteme. ZWF 10(2006):546–552

Chapter 17
Preventive Process Stabilization by Integrated Process Development

Thomas Friedli and Reto Ziegler

Introduction

Situation in Development

Compared to other industries, pharmaceutical companies still work as an assembly of functions rather than as a seamlessly integrated operation. Co-existing functions and departments do not, or only to a small extent, collaborate. This especially applies to pharma's central value stream of research – development – production. Although there are often clear interfaces between these major functions, they usually are rather narrow. Since projects from research through development to commercial manufacturing have a long lifespan, they are rarely overseen from beginning to end, but instead are independently assessed during these three distinct phases. This results in an overall lack of dedication to the success of a project; the goal is mainly to get a project successfully through one's own phase, without much consideration of subsequent requirements and specifics.

For example, this can be observed during the development of manufacturing processes of drug products: often, the future commercial manufacturing site, with its specific environment, equipment, and capabilities, is only involved at a very late stage of process development. Transfer to such sites is based on a quite low process understanding and during these transfers, only the most necessary adaptations to a process are made. This is mainly due to pressures to keep the transfer and thus the following commercial production fast, in order to timely hit the market with the finished product. Transferred and launched processes are therefore minimally stable and poorly understood from a scientific point of view. It is only at later stages, during established commercial production, that general and stability-related optimizations are addressed.

T. Friedli (✉) • R. Ziegler
University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; reto.ziegler@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_17, © Springer-Verlag Berlin Heidelberg 2013

Impacts on Commercial Manufacturing

After a launch, commercial production often faces unstable and rather inefficient manufacturing processes. This makes many minor and major adaptations necessary and at worst even post-approval changes. The latter require re-approval by regulatory authorities, and thus are time and cost intensive. Inefficient manufacturing processes can lead to a significant waste of material, human, and time resources. As a consequence, manufacturing costs are often substantially higher than they could be, with negative effects on both margin and selling price.

The lack of a thorough scientific understanding of manufacturing processes means that optimizations cannot be clearly directed, but will have to be experimental and unnecessarily effortful. As Basu (2010) appropriately remarks, "If process development is largely empirical in nature, then manufacturing becomes a 'Big Experiment' and learning on the plant floor can be very expensive" (Basu 2010, p. 30).

Integrated Process Development as Facilitator for Preventive Process Stabilization

The negative effects of an unsystematic trial-and-error approach to manufacturing processes call for measures ensuring preventive process stabilization. Process stability has to be addressed as early as during development. As this can require major organizational and managerial changes to the development and transfer process, clearly structured concepts are needed.

Existing Concepts

Many industries have designed concepts and methods to make the development process more efficient and thereby shortening it (Boyle et al. 2006; Gerwin and Barrowman 2002; Koufteros et al. 2005; Palacios and González 2002; Tessarolo 2007; Yeh et al. 2008).

As literature and case studies show, there is one specific method to avoid the issues described above: integrated development with a special focus on cross-functional teams. Central to this concept is the early integration of production during development. This allows ensuring in an early phase that the developed processes can be efficiently implemented in a commercial scale and with commercial-scale equipment. Data from practice examples demonstrate that higher collaboration of development and production in companies leads to more efficient processes (Fig. 17.1). The more advanced a company becomes in integrated development, the earlier processes are adapted and optimized to the commercial

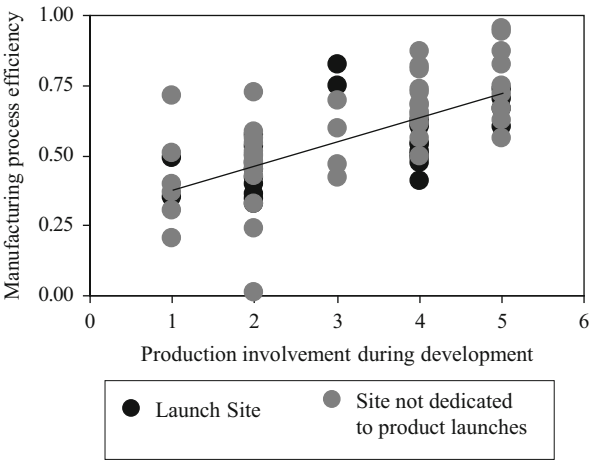


Fig. 17.1 The effect of collaboration between development and production on manufacturing process efficiency (Data taken from unpublished "Operational Excellence (OPEX) in the Pharmaceutical Industry Benchmarking 2004–2012" (Chair of Production Management, Institute of Technology Management, University of St. Gallen))

scale environment. Ideally, the processes transferred into commercial production do not need any further optimization and do not cause excessive manufacturing costs. In the pharmaceutical industry, development and production are separated and work more or less as silo-organizations. Through an improved collaboration, manufacturing costs could be significantly decreased. As a side effect, the continuous increase of development costs and time is halted.

Adoption of Existing Concepts Through Adaptation to Pharma Specifics

Due to the highly regulated development process in the pharmaceutical industry, established approaches to integrated development from other industries cannot be used without adaptations. In pharma, new products are tested for efficacy and safety in multiple clinical studies. If results are accepted by regulatory authorities, a product is approved for sale. However, the commercial production process must be identical to the process used during development and especially during production of material used in late studies. Otherwise, there will have to be additional toxicity-studies, resulting in increased development costs and time. The transfer of the production process from development to commercial production is often sped up in order not to waste time and hit the market as soon as possible. The transfer is thus often done in a rudimentary manner, with the main aim only being enabling basic commercial production. This results in inefficient commercial processes and thus excessive manufacturing costs. Major adaptations to commercial scale equipment and environment are omitted in order to not further increase time-to-market.

By now, a model of integrated development applicable to the pharmaceutical industry has been missing. Such a model should specify how to shape the integrated development process, with a focus on how to involve production into development

as early as possible, covering aspects such as when and to what extent to involve production. Through integrated development, manufacturing costs are decreased while process efficiency is increased. With a solid process design less problems will arise, and thus less costs accumulate: "quality of the development process dictates the quality of the manufacturing process that follows – and will lead to cost savings in manufacturing!" (Basu 2010, p. 33). FDA's Quality by Design initiative takes some first steps into this direction (FDA 2007).

A Reference Model for Integrated Development in Pharma

Based on findings from literature and practice experiences, we derived a simple reference model (Fig. 17.2). The model is divided into three main areas: the *organizational set-up* defines the right conditions, *cross-functional collaboration* deals with collaborations and their management, and *success factors* lead the way for a promising implementation. Together, these areas and their different characteristics form an effective concept for integrated development in the pharmaceutical industry.

Success factors are further divided into three groups – context, enabling, and team behavior factors (McDonough 2000) (Table 17.1). Context factors set the right environment for integrated development. Enabling factors facilitate context factors and make them effective. Both context and enabling factors are organizational prerequisites; however, they do not encompass collaboration, which is covered by team behavior factors. They describe how collaboration in teams can be most effective.

Capturing the Industry's Current State: An Industry Survey

To assess the current state of integrated development and cross-functional collaboration, we conducted an international survey using a questionnaire that was based on the previously described reference model for integrated development. The questionnaire was distributed electronically and contained different sections inquiring about general information, effects and benefits of integrated development concepts, organizational set-ups, success factors, and metrics. An additional section contained a RACI-matrix in which the degree of involvement of cross-functional team members along the pharmaceutical development process (Fig. 17.7) was recorded.

The questionnaire was sent out to more than 800 representatives of pharmaceutical, biotech, generics, and chemical companies from all over the world. The representatives were chosen either from development, manufacturing/operations, quality, or regulatory departments. However, representatives from the latter two departments did not feel adequate to participate and thus there were less potential participants.

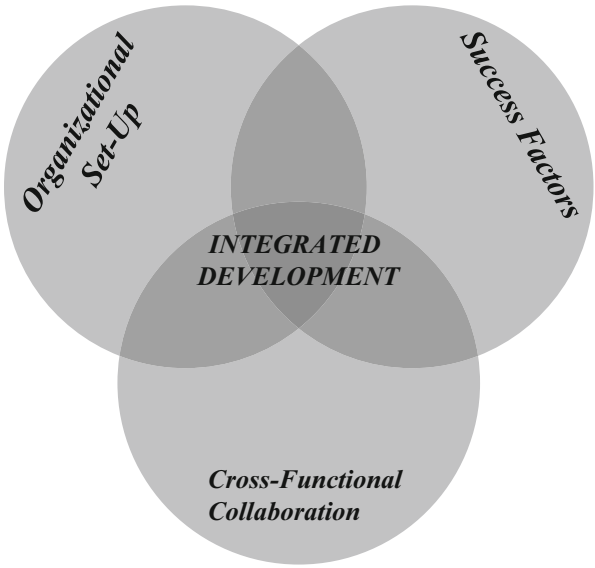


Fig. 17.2 Reference model for integrated development

Table 17.1 Success factors

Group	Success Factor
Context	Shared, common, unified goals & vision, supported by senior management
	Organizational climate supporting (cf) teams
	Team co-location
	Team reward
Enabler	Top/senior management support
	Team leadership
	Formal process
	Clear roles & responsibilities
	Resources/mix
Team behavior	Commitment
	Creativity
	Communication
	Trust & respect
	Autonomy
	Informal interpersonal relationship/social cohesion
	Cross-team coordination
	Formal knowledge transfer process

In total, there were 37 responses representing 29 companies. Out of all responses, 23 came from development, 9 from manufacturing / operations, 0 from regulatory, 2 from quality, and 3 from others (Fig. 17.3a). Participating companies were based in the following countries: Switzerland (8), Germany (8), USA (10), Netherlands (2), India (2), Austria (2), Italy (2), Israel (1), and n/a (2) (Fig. 17.3b). 12 participants were working for companies with less than 250 employees, whereas

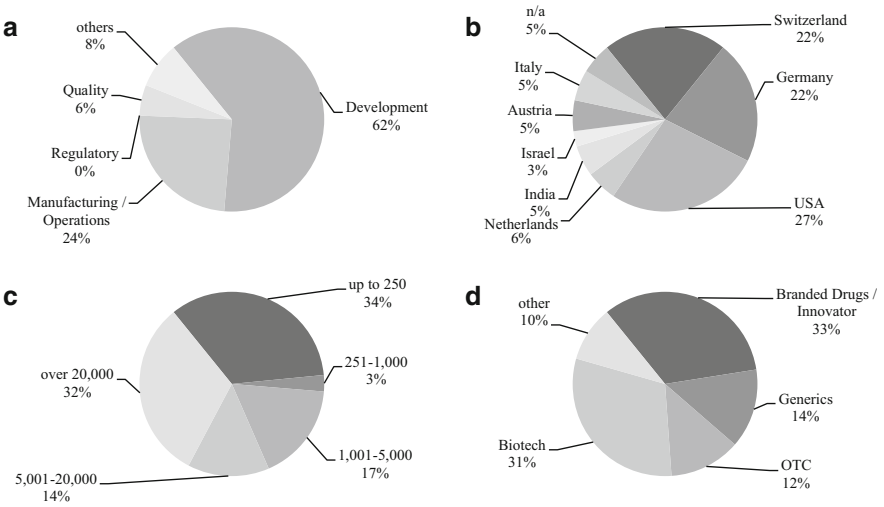


Fig. 17.3 Distribution of (**a**) participants' departments, (**b**) companies' geographical origin, (**c**) companies' size (employees), (**d**) operating fields

11 participants were working for companies with more than 20,000 employees (Fig. 17.3c). Of all participants, 24 indicated to operate in the field of branded drugs, 10 in generics, 9 to produce OTC (over-the-counter) drugs, 22 in biotech, and 7 in other fields (such as vaccines and others) (Fig. 17.3d). It is noteworthy that all participating companies were engaged in R&D as well as manufacturing activities. The participants' experience in the current position ranged from less than one to over 6 years; on average it amounted to 4 years.

Integrated Development in the Industry

Throughout the industry, integrated development is considered to have very positive effects on development (Fig. 17.4): no participant rated its impact negative, and only very few considered it to be neutral. Although integrated development's impact is considered throughout positive, there are differences between different development stages. More than 75 % of participants rated integrated development very positively, especially for full scale development and tech transfer. These are the steps that involve the most different functions and particularly combine development and manufacturing. It is obvious that manufacturing involvement during full scale development helps to develop large scale processes that are already partly adjusted to the equipment and set-up of the first manufacturing site.

Of all participants, 58 % rate their development to be *rather fully integrated* and 18 % state it to be *fully integrated* (Fig. 17.5). On average, all participants' development is rather fully integrated (72 %, Fig. 17.5). This concurs with the fact that 84 % of all participants work in cross-functional teams (Fig. 17.6). At 83%, the average of this

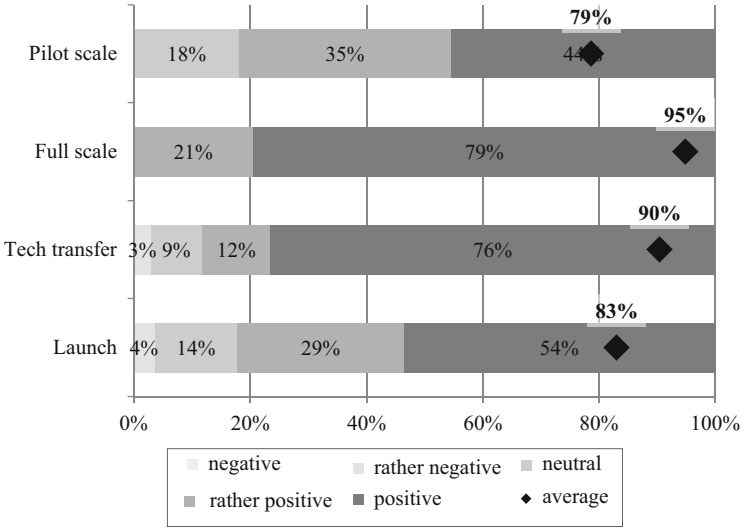


Fig. 17.4 Rating of the effect of integrated development on the performance of different development stages (n = 33)

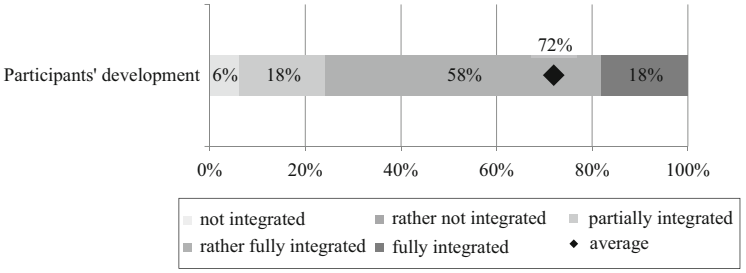


Fig. 17.5 Average integration of participants' development (n = 33)

indicator is even higher, which means that development projects are mostly carried out in cross-functional teams. However, personal ratings usually exceed the actual state. Although this value is high, there is a lot of improvement potential with regards to existing concepts of integrated development in the pharmaceutical industry.

Insights from Industry: More Integration Leads to Higher Process Performance

In order to test whether more integration in development leads to higher process performance in manufacturing, a measure was needed that would assess both indicators in a representative way and, most importantly, comparable between participants.

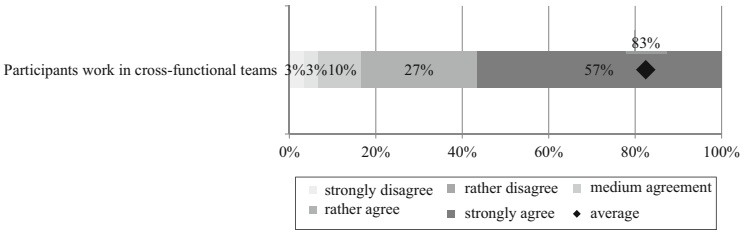


Fig. 17.6 Average degree of working in cross-functional teams (n = 30)

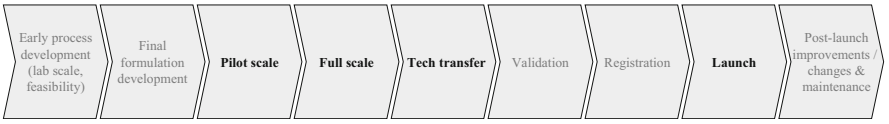


Fig. 17.7 The general pharmaceutical drug product development process

Measuring Performance

In literature on new or integrated product development, performance of investigated processes, tools, and measures is usually assessed as the amount of successful development projects, the market success of new products, or by comparing time and cost of development projects (Cooper and Kleinschmidt 1997; Griffin 1997). However, since the focus of our research is not on overall development, but rather on the development of commercial manufacturing processes, such a holistic view would distort the effects of interest, as they would be conflated with other non-influenceable events (e.g., low drug safety or efficacy). For this reason, a new indicator of performance was required.

In discussion with experienced industry representatives, it was decided to assess whether development stage objectives were met. For this, the relevant process development stages were taken from the general pharmaceutical Drug Product development process (Fig. 17.7). The following process steps represent these development stages: *pilot scale*, *full scale*, *tech transfer*, and *launch*. Additionally, it was decided to include the *manufacturing process efficiency* (in routine production). In order to get a more detailed picture, these objectives were further divided into *time*, *cost*, and *quality* objectives and assessed separately.

For each analyzed process step a general performance-index (PI_i) was generated, as shown in Eq. 17.1. It was decided to apply different weights to time (T), cost (C), and quality (Q):

Quality standards are very high in pharma and have to be maintained at such a level. Therefore, the industry is very well adapted to providing high quality. The quality part of objectives were thus only weighed $w_Q = 0.3$.

Time is a very important factor in pharma development. However, timelines are influenced by clinical development activities (e.g., clinical trials). Only in the case of early clinical success, time also gains importance in technical development. Accordingly, the time part of objectives was weighed $w_T = 0.6$.

Despite the fact that the main part of development costs is determined by clinical trials, the industry is also very cost-sensitive when it comes to technical development. Cost-related objectives were mentioned to be the most important by all industry representatives and therefore weighed $w_C = 1.0$.

$$PI_i = \frac{(T_i * w_T) + (C_i * w_C) + (Q_i * w_Q)}{w_T + w_C + w_Q} \tag{17.1}$$

The performance-indices of all five process steps ($PI_{1–5}$) were then combined into a weighted average to get an overall performance-index (PI_{total}), as shown in Eq. 17.2. According to their importance and influence on overall performance, they were assigned different weights:

Pilot scale as the first process step was considered to be the most important. In this step, early foundations of future processes are determined and basic knowledge is gathered. The more efforts at this stage are target-focused, the less effort is needed in later stages. Thus, it was weighed $w_1 = 1.0$.

The second and third process steps, full scale and tech transfer, are still important especially regarding scale-up of the previously developed process. They both were assigned a weight of $w_2 = 0.6$ and $w_3 = 0.6$.

The second to last step, launch, is considered to be less critical as it is fully based on preceding efforts. It was thus weighed $w_4 = 0.2$. This also applies to manufacturing process efficiency, which resulted in a same weight $w_5 = 0.2$.

$$PI_{total} = \frac{\sum_{i=1}^{5} (PI_i * w_i)}{\sum_{i=1}^{5} w_i} \tag{17.2}$$

Additionally, in order to measure the efficiency of launched manufacturing processes, it was assessed how many process adaptations (PA) and changes (PC) occurred on average during the first 3 years after launch. Process changes imply immense effort with regulatory authorities, resulting in time loss and high costs, therefore these were weighed $w_{PC} = 0.6$ in comparison to $w_{PA} = 0.4$ for process adaptations. The performance index PI was still considered to be the most important and objective measure, and thus weighed $w_{PI} = 1.0$. These three indicators were combined to form an indicator of overall performance (P), as shown in Eq. 17.3. Thus, the overall performance (P) gives an indication how successful technical development, and especially process development, is.

$$P = \frac{(PI_{total} * w_{PI}) + (PA * w_{PA}) + (PC * w_{PC})}{w_{PI} + w_{PA} + w_{PC}} \tag{17.3}$$

The overall performance (P) is a value between 0 and 1, with higher numbers indicating a better overall performance.

From all 37 participants, only 20 had provided enough data to reliably calculate performance (listed in Table 17.2).

Table 17.2 Participants with the corresponding values of performance (P) (n = 37), only top 10 shown

	P
Company J	0.76
Company J	0.75
Company Q	0.73
Company R	0.68
Company L	0.67
Company E	0.66
Company K	0.65
Company T	0.64
Company U	0.60
Company A	0.57

Participants with an overall performance of higher than 0.66 are considered to be high performers. This leads to a high performer quota of 25 %. Companies with multiple participants are not grouped, but treated individually. Interestingly, the five high performers were formed by four companies.

Measuring Integration

For all participants, a corresponding value of "integration" (I) was calculated. This indicator represents the degree of cross-functionality within development projects on the one hand, and the degree of implementation and application of principles of integrated development described earlier on the other hand.

It was assessed how integrated participants rated their own development (ID) as well as whether they work in cross-functional teams (CF). These two values were then combined into a weighted average, as shown in Eq. 17.4. The self-assessment of the own development was weighted $w_{ID} = 1$, whereas the degree of work in cross-functional teams was weighted $w_{CF} = 0.3$. This was mainly due to the fact that work in cross-functional teams is only one part of integrated development concepts, and thus of less influence. It has to be noted that both used values are solely based on self-assessments participants and therefore reflect a subjective perception.

$$I = \frac{(ID * w_{ID}) + (CF * w_{CF})}{w_{ID} + w_{CF}} \tag{17.4}$$

Table 17.3 shows high performers and their corresponding values of integration. The values are all between "high" (0.8) and "very high" (1). Thus it can be concluded that high perceived integration is closely associated with high process development performance.

The identified association of high performance and high integration is confirmed by a correlation analysis using Pearson's correlation coefficient. Overall performance and integration were significantly correlated at $r_{20} = 0.68$, $p = 0.01$ Pearson's correlation coefficient of both variables is $\rho = 0.75$ (Table 17.4). A linear regression also shows a clear correlation of both variables (Fig. 17.8). This is in line with previously found results in OPEX data (Fig. 17.1).

Table 17.3 High performing participants with the corresponding value of integration (n = 5)

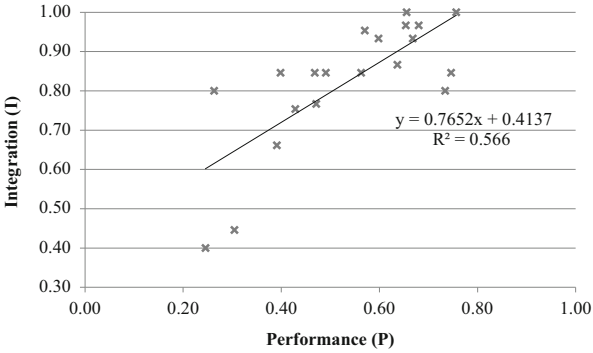
	P	I
Company J	0.76	1.00
Company J	0.75	0.85
Company Q	0.73	0.80
Company R	0.68	0.97
Company L	0.67	0.93

Table 17.4 Correlation matrix for performance and integration (n = 20)

	Performance	Integration
Performance	1	
Integration	0.75*	1

*$p < 0.01$

Fig. 17.8 Linear regression of performance and integration (n = 20)



A Descriptive Model for Integrated Development in the Pharmaceutical Industry

Insights from our international survey as well as from practical collaborations have been combined and transferred into a descriptive model. This can assist managers to develop an individual approach of achieving high integration in drug product development.

The model is comprised of three main components: (1) The actual management of the development process within approaches of integrated development, (2) the characteristics of the organizational set-up of involved organizations and departments, and (3) supporting and enabling success factors.

Managing Cross-Functional Collaboration

The RACI-matrix of involvement was analyzed. Only values that showed conformity between at least three of all five high performers were considered. This guarantees that no outliers biased the general process model. Figure 17.9 shows how high performing companies handle cross-functional process development.

	Early process development (lab scale, feasibility)	Final Formulation Development	Pilot scale	Full scale	Tech transfer	Validation	Registration	Launch	Post-launch improvements / changes & maintenance
Early stage development	**100%**	55%	*I*	*I*					
Late stage development	*I*	**45%**	**100%**	**62%**	**43%**	**38%**	29%	*C*	
Central / transfer group				*C*	28%				
Receiving / first manufacturing / launch site			*I*	38%	28%	52%	**C**	**100%**	**100%**
Regulatory	*C*	*C*	*C*	*C*	*C*	*C*	60%	*C*	*C*
Marketing		*C*				*I*			*C*
QA				*C*	*C*	10%	11%	*C*	*C*

Fig. 17.9 Model of cross-functional collaboration (involvement and responsibility) during late stage technical development

The percentages represent the amount of work done by the participant in the left column during the process step in the top row. Cells with dashed boxes indicate responsibility and leadership for the process step. Cells with "I" indicate that this participant is kept informed during the process step, whereas "C" means that the participant is actively consulted and thus slightly more involved.

Due to its non-technical nature, the process step "Registration" was not further considered; it is of course mostly regulatory-driven.

It was very obvious that in companies with the highest early manufacturing process performance (P) the involvement of the main future customer – the receiving/first manufacturing or simply launch site – started earlier during process development than in lower performing companies. Also, the extent of cross-functional collaboration was greater, meaning the different functions (mainly development and manufacturing) are actually collaborating and finding solutions together.

As expected, the analysis showed that mass work load, and with it responsibility, switched from development to manufacturing around the tech transfer step. However, the true lead switched just after the tech transfer, after the process has physically left development facilities and entered launch and commercial production plants.

Determining the Organizational Set-up

Figure 17.10 gives an overview of different ways of working in development teams. The most common form (35 %) of cross-functional collaboration in development projects is a set-up where a project leader or process owner leads and coordinates cross-functional teams through the different process stages and handles communication up-(to upper management) and downwards. Also very common (26 %) is a similar set-up where the coordinator between the cross-functional team and the responsible and decision taking management is missing. This form is less seamless but more task-and development stage-oriented and management reviews results at the end of each stage. 18 % have an overlapping system in place: parallel activities,

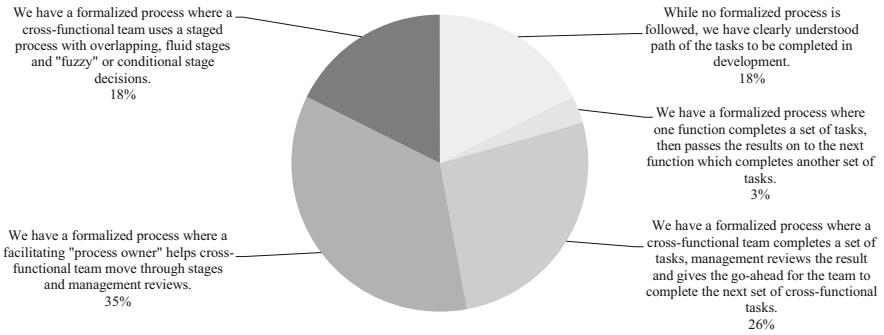


Fig. 17.10 Overview of ways of working in development teams (n = 34)

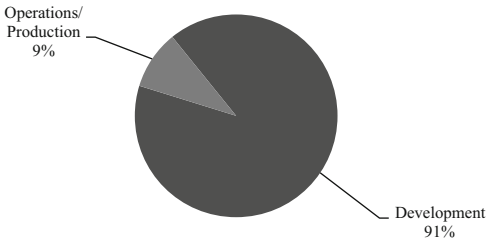


Fig. 17.11 Distribution of organizational responsibility for process development (n = 32)

seamless transitions and conditional stage decisions are top characteristics. Another 18 % have no formalized process, but still a clearly defined path and activities. Only 3 % work in a very isolated way where one team completes a task and hands over the results as well as involvement and responsibility.

In the overwhelming majority of companies, development rather than production is responsible for process development (Fig. 17.11). Although process development should be very close to commercial production, it is clearly separated and still a development task, mainly because during process development it has to be dealt with many uncertainties and changing conditions. In more than half of all participating companies, even the group responsible for the following step, tech transfer, is under development responsibility (Fig. 17.12). However, in 27 % this group is organizationally part of production. In total, 85 % of all participants do have such group facilitating transfer from development to routine production.

Surprisingly, only little more than a third (39 %) of all participating companies do possess designated launch sites (Fig. 17.13). On average, there are 2.8 launch sites per company, with a maximum number of 10 different launch sites for one of the participating companies (Fig. 17.14).

Over 60 % of all participants have designated teams for the launch of new products in place, while only a small number of companies do not (Fig. 17.15). Over 50 % of these launch teams are not directly reporting to routine production at

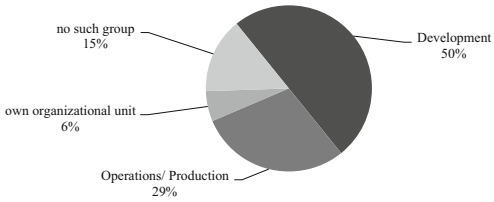


Fig. 17.12 Distribution of organizational affiliation of the transfer group (n = 34)

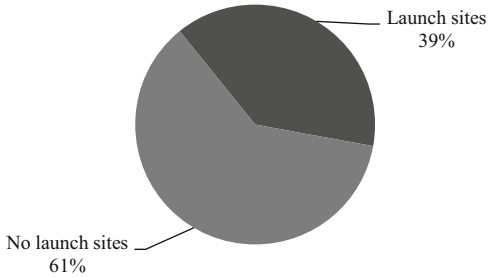


Fig. 17.13 Existence of launch sites in participants' company (n = 33)

the first manufacturing or launch site (Fig. 17.16), while the industry average is at 43 %. This means that launch teams are rather site-independent, maybe associated with or located at specific sites, but not reporting to it. It is also possible that they are identical with the transfer group and are thus, as seen in Fig. 17.14, organizationally part of and also reporting to development.

In general, transfer from one development step to the following – and associated with this often also transfer from one specific cross-functional team composition to another – is problem-free (Fig. 17.17). The more groups are involved, the less smooth a transfer at interfaces will be, and the more problems will occur. On average, smoothness of transfer at interfaces is the lowest before and during tech transfer. This is mainly due to the fact that different organizations have to collaborate closely. Employees in these different organizations, especially development and production, have different ways of thinking and approaching problems (more freely and creatively in development vs. more structured and process-oriented in production). This cultural difference, often combined with varying expectations, makes transfers at these interfaces most difficult. Especially in the end, in the time after validation up to launch, transfer is mainly within production and therefore smooth.

Supporting and Enabling Success Factors

Supporting and enabling success factors are grouped into (1) general success factors and (2) knowledge management as a special success factor.

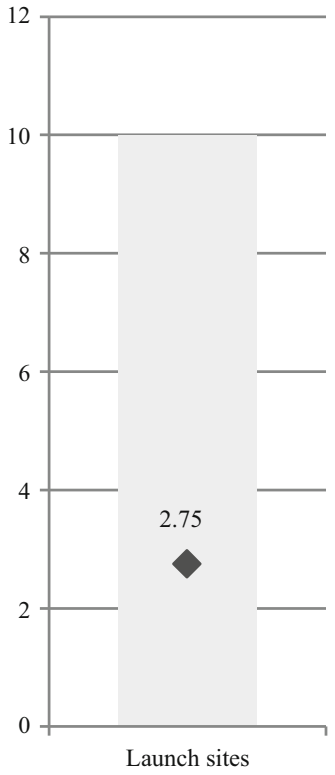


Fig. 17.14 Average and maximum number of launch sites (n = 12)

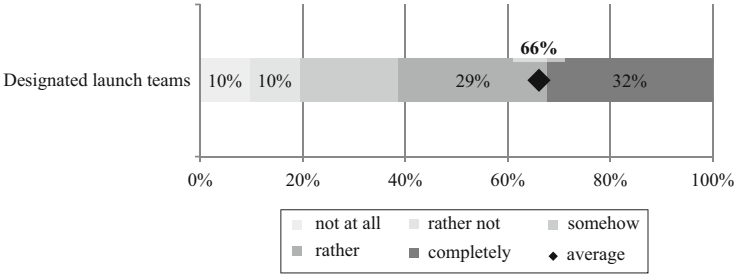


Fig. 17.15 Degree of existence of designated launch teams (n = 33)

General Success Factors

Previously identified success factors proved to be important and beneficial for cross-functional team success. As the majority of earlier studies focused on very few industries (e.g., electronics, automotive), success factors were tested for their relevance in the pharmaceutical industry.

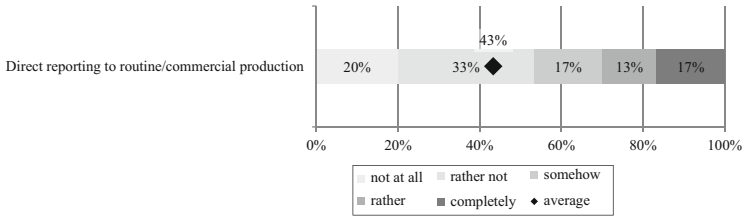


Fig. 17.16 Extent of direct reporting to routine/commercial production by launch teams (n = 33)

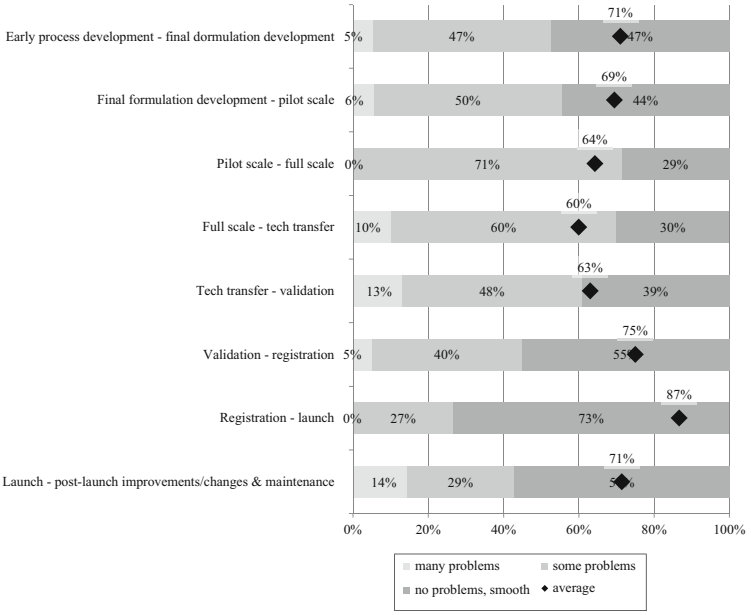


Fig. 17.17 Smoothness of transfer at interfaces during the development process (n = 21)

In general, only selected factors of each group are important. Of great influence, and widely implemented in industry are mainly contextual, enabling, and technical success (Figs. 17.18, 17.19, and 17.21). Team behavior factors seem to be less important (Fig. 17.20).

Common goals and visions, *organizational climate supporting cross-functional teams*, and *clear roles and responsibilities* proved to be the most important success factors across all and high performing participants. High performers rate the former two factors even higher than the average.

Top management support is found to be important, though its effect is not crucial for high performance. The same applies to *creativity*. Both *top management support* and *creativity* are mentioned with a below-average frequency by top performers.

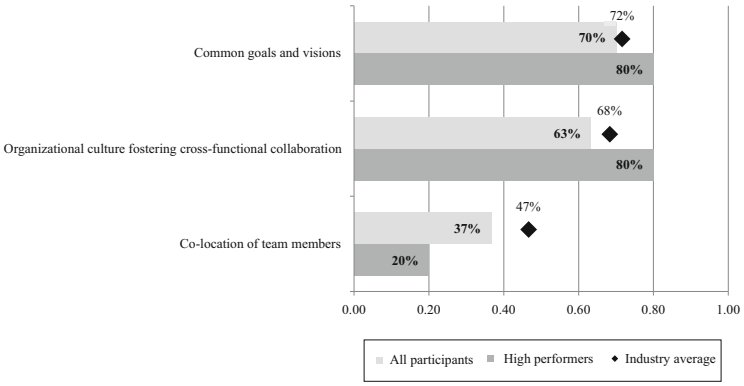


Fig. 17.18 Contextual success factors (n = 30 for all participants, n = 5 for high performers)

Interestingly, *team co-location* is rated very low across all participants, and even below average by top performers. This corresponds to the fact that most companies operate internationally, and often have separate sites for development and for (first) manufacturing. Thus, ways to bypass this distance had to be found.

Knowledge Management as Success Factor

Effective knowledge management is key to a scientific approach to development. It helps to gain thorough process understanding and thus develop stable and robust processes.

Our expectation was that a *formal knowledge transfer process* (both directions) would be highly beneficial and greatly impact process development performance. Formal knowledge transfer should be beneficial by helping gathering and reusing gained knowledge, thereby speeding up future development. However, its frequency was very low, across all participants and even more so for top performers. This means that companies have no formal process in place but rather transfer and share knowledge in an informal and possibly inefficient, unsystematic way.

High performing companies have a higher degree of *similarity of equipment in pilot and commercial manufacturing plants*. This of course facilitates development of processes tailored to the future commercial environment. *Knowledge of capabilities of launch/first manufacturing site* is a tremendous advantage for similar reasons, and therefore widely spread across the industry. *Secondary manufacturing site capabilities knowledge* is less important during development, especially for high performing companies.

During the first development steps up to product launch, almost half of all companies have *shared knowledge management solutions* in place (Fig. 17.22). Such platforms help to make knowledge available to everyone involved, independent

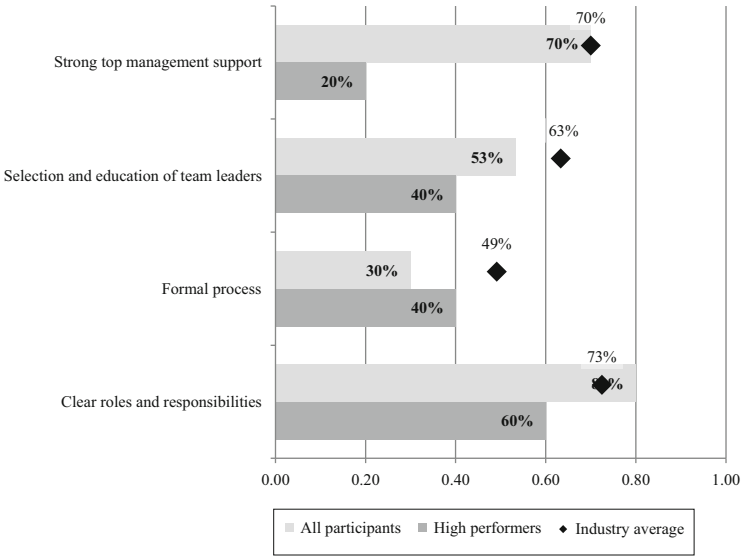


Fig. 17.19 Enabling success factors (n = 30 for all participants, n = 5 for high performers)

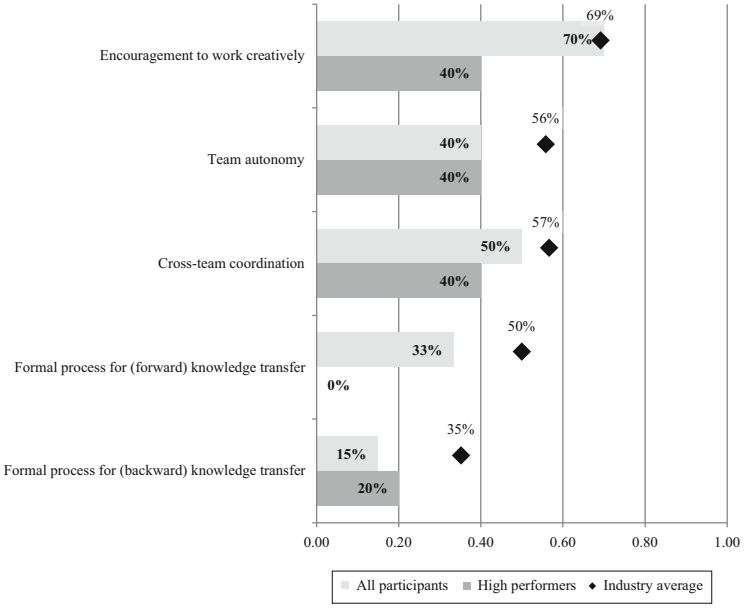


Fig. 17.20 Team behavior success factors (n = 30 for all participants, n = 5 for high performers)

of when or by whom it has been originally acquired. By this, prior knowledge can be re-used and certain development steps shortened by avoiding double work. Interestingly, only one of the high performing companies has such a solution in use.

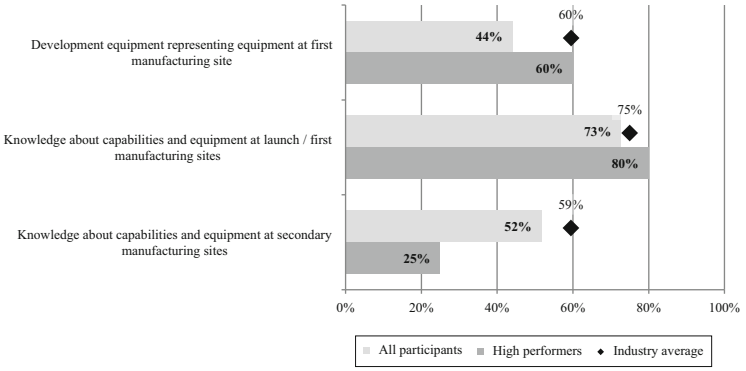


Fig. 17.21 Technical success factors (n = 30 for all participants, n = 5 for high performers)

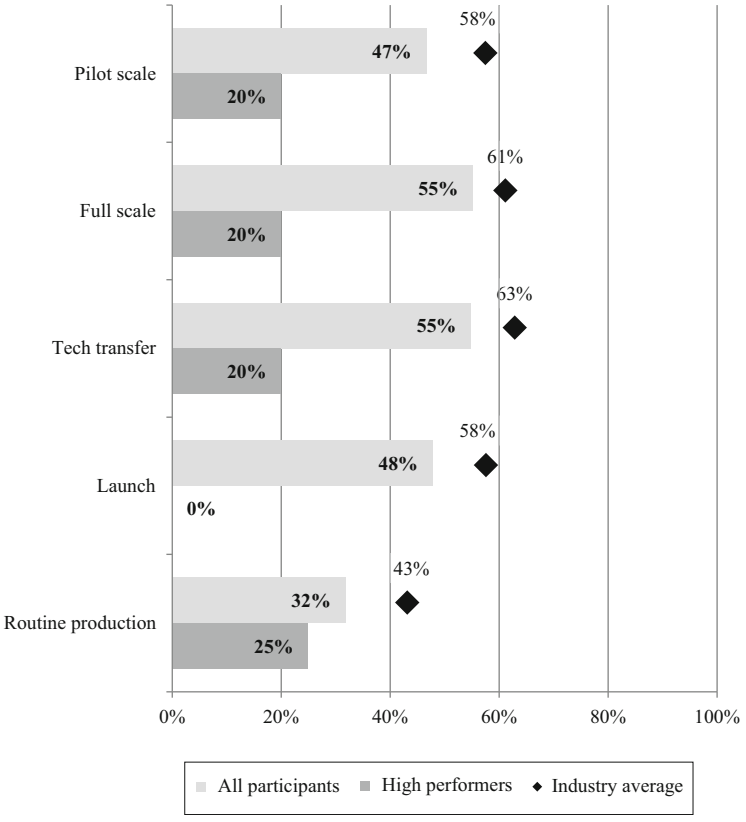


Fig. 17.22 Knowledge management solution in different development stages (n = 30 for all participants, n = 5 for high performers)

Conclusion

In a successful approach to integrated development in the pharmaceutical industry, development projects follow a formal process with clear roles and responsibilities. Process development is under development responsibility of late stage development. Ideally, a transfer organization exists, belonging to the launch site or at least to the production department and thus really representing manufacturing's capabilities. The transfer organization is involved in process development and represents the commercial manufacturing or launch site. Thereby it is assured that the environment, equipment, and capabilities of commercial production are considered and processes are specifically developed to be efficient in commercial production. The transfer organization takes over responsibility from development after successful tech transfer. As soon as commercial production is established, responsibility is transferred from the transfer organization to routine production. The transfer organization becomes active again in case the production is transferred to a secondary site at a later stage.

Top management commitment and an organizational climate fostering cross-functional collaboration are important for successful concepts. Thereby all needed resources are available and employees are encouraged to collaborate with other departments. Furthermore, common goals and visions are important for development project success, to eliminate silo-thinking and to foster individual interest in overall project success. This overall team and project performance can also be rewarded. The more equipment and capabilities of development and commercial production are aligned, the smoother the transfer runs. Harmonization efforts further increase process stabilization.

Not yet widely established but crucial are singular, integrated knowledge management solutions. They help to build up and preserve valuable knowledge, which can then be re-used for new development projects, speeding up development time and decreasing efforts. However, it is crucial that there is only one system in place, and that data is available to all responsible employees at all time. This knowledge can then also be used to resolve manufacturing issues. A scientific approach to development is based on an accessible, large amount of data and empowers preventive process stabilization.

References

Basu PK (2010) Process variability and design space (the regulatory environment for OPEX). GSIA, Basel

Boyle T, Kumar V, Kumar U (2006) Determinants of integrated product development diffusion. RD Manag 36(1):37–54. doi:10.1111/j.1467-9310.2005.00414.x

Cooper RG, Kleinschmidt EJ (1997) Winning businesses in product development: the critical success factors Robert G. Cooper and Elko J. Kleinschmidt, Research-Technology Management (July–August 1996). J Prod Innov Manag 14(2):18–29. doi:10.1016/S0737-6782(97)83946-X, 132

FDA (2007) Pharmaceutical quality for the 21st century a risk-based approach progress report. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm128080.htm. Retrieved on August 26th

Gerwin D, Barrowman NJ (2002) An evaluation of research on integrated product development. Manag Sci 48(7):938–953. doi:10.1287/mnsc.48.7.938.2818

Griffin A (1997) PDMA research on new product development practices: updating trends and benchmarking Best Practices. J Prod Innov Manag 14(6):429–458. doi:10.1111/1540-5885.1460429

Koufteros X, Vonderembse M, Jayaram J (2005) Internal and external integration for product development: the contingency effects of uncertainty, equivocality, and platform strategy. Decis Sci 36(1):97–133. doi:10.1111/j.1540-5915.2005.00067.x

McDonough EF (2000) Investigation of factors contributing to the success of cross-functional teams. J Prod Innov Manag 17(3):221–235. doi:10.1111/1540-5885.1730221

Palacios TMB, González FJM (2002) Assessing the validity of new product development techniques in Spanish firms. Eur J Innov Manag 5(2):98–106. doi:10.1108/14601060210428195

Tessarolo P (2007) Is integration enough for fast product development? An empirical investigation of the contextual effects of product vision. J Prod Innov Manag 24(1):69–82. doi:10.1111/j.1540-5885.2006.00233.x

Yeh T-M, Pai F-Y, Yang C-C (2008) Performance improvement in new product development with effective tools and techniques adoption for high-tech industries. Qual Quantity 44(1):131–152. doi:10.1007/s11135-008-9186-7

Chapter 18
Matching Problems with Tools

Thomas Friedli, Christian Mänder, and Daniel Bellm

The objective of this chapter is to provide guidance on which methods and tools should be applied for what kind of OPEX problems. The main reason for adding this topic is the observation that most of the existing approaches to Operational Excellence (OPEX) are good in providing training in diverse methods and tools from the quality management/lean sigma point of view. However, the training does not always help to be able to match a problem with the most appropriate tool. We will start with an overview about the most widespread tools in improving production, followed by a discussion about how to structure the application of tools within of an OPEX initiative.

Overview of Tools

In order to provide a profound understanding of the use of tools, it is necessary to discuss them in the context of objectives that can be reached by their application. A tool and its mere application are not just self-contained. This becomes apparent when looking at the further development of Deming's famous PDCA cycle[1] by Kaoru Ishikawa. He expanded the two steps "Plan" and "Do" by an extra step each, making six steps out of the four: Determine goals and targets, determine methods of reaching goals, engage in education and training, implement work, check the

[1] Cf. Deming

T. Friedli (✉) • C. Mänder • D. Bellm
University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; christian.maender@unisg.ch; daniel.bellm@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_18, © Springer-Verlag Berlin Heidelberg 2013

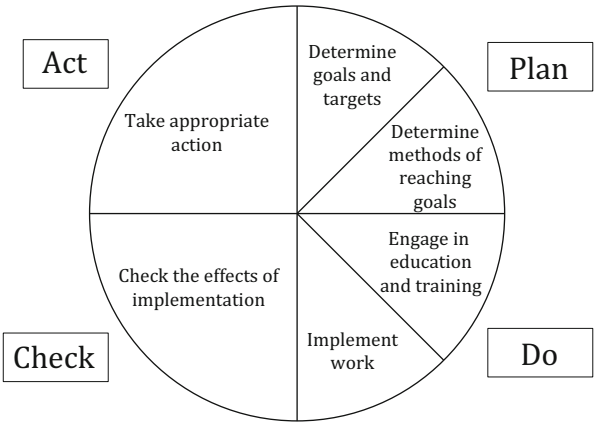


Fig. 18.1 Overview of the main PDCA cycle steps follows Deming (1986)

effects of implementation and take appropriate action.[2] These kinds of cycles are typical for many approaches in quality management/improvement. It is a pragmatic step-by-step approach for collecting data, analyzing them and deriving solutions (Fig. 18.1).[3]

In the approach shown above, the methods are derived from the goals and targets to achieve and not simply to be applied. The successful application of tools is further complicated by the fact that most of these tools rely on an underlying philosophy. Only applying the tools will therefore not have a long-term impact like Stone[4] citing Seddon and Caulkin[5] stated: "Companies that use only the toolbox without embracing the underlying philosophy [and] are unlikely to gain more than limited and temporary results."

Now, we will shortly describe some of the most widespread tools in improving production environments. Most of these tools stem from the classical quality management approaches. This is followed by separate discussions of tools which are mostly named when talking about Lean and Six Sigma. We are fully aware that these approaches could also be discussed under the umbrella of quality management in general. We finalize this overview with a look at the combination of Lean and Six Sigma and a description of a tool to prevent failures, the so- called FMEA (Failure Modes and Effects Analysis).

[2] Cf. Ishikawa (1985)

[3] Cf. Nicholas (2011), p. 51

[4] Cf. Stone (2012), p. 113

[5] Cf. Seddon and Caulkin (2007)

Basic Problem Solving and Improvement Tools

The Seven Basic Problem Solving Tools

The Seven Basic Problem Solving Tools are a set of widespread graphical techniques that foster the understanding and visualization of various issues related to quality.[6] These tools are called basic because they are suitable for people with little training. Besides, they can be applied to better understand a lot of quality problems.[7] They go back to Kaoru Ishikawa, one of the leading early quality management thinkers in Japan. A decisive factor for the introduction of these tools was the observation that a majority of workers had a reservation against more complex statistical approaches that are associated with Statistical Process Control. In today's state-of-the-art OPEX initiatives most (if not all) employees are usually trained in these seven tools so as to enable them to get involved in improvement efforts.

The Seven Tools are:

- Check Sheet
- Histogram
- Pareto Chart
- Scatter Diagram
- Stratification (alternatively, flow chart or run chart)
- Cause-and-Effect (also known as the "Fish-Bone" or Ishikawa) Diagram
- Control Chart

In summary, the Seven Basic Quality Tools help to structure quality related issues by providing simple and easily understandable means to visualize interdependencies between different factors. Furthermore, they support the analysis of the development of a figure over time or frameworks to derive possible root causes for problems. We provide a short summary of each tool below.[8]

Check Sheet (or Tally Sheet)

In a Check Sheet, data from observations is recorded and tallied. The content and format vary considerably as it is always designed to a particular purpose. It is crucial that the categories, terminology and layout of the sheet are carefully determined. It should be designed to avoid inter observer subjectivity. Figure 18.2 provides an overview of a Check Sheet and shows that the type of defects and the cause of effects can be analyzed in an easy way.

[6] Cf. Nicholas (2011), p. 37ff.

[7] Cf. Ishikawa (1985)

[8] These descriptions follow Nicholas (2011), pp. 37–44, for more details see there

	Type of defects			
Causes of defects	Number of stoppages	…	….	Data collected by: John Doe Date: Februar 18.2.2013 **Total**
Humidity	III	…	…	3
Temperature	…	…	…	…
				…
Total	3	…	…	

Fig. 18.2 Check Sheet (Rampersad (2001))

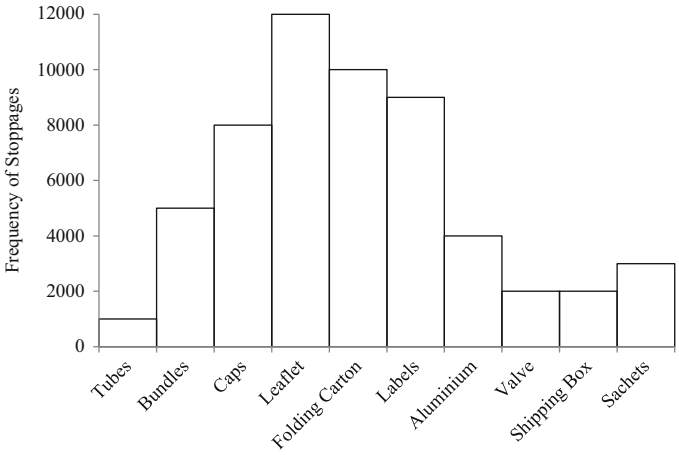


Fig. 18.3 Histogram (Modeled after Rampersad (2001))

Histogram

A Histogram graphically shows the frequency distribution of a variable. It does not show the root cause of the variation or the problem itself. This diagram just provides an idea in what frequency different problems occur within the process.[9]

Figure 18.3 shows an example of a Histogram showing the frequency of the component related stoppages for all production lines of a company. Here the variable is the stoppage of the process and the idea was to focus on the cause of the stoppages. On the horizontal bar the different components can be seen, on the vertical bar the frequency of the incidents is indicated.

[9] Cf. Nicholas (2011)

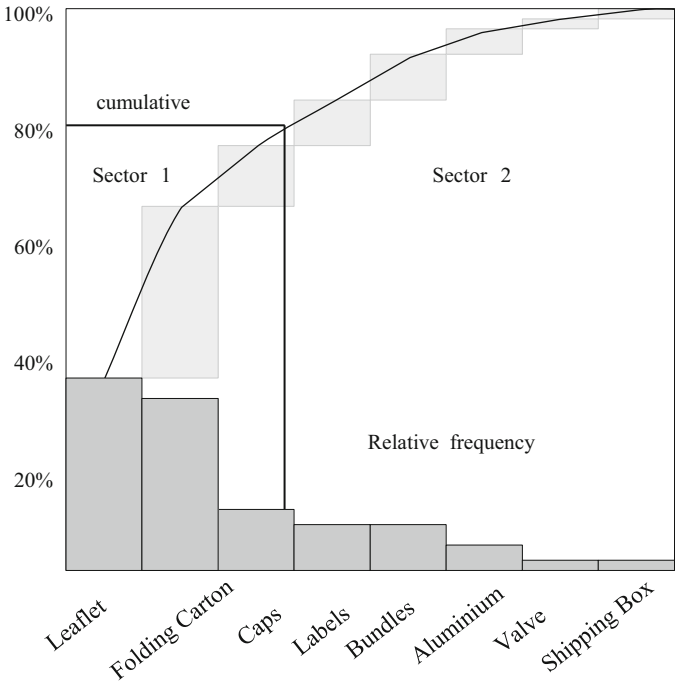


Fig. 18.4 Pareto Chart (Modeled after Rampersad (2001))

Pareto Chart

The Pareto Chart is a tool to help to focus on the important problems, e.g. the ones with the biggest impact on the topic we are dealing with. Typical applications might be the identification of influencing factors on a specific quality critical process parameter or the analysis of the usage of units that have to be held on stock (stock keeping units). The main idea is to identify the few problems that occur with the greatest frequency. Those problems have the biggest impact on the considered issue. The Pareto Chart supports the Pareto Analysis. It looks similar to a Histogram except that the bars are ordered starting on the left with the bar representing the greatest frequency. Usually the cumulative contribution of the total problem is shown as well. In Fig. 18.4 below the example of the Histogram is translated into a Pareto Chart. In contrast to the bars of a Histogram which indicate the absolute frequency, the bars visualized in the Pareto Chart (Fig. 18.4) show the relative frequency of a problem's items. In addition they are ordered based on this frequency. Usually as a rule of thumb for the subsequent improvement steps, factors contributing to 80 % of the total problem are investigated in more detail.[10]

[10] Cf. Rampersad (2001)

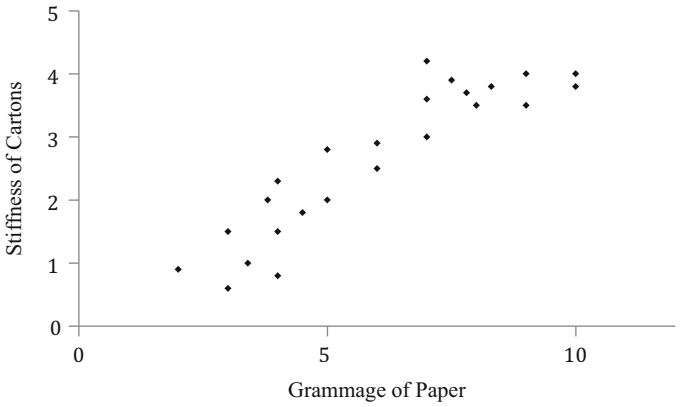


Fig. 18.5 Scatter Diagram (Modeled after Rampersad (2001))

Scatter Diagram

A Scatter Diagram reveals possible relationships between variables. Such a plot shows if there are possible correlations between two of the focused variables. However, it does not show which lever is the root cause for correlations. It simply suggests a potential relationship that needs further investigation. Possible relationships can be evaluated based on the trend of illustrated data points within the diagram. Typically observations in a Scatter Diagram are positive or negative relationships as well as no correlations.[11]

Figure 18.5 shows an example of a Scatter Diagram with a strong positive relationship of the grammage[12] of paper and the stiffness of folding cartons. The result of this diagram indicates that with a higher grammage of the used paper the stiffness of cartons increases.

Process Flow Chart

A Process Flow Chart shows the different process steps and helps to pinpoint sources of problems. There is no standard for visualizing the process flow. However, everything that helps to describe the process in an understandable way is appropriate. That is why the main purpose of a Process Flow Chart is to portray the main steps and elements of a process. Another main focus is how the individual

[11] Cf. Nicholas (2011)

[12] Grammage is a metric measure of paper weight based on the same square meter sheet of paper (g/m^2)

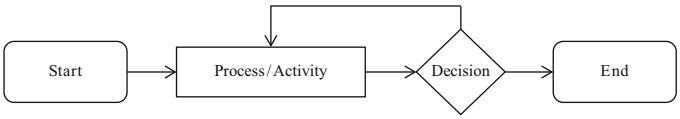


Fig. 18.6 Standard symbols for a Process Flow Chart (Cf. Rampersad (2001))

steps correlate. In the end, the chart should show all relevant activities. This includes value added and non-value added activities. How detailed the chart is drawn will depend on the individual problem and process (Fig. 18.6).[13]

Cause and Effect Analysis

This tool is used to identify all possible causes for an outcome (effect). Another, more famous name, of the Cause and Effect Analysis Diagram is the Ishikawa Diagram. The main categories in the Ishikawa Diagram are environment, materials, people, methods, equipment and measurement. Those influence factors are shown as the six categories in Fig. 18.7. The Cause and Effect Diagram Analysis is usually conducted by a small team. In a brainstorming session, as many ideas for root causes as possible, are generated. All ideas listed on the diagram are considered at a next step as possible root causes or as starting points for more detailed scrutiny. This approach leads to an overview of the influence factors that may help to find reasons for the problem being investigated. This procedure also helps to identify who and what is involved in the process.[14]

The result of the mentioned analyses is shown as an example in Fig. 18.7.

Process Control Chart (Run Diagram)

A Process Control Chart shows the results of observations along pre-given intervals. These observations are plotted against time to reveal any extra-ordinary incidents. In case the period of observation is not long enough, the diagram often shows no clear pattern. Otherwise, trends and variations in long running processes can be detected. For this reason, the Process Control Chart is limited with an upper control and a lower control limit line that helps to identify when the operators have to intervene in the process.

Figure 18.8 shows a data point that is located outside the defined target area. In this case the project team has to react and must identify possible root causes for the abnormality.[15]

[13] Cf. Nicholas (2011)
[14] Cf. Nicholas (2011)
[15] Cf. Nicholas (2011)

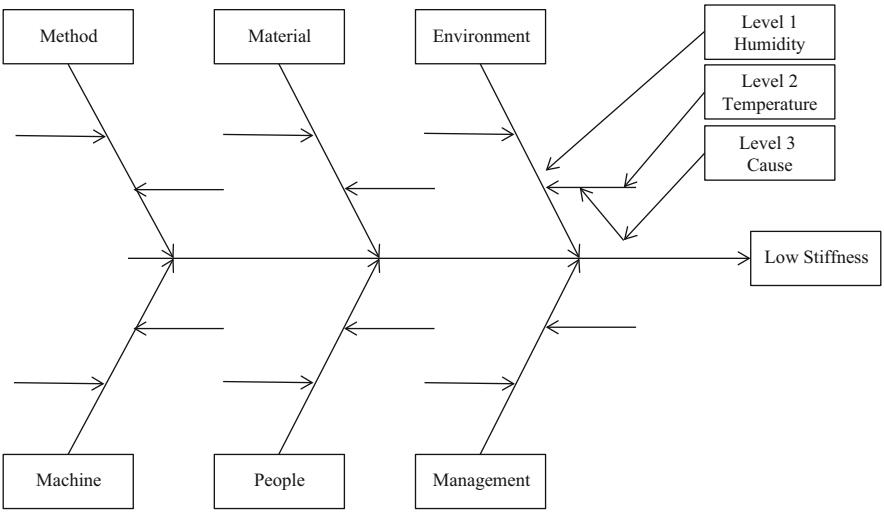


Fig. 18.7 Cause and Effect Diagram (Cf. Rampersad (2001))

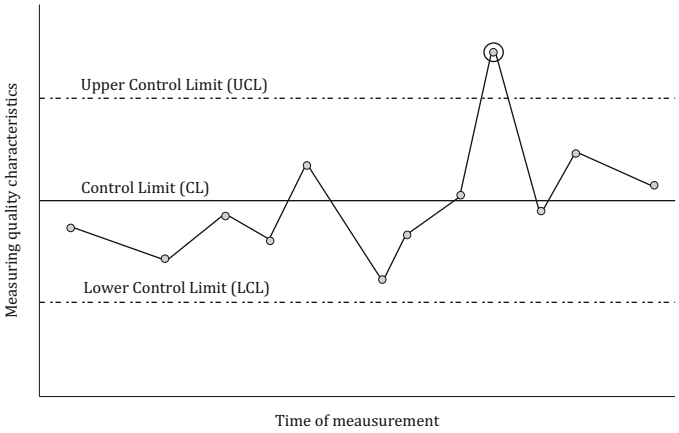


Fig. 18.8 Process Control Chart (Cf. Rampersad (2001))

The Seven New Tools are like the Basic Problem Solving Tools rather graphical than language based. They are used for a more networked analysis and for structured discussions in groups. In general, the tools help to make complex processes and problems understandable and easier to illustrate for further steps. In the following section we will provide an overview and a short introduction of the Seven New Tools:

The Seven New Tools are:

- Affinity Diagram
- Interrelationship Diagraph
- Tree Diagram
- Prioritization Grid
- Matrix Diagram
- Process Decision Program Chart
- Activity Network Diagram

Affinity Diagram

An Affinity Diagram is a useful tool that uses brainstorming methods to generate a large number of ideas for a specific topic. It allows the participants of the project team to work creatively and logically at the same time. For generating ideas, the participants are tapping into their creative side. While organizing those ideas during the design of an Affinity Diagram, the user exercises logically.

According to Mizuno,[16] an Affinity Diagram is especially useful when the topic being handled is complex, hard to understand, or if little information is available about the specific problem. In case the event is large, and requires an intensive collection of information in multiple directions, the tool can also lead to a final conclusion. In addition, it helps to find a useful solution if the involvement of another group of people is required.

There are six basic steps to create an Affinity Diagram:

1. Identify the problem or issue
2. Each person writes issues related to the problem on note cards or sticky notes
3. Organize the cards or sticky notes into logical piles
4. Name each pile with a header
5. Draw an Affinity Diagram
6. Discuss the piles created

The figure below gives an example of an Affinity Diagram (Fig. 18.9):

Interrelationship Diagraph

The main purpose of the Interrelationship Diagraph is to depict the relationships in complex problems to find a useful solution. It can be very powerful since it reveals the impact one issue can have on another. While drawing the diagraph several times, many new ideas can be generated. It is expected that those ideas will lead to

[16] Cf. Mizuno (1988)

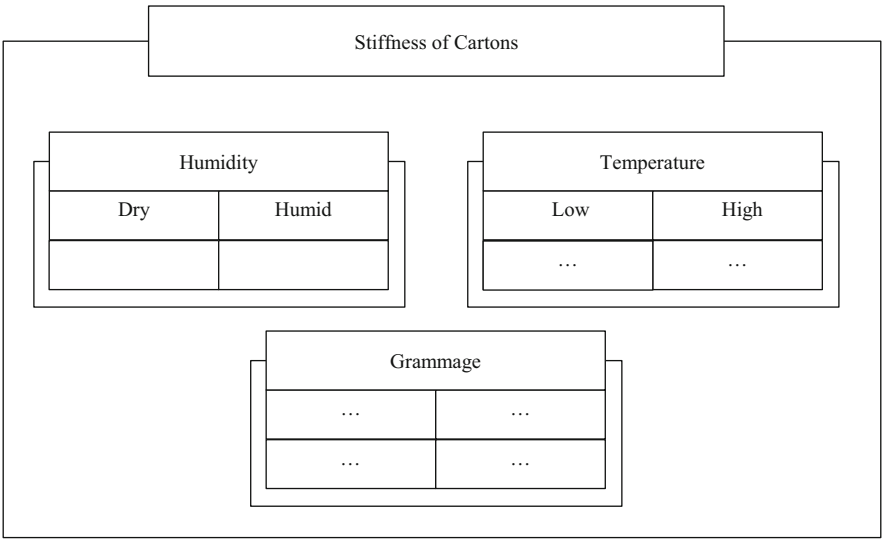


Fig. 18.9 Affinity Diagram (Follows Mizuno (1988))

an appropriate solution. Often times, this diagraph is used in conjunction with other methods as for example the Affinity Diagram.[17]

There are seven steps to create an interrelationship diagram:

1. Identify the problem or issue
2. Write each element that relates to the problem in a box
3. Draw arrows from the element that influences to the element that is influenced
4. Draw the strongest influence if two elements impact each other
5. Count the arrows
6. Elements with the most outgoing arrows will be root causes or drivers
7. The elements with the most incoming arrows will be key outcomes or results

The Fig. 18.10 below gives an example of an interrelationship digraph:

Tree Diagram

A Tree Diagram is used to discover the steps needed to solve a given problem. It shows the problem separated in different included elements. The analysis allows the user to gain further insight into the problem and helps the team to focus on specific tasks. As a final step, the specific issue can be solved based on the new insights of the problem.

[17] Cf. Mizuno (1988)

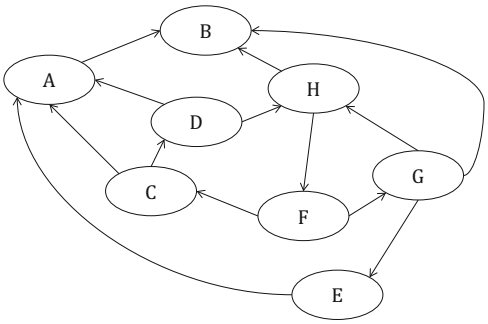


Fig. 18.10 Interrelationship Digraph (Follows Mizuno (1988))

There are five major steps in creating a Tree Diagram[18]:

1. Determine the main goal
2. Be concise
3. Brainstorm the main tasks involved in solving the problem and add them to the tree
4. Brainstorm subtask that can also be added to the tree
5. Do this until all possibilities have been exhausted

Below is an example of a Tree Diagram (Fig. 18.11):

Prioritization Grid

A prioritization grid is typically used to make decisions about the importance of a list of different items. This prioritization is based on a "divide and conquer" approach in which you work with a list of preference of the items and compare those to every other item, working in pairs, one pair at a time. The comparison leads to a specific weight of the items in relation to the remaining. This weight is calculated in the dependence of the amount of items we are focusing on. The sum of all weights equals one. In the next step the influence of the specific items on the problems needs to be subjectively indicated. With the calculated weight and the subjective influence of the items on the problem an individual ranking can be created. This ranking reflects the influence of the items on the specific problem. This rank system is the basis to initiate further steps.

The prioritization grid visualizes the data in an easy and understandable way. It helps to focus on the most important topics of highly complex problems. Moreover it shows large data volumes in an easy and comprehensive way.[19]

[18] Cf. Rampersad (2001)

[19] Cf. Mizuno (1988)

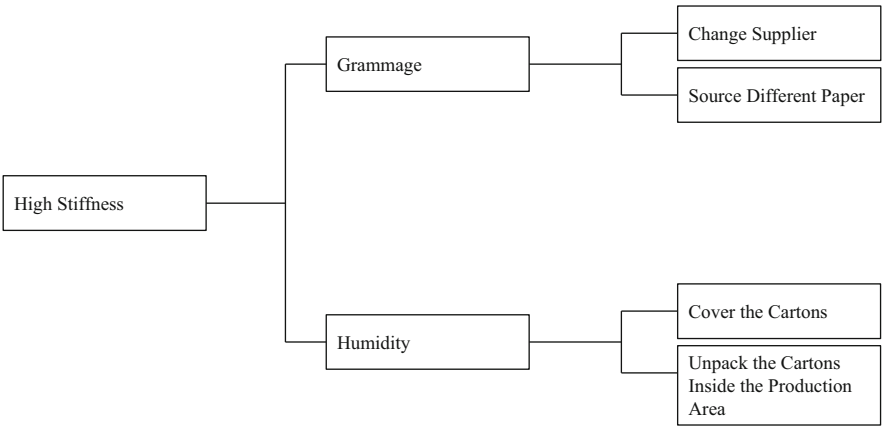


Fig. 18.11 Tree Diagram (Follows Rampersad (2001))

There are seven steps to develop a prioritization grid:

1. Identify your goal
2. Rank the items in order from least important to most important.
   Compare the criteria to each other. The possible values to insert in the matrix are stated as 2:0 (criteria one is more important than criteria two), 0:2 (criteria two is more important than criteria one), 1:1 both criteria are seen as equally important
3. Assign each item a weight in dividing the individual sum of the comparison with the sum of the overall ranking. The sum of all weights equals one
4. Rank the options in order with the specific item. To get this result compare each item with the individual option. Use the range "1 to 10" to evaluate the affection of the item on each option
5. Multiply the criteria weight with its associated criterion/option comparison. The result in each cell of the matrix is called an importance score
6. Sum the importance scores for each alternative
7. Rank the alternatives in order of importance

Below is an example of a Prioritization Grid (Fig. 18.12):

Matrix Diagram

The matrix diagram uses the relationship of criteria to identify interfering elements in a complex problem. It is for example a good tool to compare the efficiency and effectiveness of alternatives. It uses criteria and symbols to visually depict the relationship between collected elements. For example, a user could analyze the relationship between cost and performance. The Matrix Diagram will then show the

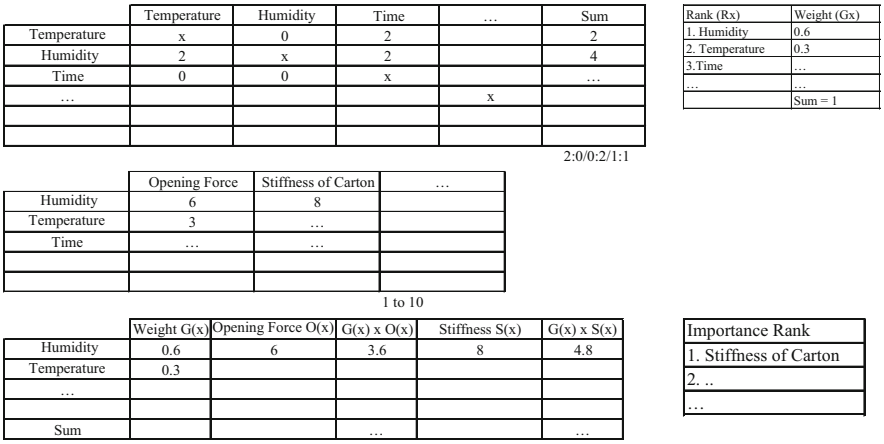


Fig. 18.12 Prioritization Grid (Modeled after Mizuno (1988))

leverage of the selected aspects. Matrix diagrams can be used with up to four dimensions. There are several styles of matrix diagrams. The most common styles are the L-shape, the T-shape, the Y-shape, X-shape and the C-shape matrix.[20]

There are five steps in constructing a matrix diagram:

1. Decide the factors that are most important to make the decision
2. Select the style of matrix that will help the best
3. Select the symbols to be used to represent the relationships
4. Complete the matrix using the determined factors and symbols
5. Analyze the completed matrix

Figure 18.13 shows an example for a Matrix Diagram in L-shape:

Process Decision Program Chart

The Process Decision Program Chart helps to indicate a successful practice to get the required result for a defined process. Moreover it is a good tool to use for contingency planning. The analyses helps to outline what possible impacts could occur while implementing new programs or improvements. Likewise the method is a good tool to handle changes in a long process of e.g. problem solving. With a Process Decision Program Chart processes and difficult problems of quality can be solved.[21]

There are four main steps to create a Process Decision Program Chart:

1. List the steps in the process you intend to analyze
2. List what could go wrong at each step

[20] Cf. Mizuno (1988)

[21] Cf. Mizuno (1988)

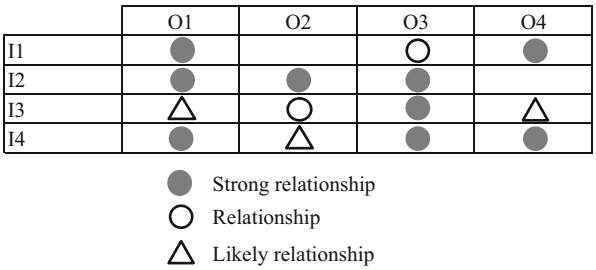


Fig. 18.13 L-type matrix (Cf. Mizuno (1988))

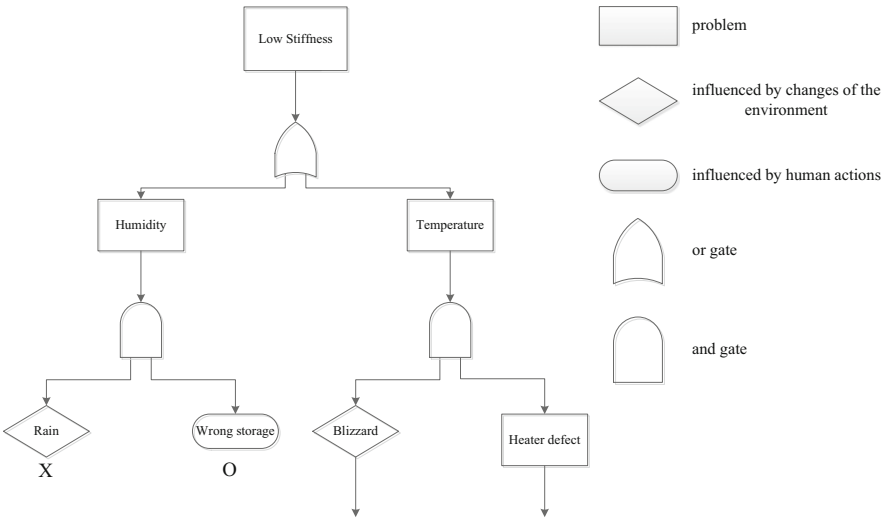


Fig. 18.14 Scheme of a Process Decision Program Chart (Modeled after Mizuno (1988))

3. List the counter measures to the problems
4. Evaluate the counter measures by placing an "O" for feasible or a "X" for not feasible

Below is an example of a Process Decision Program Chart (Fig. 18.14).

Activity Network Diagram

The Activity Network Diagram is also known as the Program Evaluation and Review Technique diagram (PERT diagram) or the Critical Path Method diagram (CPM diagram). It evaluates the time it takes from the beginning of a process to its

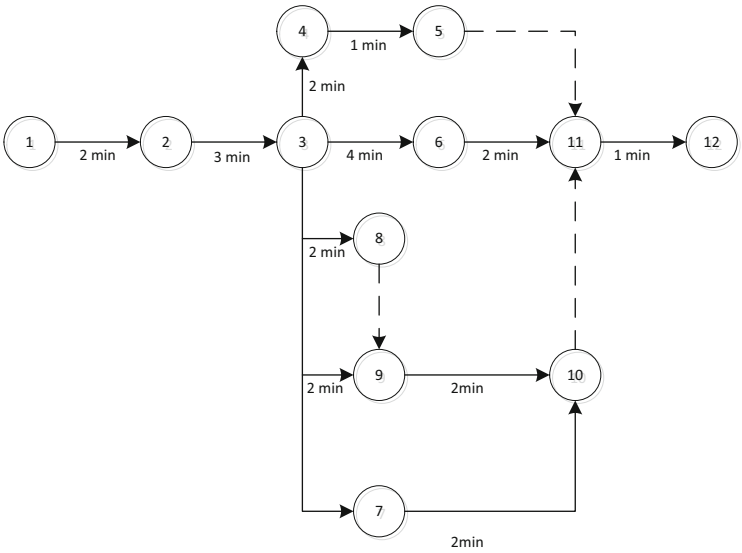


Fig. 18.15 Activity Network Diagram (Cf. Mizuno (1988))

end. Thus, processes can be improved in relation to the required time by determining slack time between process steps. This becomes obviously important as timing, likewise quality is considered as a critical market requirement.[22]

The following bullet points list the steps to develop an Activity Network Diagram.

1. List all tasks
2. Determine the time it takes for each task
3. For each task, determine the task that must happen before the current task can take place
4. Draw the network diagram
5. Compute early start and early finish times for each task
6. Compute the late start and late finish times for each task
7. Compute slack time
8. Determine the critical path

Below is an example of an Activity Network Diagram (Fig. 18.15):

The Seven New Tools do not replace the Seven Basic Quality Tools. Likewise the tools help to solve highly complex problems, situations and simplify challenges. Furthermore, they support to analyze huge sets of data and help to indicate the most important facts in many areas in the modern industry. With their visualization of

[22] Cf. Mizuno (1988)

interdependencies the Seven New Tools help to solve quality related issues. Moreover, the tools allow using the creativity of interdisciplinary groups and leading to a prioritization of facts.

Summary

The Seven Basic Quality Tools and the Seven New Tools, as described above, all help to get a better, visualized understanding of a problem. This prevents someone thinking in a box and helps to get a better overview about problems and processes. The tools give the opportunity to work in an interdisciplinary team on the same level.

The tools provide a guideline for a structured discussion in interdisciplinary teams. After the discussion there is usually a common understanding of the problem and a basis for further steps is founded. Even if this seems to be simple, it needs a lot of discipline and training to apply these tools as it is not in the nature of most people to first make a more profound analysis of a given situation by using their creativity in a structured way. It prevents people to come out with the very first solution that comes to their mind. Instead many ideas can be collected and an overall solution tackling the root causes will be found.

For some of the tools, a collection of data is required, others simply rely on brainstorming. The tools can be applied to rather simple problems with not too many interdepending factors. They do not rely on statistical methods and analyses. Mostly the tools are trained over the majority of co-workers in the manufacturing environment to provide operators with a basic understanding of how they can help to improve weaknesses in their daily operations.

Lean and Six Sigma

The following excerpt gives an introduction of the background and the main ideas of the Lean and Six Sigma concept.

Six Sigma translates a TQM quality concept into a concrete quality model and finally in a quality system. It is much more than a mere toolbox. Six Sigma starts at the very top of the company with a visible management commitment, comes with an organizational structure and is based on a well working project management approach. A special focus lies on the involvement of every single employee. Some parallels between Six Sigma and Lean (Cf. also Chap. 2) can be noticed. Lean is also much more than a tool box, since it requires an organizational structure, top management commitment and the commitment of all employees. While Six Sigma deals strongly with quality issues based on process variation, Lean focuses on waste reduction in every single activity. The name “Lean” has been introduced as an

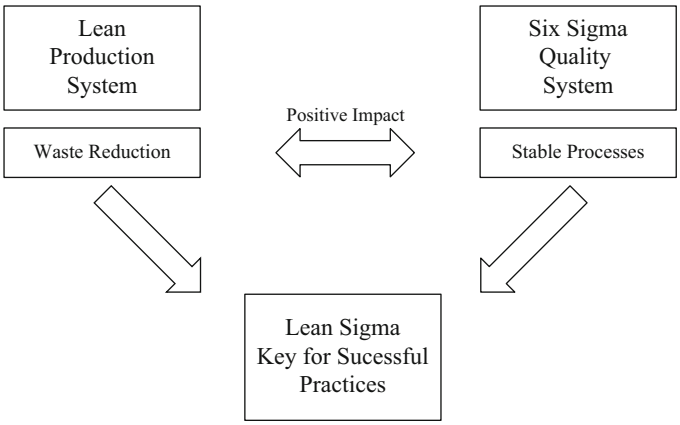


Fig. 18.16 Lean and Six Sigma

antipode to "buffered",[23] therefore aiming at all intermediate inventories and routines that helped to hide weaknesses in processes. Lean and Six Sigma are often used in combination, combining the focus on reducing process variations with the relentless search for and elimination of waste. Figure 18.16 reflects the interplay of Lean and Six Sigma.

Neither Six Sigma nor Lean is easy to implement or valid in the same way for every company. Combined they can be a powerful competitive weapon. Six Sigma, to some degree, can be considered as a prerequisite for Lean since Lean can't work without a certain underlying process stability which is exactly what Six Sigma aims for. Interestingly this required stability is very well known by companies who are quite advanced in Lean, but has been often neglected in practical applications. In the following sections we describe some of the typical tools out of both toolboxes.

Six Sigma (Tools)

The start of Six Sigma dates back to the years from 1985 to the beginning of the 1990s. In those years Motorola was the first company in the world to use the Six Sigma thoughts in its production area. It was a big success for the company saving billions of dollars with the usage of these tools. The success story of Motorola brought the idea of Six Sigma subsequently on the agenda of other leading companies in the Western world. The main objective of Six Sigma is to keep processes controlled, especially their variability and therefore to improve the stability of the processes.

[23] Cf. Krafcik (1988)

The focus of Six Sigma tools is on the area of problem solving and the reduction of variation within the processes. They range from easy to use applications to tools with a complex statistical background.

The ultimate goal of a Six Sigma tool application is Zero Fault. To achieve this, the Six Sigma tool box contains also a standard procedure to deal with problems. The following section will introduce this so called Six Sigma DMAIC procedure; it will than provide an overview of the Six Sigma Tool Box and will explain two selected Six Sigma tools more in detail. Those tools are helpful to establish stable processes in the production environment. To finalize and to illustrate the usage of the Six Sigma tools, a real case will be introduced.[24]

DMAIC: Define, Measure, Analyze, Improve, Control

Most Six Sigma projects are based on the DMAIC procedure. DMAIC is an acronym for Define, Measure, Analyze, Improve and Control. The procedure is used as a guideline to lead a project team through complex and not easy to handle tasks. Every step itself leads to an individual output. This output becomes the subsequent starting point of the following individual step. In the end, the improvement can be evaluated, and the way to reach the stated goal is easy to reproduce.

In the following passage the different steps are described[25]:

- Define: In this step the problem to be solved is described and therefore the necessity to improve is clarified. Additionally, the specific timeline, the group of people involved and the main goals are finalized
- Measure: The deviation from the target is measured
- Analyze: The main question in this stage of the project is to find out reasons (root causes) for deviations based on the analysis of the collected data
- Improve: In this phase possible strategies and projects are defined to remove the causes of deviations
- Control: Main focus is to measure, if the defined improvements have helped to solve the problem, if there are any additional deviations to the target and to decide about the need for adaptions

Six Sigma Tool Box

The Six Sigma Tool Box includes a wide range of different tools to analyze and to improve processes and to state the Six Sigma goals. As the implementation process of Six Sigma follows DMAIC, the tools can be related to specific phases of the cycle. Different tools are used for different steps and lead to specific results.

[24] Cf. Chiarini (2013)

[25] Cf. Chiarini (2013)

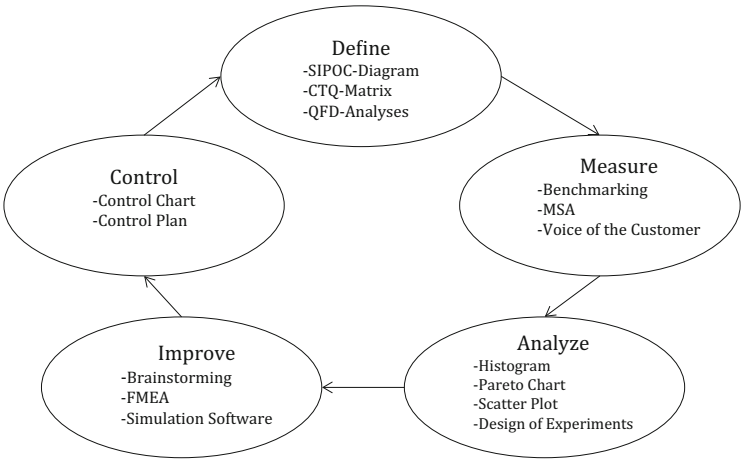


Fig. 18.17 Examples for Six Sigma Tools used in the DMAIC pattern (Cf. Chiarini (2013))

An indication of which tool is best for which phase of the DMAIC circle is often not easy and requires experience. An overview about the correlation of the respective DMAIC phase and several Six Sigma Tools gives Fig. 18.17.

The following tools are examples of well-known Six Sigma tools that are especially used in the steps Define and Analyze of the DMAIC circle.

SIPOC-Analyses

The SIPOC tool supports the analysis of a system including its involved elements. It separates the Input of a process, the result of the process (Output) and the interdependences of the processes. It leads the observer through the complete process from its beginning to the end and provides an overview of the individual steps. That is why the tool is often used in the Define phase of the DMAIC cycle.

SIPOC is an acronym for the following words[26]:

S – Supplier	Every internal or external supplier of the process
I – Input	States the required input for the process to get the final product
P – Process	The actual process to realize the transformation of the inputs. The process converts the input to the final output
O – Output	The result of the process. In a process chain the output of a process step is the input for the following process
C – Customer	The receiver of the process result is the customer

[26] Cf. Lunau (2007)

The main goal of SIPOC is to identify the supplier/customer of the individual processes and to clarify the procedure in detail. It states the basis for a process improvement.[27]

Design of Experiments (DOE)

The main goal of DOE is to analyze an individual process systematically and efficiently. A further objective is to analyze the interdependencies of the process and the product characteristics with a minimal amount of experiments. Out of this knowledge, the optimized settings of the process can be defined. The DOE tool is usually used in the Analyze phase of the DMAIC pattern, but sometimes interdependences with other steps are possible.

The procedure for the Design of Experiment tool follows the hereinafter steps[28]:

1. Define the optimization task and set the central objectives
   - Product and process
   - Define goals
   - Quantify the goals
2. Define the influencing variables (Ishikawa Diagram, FMEA)
   - Precision of the variable (Regression Analyses)
   - Reproducibility of the variable
3. Set factor levels
   - Set a maximum and a minimum
   - Constant influencing variables
   - Discreet influencing variables
4. Define the design and the sample size for the experiment strategy
   - Set sample size
   - Set factor level combination
   - Full factorial design
   - Fractional factorial design
   - Usually the full factorial design is very work intensive

   Consequently for the complex factorial design the following procedure is used:

   1. Good-Bad comparison
   2. Screening experiments
   3. Fold over experiments
   4. Closing experiments
   5. Optimization experiments

[27] Cf. Lunau (2007)

[28] Cf. Lunau (2007)

5. Ensure the equipment (measurement systems, etc.) ability
   - Analyze the measurement system
6. Perform the experiments and get the data
   - Before starting the experiments it is helpful to perform several pilot experiments
   - While performing the experiments a fulltime observation is necessary
7. Analyze the data and conduct actions
   - A statistical analyses is necessary
   - The results need to be evaluated, the DOE might be iterative
   - All results have to be evaluated by several experts to ensure the meaningfulness of the data

In an earlier case study we attended a problem solving process, where the methodology of the DMAIC pattern was used to solve the problem of a high number of stoppages in the packaging line of the Geneva site of the company GlobePharm Ltd.[29] The following example will illustrate the DMAIC-Six Sigma problem solving approach to find an appropriate solution for the stated problem.

Step 1: Define

In the first step, a better understanding of the overall process from the carton manufacturing to the packaging of drugs was in the focus. It started with a mapping of the manufacturing process for cardboards and ended with the processability of the folding carton at the packaging line. The team focused on all necessary steps and outlined the input and output parameters that may influence the problem being analyzed. This helped the team to better understand the processes, including from the supplier's point of view. For this analysis, the team used the SIPOC tool as described above. In addition to the SIPOC tool, the team also used as a next step the tool of Value Stream Mapping which is going to be explained later in this article. With both of these tools, the team obtained a good overview of the process and was able to highlight the main problems more easily.

Step 2: Measure

As a next step, after the team had a better understanding of the processes, it was necessary to identify the key parameters to measure. The result of this identification step based on the SIPOC analyses, were the parameters that may influence the folding process as stated below:

- Grammage[30]
- Humidity
- Temperature

[29] Company name is changed for this article

[30] Grammage is a metric measure of paper weight based on the same square meter sheet of paper (g/m^2)

- Stiffness
- Force required to open a folding carton
- Storage time
- Three supplier 1 cardboards (230, 240, 255 g)
- Three supplier 2 cardboards (235, 250, 260 g)

In addition to those parameters, the machines needed to be analyzed and therefore nine mechanical elements that are influencing the result of the measurement were defined. Those nine elements were:

- Load of the cartons in the store
- Spacing of the loaded cases
- Position of the suction cups on the carton
- Taking of the carton by two or four suction cups
- Air limiter
- Perforation rod
- Opening of the fingers
- Jack compartment to let the cartons fall
- Incline of the plate

After setting up the influencing parameters, the team started to design test protocols to collect the required data. To validate the measurement system the team evaluated the reproducibility of the tests to ensure that the data was usable. During the test period 54 protocol sheets were used to record the specific events.

Step 3: Analyze

This phase of the analysis was necessary to understand the collected data. In a first step, the humidity and temperature were focused. As a result of the analyses, it could be stated that the effect of the variability in temperature was minimal but the effect of the variation of humidity was quite significant. However it was not yet possible to understand how and if fluctuating humidity was also influencing the physical properties of the folding carton in a way that had a negative impact on the stability of the machine.

The next step was to deal with the machine-ability, the stiffness of the folding carton and the opening force. The actual manufacturing process was recorded by a high-resolution camera. From the recordings, it could be visualized that a lack of stiffness and the bend of the folding carton were causing machine stops. With this knowledge, the next step was to analyze the change of stiffness over the time. The result of this analysis was that stiffness is one of the key parameters causing machine stoppages. A high stiffness indicates a high machine-ability. Another finding was that stiffness does not change over time, but the humidity somehow correlates with stiffness. This fact indicated that humidity was the key influencing factor for variation in stiffness. Another finding was that a high grammage implied a high stiffness. (For this analysis complex statistical methods were used).

All of the described analyses were interesting and further helped to deepen the understanding about the correlations of the influencing parameters. However, even with the collection of additional information, the root cause of machine stoppage could still not be identified. With the assumption that the variation of temperature and humidity during transport influenced the number of stoppages, the team decided to use another Six Sigma tool to identify the root cause. This tool was the above described tool "Design of Experiments". The team further decided to design two experiments to identify the cause and effect relationship. In the following write-up, we will describe the two experiments:

DOE 1: Reproduction of the Transport Stress

The first experiment was dealing with the transport stress, the variation in temperature and humidity of folding cartons while they were on a truck and the influence of the variables on the stiffness and the opening force of the cartons. The result of this experiment was that low temperature was influencing the stiffness and the opening force. Since the stiffness retains very quickly under normal conditions the opening force was influenced in a different way by the factors. The experiment did not lead to a final conclusion and solution for the problem.

DOE 2: Impact of Temperature, Humidity and Time

For the second experiment the variable factors grammage, humidity, temperature and storage duration were focused on. As a first result it was possible to indicate that temperature and storage duration had no effect on the folding carton properties. The experiments indicated that the stiffness increases if the grammage is increased or the humidity is decreased. As a last result, the team came to the conclusion that for the force required to open the cartons, all mentioned factors are relevant.

To summarize the findings of the analysis, it was highlighted that the stiffness is the critical factor for the packaging line. As a consequence, the grammage was increased and cartons that were delivered with low temperature were stored for a minimum of 24 h before usage. Additionally, a main finding was that the humidity had a negative impact on the OEE by decreasing the stiffness of cardboards.

Step 4: Improve

Based on the above analysis, the project team decided as a short-term improvement to use a higher grammage to compensate the humidity problems. As a long-term solution, to solve the humidity problem, the team decided to store the cartons in fiberboard boxes with a waterproofed layer or to build a hood for the pallets after they leave the process of printing.

Step 5: Control

To control the influences of humidity on the stiffness, the team kept operating with the designed experiments on other machines. Additionally, the humidity in the warehouse was measured continuously.[31]

Conclusion

This case provides an insight in how a company can use several Six Sigma tools to solve problems and how to handle difficult, not easy to solve issues, by working in interdisciplinary teams. Every case will be slightly different and no overall user guideline can be found. But the Six Sigma tools help to handle such a project in a structured and well planned manner. Furthermore, the traceability of such a project is very high.

The Six Sigma Tool Box includes several tools that are also well-known in the transformation of lean thoughts in production fields. As an example, a Kaizen Workshop (we will introduce this tool in the following section) can be stated. Additionally, many quality tools out of the described Seven New Tools and these Seven Tools are used in the Six Sigma Tool Box. Those tools are especially found in the stage "Analysis" of the DMAIC-Cycle. Examples for those tools are Brainstorming, Histogram, Pareto Analyses and the Scatter Diagram.[32]

Summary

The main focus of the Six Sigma tools is to establish stable processes that are controlled permanently. The Six Sigma Tool Box varies from very easy basic tools to tools that require advanced statistics. Easy to use tools help to make processes understandable and help to focus on possible problems in advance. Tools with a high statistical background are used to identify the true root causes for deviations and to help to develop a scientific process understanding. As seen in the above described case, one can understand how a very complex problem can be solved in a very structured, repeatable way. The example shows how easy tools and complex tools are used in combination for application in the industry. The use of Six Sigma helps to involve all layers of employees in a company and to improve the overall understanding of the internal products and processes. This leads to a better internal communication and better internal approach based on the improved knowledge to tackle problems.

[31] Cf. Werani (2010a)

[32] Cf. Chiarini(2013)

Lean Production (Tools)

Lean and lean tools are the heart of the Toyota Production System. Through the dissemination of the system's philosophy, progressively more tools have been generated.

A main goal of all these tools is to reduce waste in the processes (Cf. Chap. 2). The eight wastes in the production area are[33]:

"Overproduction" (Too many goods are produced, they are produced too early or too late to match the customer's demand)
"Excess Inventory " (Stored raw material, work in process or finished goods)
"Motion" (The body is moved without value adding background)
"Defectiveness" (Non-conforming products)
"Transportation" (movement of products between the processes)
"Over-processing or incorrect processing" (Processing over the customer requirements)
"Waiting (Time on hand)" (Waiting time for the commence of the next activity) and
"Non-Utilized talents" (waste of human talent).

The types of waste with the biggest influence are stated as Inventory and Overproduction, as tied capital in the company without any benefit. To work on waste reduction initiatives the basic problem-solving tools as described in the previous paragraph are used. To get an idea about which processes should be focused on, a Pareto Analysis can be useful.[34]

The bulk points below provide an overview about three well known lean tools:

- Value Stream Mapping
- Kanban Cards
- Kaizen Workshops

In the following intercept the mentioned lean tools are introduced and described.

Value Stream Mapping

Value Stream Mapping is a method to visualize production processes including the interaction of different departments. The focus of the tool is on information and direct process influences. The tool helps to analyze downtime in and between processes. Its goal is to line up all activities that are required for the production process. It summarizes the processing time and the downtime between the individual process steps. As a final output it is possible to calculate the quotient of the value added time and the non-value added time. With this Key Performance Indicator (KPI) it is possible to get an idea about how lean the investigated process is. It is

[33] Cf. Liker (2004)
[34] Cf. Chiarini (2013)

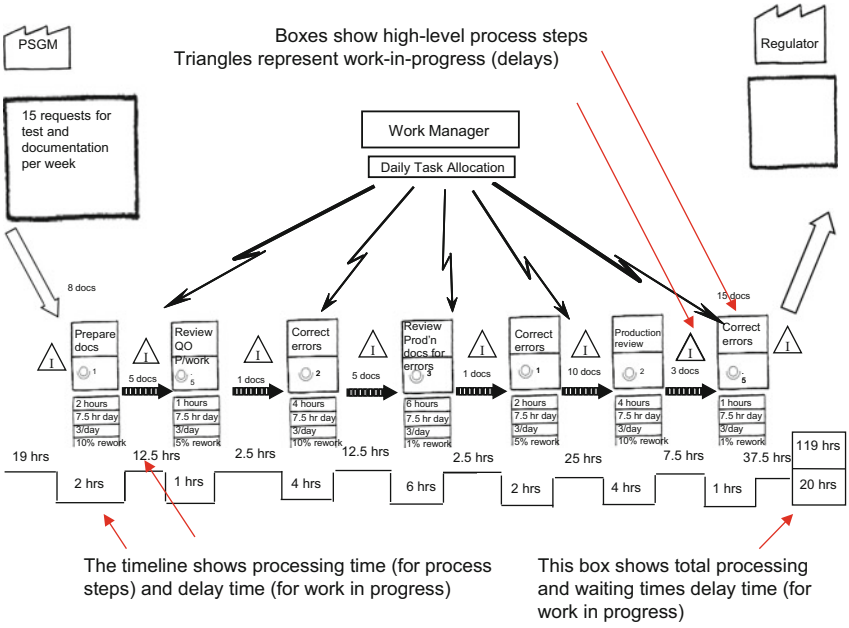


Fig. 18.18 Value Stream Map of the production process (Cf. Werani et al. (2010a))

also a good way to visualize the internal process for information exchange in and between the different departments and it shows potential improvements for information exchange.

To give an example how a Value Stream Map can be developed, we want to introduce this tool following the case of the company PharmSpec.[35]

Figure 18.18 shows the Value Stream Map developed in the PharmSpec case.

Initial Situation at PharmSpec

The major site of the PharmSpec Company was facing a rise in the production volume based on the increase of market demand of their Chewix[36] product. The production of this product contains three major steps, bulk manufacturing, coating and packaging. Additionally the amount of variants was exploding caused by different flavors and a massive increase of variants in the packaging area. As part of a holistic OPEX program, Value Stream Mapping was trained in this company. The following excerpt will reflect the usage of this tool in the production of the Chewix product.

[35] Company name is changed for this article

[36] Product name is changed for this article

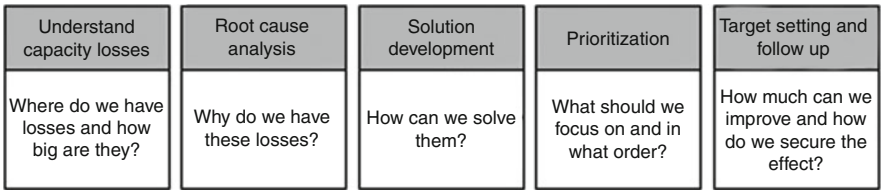


Fig. 18.19 Structure of the VSM project

The project required a guideline for the project members and participants that included the major questions of the necessary steps to concern. The five major steps are shown in Fig. 18.19.

As a first step it was necessary to understand the reasons for the capacity losses. With this knowledge bottlenecks could be identified and potential savings could be estimated. This analysis indicated large variances in lead times and a low overall value added time. The final idea of this phase was to create stable and standardized processes. Based on this knowledge a root cause analysis followed. This tool led to the determination of the main causes of the losses. For the production process the variances in the changeover times were identified as the root cause. In the packaging area, the different "ways of working" seemed to be the main cause for losses. Additionally the explosion of variants in the packaging area was outlined as a key issue. As a last cause the large average campaign size for low and medium volume items was indicated.

The derived improvement suggestions were related to the estimated "value" and the "ease of implementation" to achieve a reproducible prioritization. A first improvement step was the stabilization of the processes by the introduction of standard operations. Second the daily management and planning had to be improved. To achieve the defined goals daily and weekly production schedules were communicated. Additionally, the used technology in the production area needed to be improved. With a low financial effort remarkable improvements could be reached. As an example, error-proofed machine installations can be mentioned. Step four was the reduction of machine downtimes through the introduction of a better working maintenance team. A further point was to identify a new planning solution. Two different options were considered to achieve this scope. The goal of option one was to minimize the early allocation of batches through an implementation of a bulk supermarket between coating and packaging, pull replenishment of the central weighting process, and through a standard QA/QC analysis. Option two was dealing with the idea of cyclical planning in manufacturing. With the knowledge of the product volume, the product mix and the product sequence a repeatable production schedule was implemented. This improvement was leading to a more stable manufacturing process. The last source of improvement was focusing the packaging of selected high runners. Here the demand variations over time were leveled to further improve the efficiency.

In the next step the prioritization of the mentioned options was followed up. The output of this prioritization was an implementation plan for each working group.

The criteria for the prioritization was as mentioned the "value" (lead time reduction) and the "ease of implementation". The effective implementation plan summarized the necessary steps and finalized the process of the VSM.

The positive effects of the Chewix project were an improvement of the OEE of 40 %, a reduction of the inventory level by 20 % and a reduction of the throughput time by 40 %. The drug average lead time was reduced from 125 days to 75 days.[37]

Kanban Cards

Pull Production is an essential element of lean. It helps to keep a production lean and supports the reduction of waste in the production area. Furthermore it is a method where parts are only produced if they are required for further steps. The Kanban control system with the Kanban Cards is the essential tool to get the idea of lean and therefore pull production implemented in the company. In general we can differentiate the Conveyance Kanban and the Production Kanban. Both are using the same tool, the Kanban Card, but are focusing different sectors in the production.

Conveyance Kanban

The idea of the Conveyance Kanban (move or withdrawal Kanban) is to authorize the movement of a container from an upstream buffer, outbound buffer, to a downstream, inbound buffer. Without the usage of a Conveyance Kanban no container can be retracted from an outbound buffer. The first working station in a production area has to produce following the daily production schedule. With this sum of parts that are produced the necessary amount of containers at the other stations can be calculated. With this knowledge the total amount of Conveyance Kanban cards can be fixed. This option of Kanban helps to keep the logistic process lean and reduces stock directly at the stations. All the Cards can be reused and the whole process only needs to be implemented one time.

Production Kanban

The Production Kanban is the second possibility to use the Kanban tool in the production field. As the name is saying this tool is focusing on the production. The Production Kanban authorizes the production and the assembly of parts. In a production that has implemented this kind of Kanban the production without it is not allowed. Only the final operation is scheduled by a daily production schedule, all the other processes are authorized by the Production Kanban system.

In practice the Conveyance and Production Kanban is often combined. This kind of Kanban control is called a Two-card Kanban system. This Kanban process is an iterative process that starts when an operator is taking a full container at his work

[37] Cf. Werani et al. (2010)

station. After taking this container, the worker puts the Conveyance Kanban in the Kanban mailbox. The information on the Kanban Card defines the required parts with the name, the product and the container capacity. As a next step, a material handler takes the card out of the mailbox and takes an empty container to the defined upstream station. After he reached the upstream station the material handler is removing the Production Kanban from a full container and is putting the Card in the Kanban mailbox. At the same time he is putting the Conveyance Kanban card, he was removing before, in the container. As the final step the material handler leaves the empty container with the Production Kanban at the upstream station and brings the full container with the Conveyance Kanban Card to the station where the material is required.

A Kanban Card is the essential tool to implement a Kanban system and with it the Pull Production. The main goal of a Pull Production is to reduce the inventory in the production area. Kanban Cards constitute an essential tool to reduce waste in the production. The underlying idea to only produce what is required by customers is the lever for the elimination of overproduction. The usage of Kanban Cards requires the introduction of Pull Production in the production environment. As such, customer orders give a guideline for the production plan that is to fulfill.

Pull Production is crucial to build the basis of lean production. The Kanban cards are an appropriate possibility to get the "lean idea" into internal production processes. For an implementation of Kanban it is necessary to get an overview about the parts needed in the company and the daily production schedule. With this information every company can implement its individual Kanban controlling process. After implementing this way of production controlling in the entire production area, overproduction and therefore non-value adding, tied capital can be reduced in all processes.[38]

Kaizen Workshops

A Kaizen Workshop is a tool that should be used continuously in a company that lives the lean thought. A Kaizen project usually runs in between 2 and 5 days and is performed by a team with an expert and led by the person in charge of the focused process. The idea is to get involved into the waste reduction of a process and to teach internally lean principles and tools. The Kaizen Workshop is a platform for the expert to show the process owner and its team the potential of waste reduction and to redesign the focused process in a lean way. In a kick off meeting the scope of the project is defined. Kaizen Workshops deal with observations directly where the work is done and possible improvements are to make. With this knowledge and collected data the project team deals with possible strategies, improvements and finally with changes. The Kaizen teams are mostly cross-functional groups from the shop floor, the management and other persons that might add constructive ideas.

[38] Cf. Nicholas (2011)

Kaizen projects often use the DMAIC cycle. Within the process basic problem solving tools e.g. the Check Sheet, the Histogram or the Pareto Analyses are applied.[39]

The Common Basis and the Interplay of Lean with Six Sigma

Several tools applied in basic quality or Operational Excellence activities are rather a pre-condition than a means for continuous improvement. A core message and the very basis of the Toyota Production System[40] is the requirement for stability of the production system in general. This necessity could also been shown in the St.Gallen Operational Excellence Benchmarking. The Benchmarking indicates that only based on stable processes a superior overall performance is possible. The data is giving a clear indication that without a high performance in the two building blocks of Total Productive Maintenance and Total Quality Management (the stabilizing building blocks of the model) an overall superior performance is not achievable. The bases for successful practices are stable processes. Therefore we describe in this part tools with a stabilizing character. Additionally we show the complementarity of lean and six sigma tools.

The following tools are basic tools to implement a stable and standardized fundament for lean processes.

- 5S
- Standardization & Standard Operations Sheet (SOS)

5S: A Tool for Order and Cleanliness

The 5S thought is a guideline to obtain and maintain a clean workplace. The 5S' stand for the Japanese expressions Seiri, Seiton, Seiso, Seiketsu and Shitsuke. This tool is part of the internal Housekeeping initiative in the production area. The idea of Housekeeping is to create with a clean and organized workplace the basis for good quality, a higher safety and an increase of the productivity. 5S is an appropriate tool to achieve the improvements of the Housekeeping methodology.

An overview of benefits of 5S gives the following bulk points:

- Higher Productivity
- More space
- Less defects
- Less accidents and injuries

[39] Cf. Nicholas (2011)

[40] Cf. Womack (1990)

The 5S in detail are explained in the phrases below[41]:

Seiri (Proper arrangement):
Seiri means to remove all activities from the workplace that are not useful for the essential activity. This leads to a reduction of defects and therefore to an increase of the quality level

Seiton (Orderliness):
Seiton means that every tool in use has its specific place and is tied up. This counts for tools, equipment and everything that is in use for the specific process. The operator is much quicker in finding the necessary tools.

Seiso (Cleanliness):
Seiso is the word for cleaning up and keeping the work environment clean

Seiketsu (Neatness):
Seiketsu has the meaning of standardization. The main goal is to make e.g. manuals easy to understand for workers

Shitsuke (Self-discipline):
Shitsuke means that every worker must be disciplined and has to live the 5S thought every day

Standardization and Standard Operations Sheet (SOS)

A very effective way to keep processes lean and to avoid waste in the production is to standardize working procedures. This includes standard work stations, standard work flow and standardized working instructions. An example for this kind of working instruction is the Standard Operations Sheet. This manual includes the tact time, the Standard Operations Routine, the completion time, the standard lead time and the location in the process to check the quality. A SOS should be available for each operation and should be visible for the operators. With this tool the workers get information about the processes they are involved in and it highlights the important aspects of their operations. For the supervisor it is a good tool to keep an overview whether the processes are handled according to the standards.

An additional benefit of the tool is the possibility to evaluate the performance and respectively improvements of the processes.

Standardization in the production field is a good tool to keep processes lean and to retain them under control. It helps operators and supervisors to avoid mistakes and is an opportunity to easier understand the individual processes.[42]

[41] Cf. Chiarini (2013)
[42] Cf. Nicholas (2011)

Lean and Six Sigma: An Integrated Approach

The following passage provides an overview and opinions of the interplay of Lean and Six Sigma with a future outlook.

Corbett states in a 2011 article that "in an overview of continuous improvement approaches, researchers have identified that some organizations have developed "hybrid methodologies" to overcome weaknesses or shortcomings in one program or another. They identify Lean Six Sigma (LSS) as the most well-known hybrid methodology but note that its relative newness means it has not been studied in great detail."[43] He cites also Bendell who notes that: "[. . .] the literature on the compatibility and combination of Six Sigma and lean is limited and moreover, disappointing when examined for a common model, theoretical compatibility or mutual content or method."[44] However, it is a fact that almost every major Operational Excellence program in today's practice is a Lean Sigma program. De Koning et al. (2006) have proposed an integrated framework for LSS that consists of the following elements:

- A structured approach based on Six Sigma organizational mechanisms, i.e. taskforce deployment strategy with black belts, green belts, etc.
- Project-based deployment where a project aims at a chronic problem scheduled for solution.[45]
- Organizational competency development through the training of project champions, black belts, etc. in a curriculum of Six Sigma and lean components.
- Organizational anchoring of solutions and guarding against backsliding by standardization of new processes and imposition of process controls.
- The linking of strategy with project selection by translating strategic objectives into performance indicators and tactical goals, by using these as a basis for project selection and to help secure an alignment of projects with the overall organizational strategy.[46]

Tools for Prevention

So far the tools described are meant to be applied after start of production helping to optimize existing operations. The history of Quality Management shows that it makes a lot of sense not to repair processes but to design them fit for production from the beginning. Therefore we add a description of the most well-known tool for failure prevention, the so called FMEA.

[43] Corbett (2011), S. 118f. quotes Bhuiyan and Baghel (2005)

[44] Bendell (2006), p. 259

[45] Cf. Juran (1989)

[46] Cf. Corbett (2011), p. 122

FMEA-Failure Mode and Effects Analyses

The FMEA analysis is known as a risk-based analysis and is used to point out causes, effects and possible actions to avoid failures. The tool can be separated into a product and process FMEA. As the result of the FMEA, a list with critical points, including a manual what steps are required to minimize process failures, can be created.

The process of implementing a FMEA is described below[47]:

1. A team consisting of 5–8 multidisciplinary members is formed
2. A kick off meeting is held where the objective, the FMEA approach and the role of the team members is explained
3. The available information is shared with all team members
4. An overview of all relevant process steps is created
5. Every process step needs to be then analyzed and possible failure modes need to be checked. In addition the interaction to other process steps needs to be investigated
6. The causes of the failure modes have to be indicated
7. The purpose is to analyze what influence the effect has on the controllability of the process step
8. A quantification of the Probability of Occurrence (O) and the Probability of Undetected Faults (P) and the Severity of the Failure (S) for the individual failure mode hast to be set. The product of O, S and P leads to the Risk Priority Number (RPN). O, S and P are numbers starting from 0 to 10. 0 indicates that a problem will not occur (O), that it has no influence on the process (S) or that the failure will be detected before the product reach the customer (P), 10 means that an occurrence is certain (P), the problem is in fact dangerous for people (S) and the failure will not be detected before the product goes to the customer (P).
9. For each failure mode the necessary actions for improving the process have to be stated. The RPN indicates the problem with the highest priority
10. A responsible problem solver has to be appointed
11. The period for the verification of the solutions has to be communicated
12. FMEA results have to be reported and communicated to the management
13. Internal feedback for the team members
14. Evaluate and verify the essential actions to solve the problem

[47] Cf. Rampersad (2001)

Structuring Tools

Top Down Versus Bottom-Up Applications

Several of the tools described allow a systematic identification of priorities for the further focus of improvement projects. Based on an overview about a specific situation a focus is set for improvements. We call this procedure top down considering the systematic selection for the improvement activities. Other approaches let people decide based on their daily work experiences what to improve next. Therefore it is a bottom-up application and not managed from the top.

Simple and Complex Problems

A common mistake in improvement initiatives is that the same tool is used for any kind of problem without taking into consideration if this really makes sense. The classical Six Sigma tool set with e.g. DOE and corresponding statistical evaluations does not really fit together with a one-time deviation in a packaging process. The complexity and the character of a problem should be the starting point for the selection of the problem solving methodology not the other way round.

Matching Tools and Problems

There are several possibilities now for further structuring a meaningful application of tools. Based on the idea of the sand cone model[48] a good structure could be to start with the stabilizing tools and introducing the efficiency/waste-oriented approaches later. Another structure could be to identify priorities, starting with the broadest tool to get an understanding of existing challenges and improvement potentials and streamlining the tools later to the identified priorities. A third way would be to structure the tools in line with the complexity of the problems under consideration, and a fourth way would be a customized combination of the variants just introduced. At the end of the day the right way to apply methods and tools will have an impact on the acceptance of the whole Operational Excellence initiative.

[48] Ferdows K, De Meyer A, Lasting Improvements in Manufacturing Performance : In Search of a New Theory, in : Journal of Operations Management, vol9, no 2, 1990, p. 175

1. *Structuring along of the sand cone model*[49]

The sand cone model keeps a simple message. It says that the successful buildup of capabilities in a production environment follows a logical sequence and is cumulative: "...: to build cumulative and lasting manufacturing capability, management attention and resources should go first toward enhancing quality, then – while the efforts to enhance quality are further expanded – attention should be paid to improve also the dependability of the production system, then – and again while efforts on the previous two are further enhanced – production flexibility (or reaction speed) should also be improved, and finally, while all these efforts are further enlarged, direct attention can be paid to cost efficiency."[50]

This is the main reason and the real importance of approaches like 5S. Without this very basic approach, the system will not get the needed stability to increase the efficiency to the next level.

This message is similar to the outcomes of our benchmarking and the learning from the implementation of many other production systems. Without a stable base every move towards fewer costs is doomed to fail or fire back on quality (stability). We know that it can be the very objective to challenge this stability by driving down inventories and taking out waste to let the weaknesses come to the surface and therefore become open for remedy. But this philosophy comes with some risks and risks are mostly incompatible with the underlying culture and nature of the pharmaceutical industry.

2. Structuring along of the complexity of the problems

Some companies have tried to structure the application of methods along the complexity of problems. One concrete example is shown below. We believe that it makes a lot of sense to first reflect on the character of a problem before taking a sledgehammer to crack the nut. However the challenge is to identify with a certain guarantee the true character of a problem. This is heavily dependent on the experience of the company's experts (Fig. 18.20).

3. Structuring from a broad overview to the top priorities

This approach starts with the application of tools that provide an overview about the situation and make it possible to select priorities. Based on the selected priorities, the further tool application is defined depending on the character of the problem. The broadest tool for getting an idea about possible improvement potentials is Value Stream Mapping or Process Mapping in general. The visualization of the current activities makes weaknesses visible, discussable and opens them for further analysis. We suggest that based on the discussion of the process the apparent weaknesses are collected, prioritized and a decision is taken which tools should be used (and are appropriate) to overcome these weaknesses. The complexity of the problem again

[49] Cf. Ferdows/de Meyer (1990), p. 168ff.

[50] Cf. Ferdows/ de Meyer (1990), p. 168

Example –Tools application based on problem characteristics

Topic	Yellow Belt	Green Belt	Black Belt	Lean
Business Case	Resolve basic deviations	Eliminate Deviations	Eliminate variations	Eliminate Waste Improve Flow
Type of Issue	Effectiveness & Efficiency	Effectiveness & Efficiency	Effectiveness & Efficiency	Efficiency
People	Individual initiative or team	Teamwork Green Belt	Interdisciplinary teams Black Belt	Interdisciplinary teams Green and Black Belts
Skill Set	Basic knowledge in Problem solving tools	Specialised in methodology	Standardised and certified trainers	Standardized and certified trainer
Special Cause	Yes	Yes	No	No
Common Cause	No	No	Yes	No
Complexity of Problem	Low	Medium-High	Highly complex	Medium-Highly complex
Typical Tools	• Problem Definition • Process Mapping • Cause & Effect • Brainstorming • *Time Series Plot* • *Pareto Diagram* • *Control Charts*	All from Method 1 and • Capability Indices • Frequency Plots • Scatter Diagrams • Gauge R&R	All from Method 2 and • Hypothesis Testing • Regression • Design of Exp'ts	All from Method 3 • Value Stream Mapping • Value Analysis • Creating Flow • Cell Design • Standard Work • Mistake Proofing • 5S and Visual Workplace • Setup Reduction • Total Productive Maintenance • Material Flow (Pull) • Extended Value Stream
Examples	• Invoicing Problems • Quality Deviations • EHS Incidents • Production Bottle Necks	• Recurring errors or operational failure • Change over reduction	• Sustaining Yield Performance • Product Dissolution • Glass particles in steriles	• Capacity Problems • OEE Improvement • High Inventories • Cycle Time

Fig. 18.20 Link of tools and problem characteristics (Migliaccio et al. (2010))

determines the selection of the tools. For simple, not heavily dynamic or interdependent weaknesses in most cases one or a combination of the classical or new quality improvement tools will be adequate. If we have major issues in process stability, e.g. a high number of stoppages of packaging lines, a sophisticated application of Six Sigma is the appropriate answer. If we do not have to deal with process variations but with inefficiencies, like double work or other wastes along the process we will have to reflect about waste removal. If bottlenecks become visible or the flow of the process is hindered in another way, layout optimizations, super markets and other approaches from the Lean Tool box should be applied.

4. A combined approach to problem – tool matching

Based on our experience we would suggest a combination of the before mentioned structuring approaches. The main underlying philosophy should be the thinking behind the sand cone model. This means that first all simple deviations in processes should be addressed by engaging and enabling workers and teams so as to spread the application of simple tools throughout the organization. For the initialization, a broad training of as many workers as possible should take place. This, together with an early introduction of 5S, will ensure a stable base to tackle the more complex deviations in addition, to the efficiency issues addressed by most of today's lean tool boxes. There will be a combination of bottom-up ongoing applications with a top-down strategy-oriented derivation of priorities. Besides this, the application of preventive tools at the beginning of process development should be part of every approach.

References

Bendell T (2006) A review and comparison of six sigma and the lean organizations. TQM Mag 18 (3):255–262

Bhuiyan N, Baghel A (2005) An overview of continuous improvement: from the past to the present. Manag Decis 43(5):771–781

Chiarini A (2013) Lean organization: from the tools of the Toyota Production System to lean office. Springer, Milan

Corbett LB (2011) Lean Six Sigma: the contribution to business excellence. Int J Lean Six Sigma 2 (2):118–131

Deming WE (1986) Out of the crisis: quality, productivity and competitive position. Cambridge University Press, Cambridge

De Koning H, Verver JPS, van den Heuvel J, Bisgaard S, Does RJM (2006) Lean six sigma in healthcare. J Healthcare Qual 28(2):4–11

Ferdows K, De Meyer A (1990) Lasting improvements in manufacturing performance: in search of a new theory. J Oper Manag 19(2):168–184

Ishikawa K (1985) What is total quality control? The Japanese way. Prentice Hall, Englewood Cliffs

Juran JM (1989) Juran on leadership for quality, an executive handbook. The Free Press, New York

Krafcik JK (1988) Triumph of the Lean production system. MIT Sloan Manag Rev 30(1):41–52

Liker KL (2004) The Toyota way: 14 management principles from the world's greatest manufacturer-. McGraw-Hill, New York

Lunau S (2007) Six sigma + lean toolset. Springer, Berlin/Heidelberg/New York

Migliaccio G, Ricciardi N, Scott J, Winskill N (2010) Building a continuous improvement culture: Pfizer moves beyond "Right First Time". In: Friedli T, Prabir KB, Gronauer T, Werani J (eds) The pathway to operational excellence in the pharmaceutical industry. Editio Cantor, Aulendorf, pp 43–63

Mizuno S (1988) Management for quality improvement: the seven new QC tools. Foreword by Norman B. Productivity Press, Portland

Nicholas J (2011) Lean production for competitive advantage: a comprehensive guide to lean methodologies and management practices. Productivity Press/Taylor & Francis, New York

Rampersad HK (2001) Total quality management: an executive guide to continuous improvement. Springer, Berlin/Heidelberg

Seddon J, Caulkin S (2007) Systems thinking, lean production and action learning. Act Learn Res Pract 4(1):9–24

Stephan L (2012) Six Sigma + Lean toolset: innovationen erfolgreich realisieren. Springer, Berlin/Heidelberg

Stone KB (2012) Four decades of lean: a systematic literature review. Int J Lean Six Sigma 3 (2):112–132

Werani J, Friedli T, Goetzfried M (2010a) Unlocking potentials: a value stream mapping project. In: Friedli T, Prabir KB, Gronauer T, Werani J (eds) The pathway to operational excellence in the pharmaceutical industry. Editio Cantor, Aulendorf, pp 271–294

Werani J, Friedli T, Gronauer T (2010b) Six Sigma application: successfully integrating suppliers into operational excellence projects. In: Friedli T, Prabir KB, Gronauer T, Werani J (eds) The pathway to operational excellence in the pharmaceutical industry. Editio Cantor, Aulendorf, pp 295–313

Womack JP, Jones DT, Roos D (1990) The machine that changed the world. Rawson, New York

Chapter 19
Introducing Complexity in the Equation: How Pfizer Made Complexity on a Plant Level Transparent

Colin Seller, Richard Davis, Matthias Götzfried, and Thomas Friedli

Introduction and Relevance

Product variety proliferation is a trend in many industry sectors (e.g. Fisher et al. 1995; Scavarda et al. 2009; Klingebiel et al. 2011) due to the fact that offering product variety is considered an effective "strategy" to maintain and increase market share. Broadening the product portfolio enables companies to serve heterogeneous market segments and to satisfy variety seeking behavior of customers (Staeblein et al. 2011). However, Ramdas and Sawhney (2001) state that simply increasing variety does not guarantee an increase in long-term profitability and can in fact worsen competitiveness due to the complexity induced by product variety. As complexity increases, a company typically experiences difficulties in its internal operations because of higher direct manufacturing costs, manufacturing overhead, delivery times, and inventory levels (MacDuffie et al. 1996).

Building transparency on complexity induced by product variety and its effects on processes is therefore crucial (Child et al. 1991; Kreimeyer and Lindemann 2011). Recent research is mainly concerned with the complexity assessment of product portfolios (Jacobs and Swink 2011) or the role of complexity in supply and logistics (Lechner et al. 2011). When turning to the manufacturing part of the

C. Seller (✉)
Pfizer, Sandwich, Kent, UK
e-mail: Colin.M.Seller@Pfizer.com

R. Davis
Pfizer, Groton, Connecticut, USA
e-mail: richard.m.davis@pfizer.com

M. Götzfried
Freudenberg Sealing Technologies, Weinheim, Germany
e-mail: Matthias.Goetzfried@fst.com

T. Friedli
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_19,

company, existing researchers as well as practitioners are clearly focused on one dimension, namely the cost dimension for evaluating complexity (Gottfredson and Schwedel 2008; Sivadasan et al. 1993). However, calculating complexity costs remains highly difficult and is typically not successfully implemented in industry practice (Cooper and Kaplan 1988a, b; Schuh and Schwenk 2001). There have been only a few alternative indicators, besides costs, discussed in research yet to evaluate the complexity impact (Cargille et al. 2005; Orfi et al. 2011). A few complexity indices have been developed which are typically used to measure the success of complexity management approaches such as product platforms or mass customization (e.g. Orfi et al. 2011; Martin and Ishii 1997). They do not provide a guideline to evaluate complexity on a production plant level in a comprehensive manner. A holistic concept or model going beyond complexity cost estimations or single indicators (e.g. stock-keeping units) is not yet presented by researchers. Additionally, an investigation on the impact of external and internal complexity on plant performance by applying a comprehensive evaluation concept has not been conducted.

Objectives

The project that was launched by Pfizer had two objectives. First, the study was intended to design a holistic baseline metric to evaluate complexity on a production plant-level. Second, the study investigated the impact of complexity on operational performance and the study of the connection between Operational Excellence practices and the complexity – performance correlation.

Approach

In order to investigate the questions raised above, an exploratory research approach has been chosen due to the fact that existing approaches in research are rather limited to single dimensions (e.g. product portfolio complexity, product architecture commonality, or mass customization). The analysis presented in this chapter consists of two main building blocks: literature review combined with focused discussions with company experts and an empirical analysis of operational data from 158 pharmaceutical production plants. The project was conducted in a joint team of Pfizer representatives and two researchers of St.Gallen University.

Starting with a review of scientific and managerial literature, enhanced with specific discussions with practitioners, a comprehensive set of potential *complexity* indicators has been identified. These 42 operational indicators built the first draft of the complexity index. Subsequent, focused discussions within the project team led to a narrowing down of this comprehensive list to 29 potential indicators. From this set of 29 potential indicators, ultimately 20 indicators were identified and used in the comprehensive evaluation metric, called the complexity index (CI). The focus

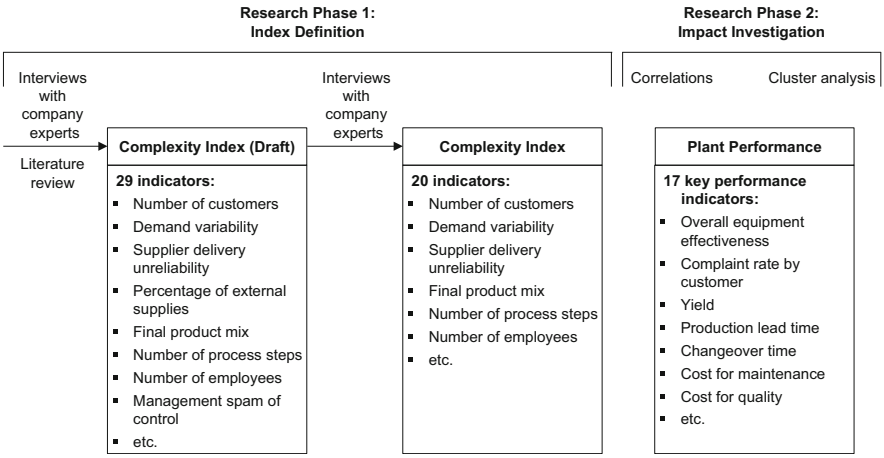


Fig. 19.1 Research process

of the first project phase had been set on the qualitative research including opinions and experiences of Pfizer experts which provided crucial thoughts and new perspectives on the issue of complexity evaluation.

After defining the complexity index, an investigation of the impact on single key *performance* indicators has been done to identify the indicators which are affected by a high level of production plant complexity. Correlations are calculated to identify these highest-impacted performance indicators. Additionally, an analysis has been conducted based on the identification of two clusters within the sample of 158 production plants from the St.Gallen OPEX database.

In summary, two main data sources have been used within the research:

- Data from interviews/workshops with practitioners (semi-structured/open-ended)
- Operational data (metric-scaled) gathered over the previous 3 years from 158 pharmaceutical production plants with a structured questionnaire
- Figure 19.1 illustrates the research process and points out the data used within the research stages.

Defining the Complexity Index

The development of the complexity index is framed by operations management literature differentiating between external and internal complexity (Pil and Holweg 2004). On the one hand, external complexity is a result of actors and stakeholders in the company's environment who are in a direct relationship with the manufacturing plant. Markets, corresponding customers' demand and suppliers playing a key role for most manufacturers influence internal assets and plant processes. On the other

hand, internal complexity is experienced inside of the plant when translating customer requirements into physical products. This requires a certain product portfolio, defined product creation processes and people. Consequently, the complexity index consists of five dimensions:

1. Market/customer (external complexity)
2. Supply (external complexity)
3. Processes (internal complexity)
4. Products (internal complexity)
5. People (internal complexity)

The differentiation between external and internal complexity as well as the breakdown into five dimensions, derived from literature, has been verified in the discussions (workshops) with experienced representatives from Pfizer coordinating a production network comprising of more than 50 plants. While some of the internal complexity may be the direct result of the external factors, they were ultimately considered internal because the company had some level of control over the indicator, even if the individual plant may not have ultimate control (e.g. new product launches).

Operationalization of the Dimensions in the Complexity Index

To provide operational feasibility of this baseline metric, each dimension has been detailed by defining its underlying complexity indicators (or drivers). 42 single complexity indicators were identified from literature as well as in open-ended discussions with company representatives. In the next stage, these 42 indicators were discussed and qualitatively evaluated with the company representatives with the objective of identifying the most relevant to pharmaceutical manufacturing. The result was the definition of the index along the five major dimensions noted above, differentiating between external and internal complexity.

Within these five major dimensions, 29 potential complexity indicators were identified of which 20 had significant contribution to the overall plant complexity. The data sets for these 20 key complexity indicators are typically available at a production plant level, which eased the second phase (quantitative investigation) of the project. Table 19.1 presents the final set of 20 indicators used to calculate the complexity index including definitions and units.

Math Behind the Complexity Index Calculation

The complexity index is calculated with an equal weighting of the complexity indicators. The decision for this equal weighting was done in close discussion with the project team and participating plants with the objective of keeping the

Table 19.1 Final set of complexity indicators used in the complexity index

Scope	Dimension	Indicator	Definition	Unit
External	Market & customers	Customer base globalization	The number of customer regions served by the plant	No
		Customer count	The number of customers served by the plant	No
		Type of customer	The number of company-external customers as a percentage of all customers	%
		Customer orders	The number of customer orders at the plant	No
		Sales forecast inaccuracy	The inverse score of the percentage of actual orders received compared to the annual sales forecast	%
	Supply	Supplier count	The number of active suppliers delivering to the plant	No
		Supplier unreliability	The inverse score of perfect order fulfillment (percentage of deliveries shipped in time, in the right quantity and right quality from your supplier)	%
		Supply frequency	The number of suppliers that deliver to your site not frequently as a percentage of all suppliers	%
Internal	Products	Bulk product mix	The number of different bulk products produced at the plant	No
		Product type	The number of different product types	No
		SKU count	The number of stock-keeping units	No
		Final product mix	The number of different final products produced at the plant	No
		Product launches	The number of new product introductions	No
	Products	SKU launches	The number of newly launched stock-keeping units at the plant	No
	Processes	Process count	The number of process steps performed at the plant	No
		Lot/batch count	The number of lots or batches produced at the plant	No
		Non-dedicated equipment	The inverse score of the percentage of dedicated production lines/production equipment	%
		Changeover count	The (average) number of changeovers performed per month	No
		Manufacturing planning instability	The percentage of production orders released within your freezing period as percentage of all production orders	%
	People	Employee count	The number of full-time employees at the plant	No

Fig. 19.2 Complexity index scores for the production plants in the dataset

calculation simple, understandable, and therefore, applicable in practice. As the indicators in the index have different units, each of the single indicators is normalized on a 0–100 % range based on the empirical data from the 158 production plants. The complexity index is then calculated in per cent ranging from 0 to 100. In line with this calculation, the external and internal complexity index is calculated accordingly by using the indicators assigned to either external or internal complexity. Figure 19.2 illustrates the distribution of the complexity index across the 158 production plants included in this research. Each of the bars in this figure represents one production plant from the dataset.

The Impact of Complexity on Plant Performance

The relationship between complexity and plant performance is analyzed in two parts. First, the correlations between single key performance indicators and the complexity indicators are calculated to reveal the performance indicators significantly impacted by complexity. Second, two clusters are identified based on the differentiation between external and internal complexity. These are compared in detail by looking at the performance details. Plant performance is categorized in four categories:

1. Quality
2. Productivity
3. Inventory
4. Speed

Table 19.2 shows the operationalization of the performance categories including definitions units, and the correlation of the indicator to the overall complexity index

Table 19.2 Key performance indicators investigated and their correlations with the CI

Category	Indicator	Definition	Unit	Correlation coefficient with CI
Quality	Rejected batches	Number of rejected batches as a percentage of all batches produced	%	0.49[a]
	Deviations	Number of deviations that arise from raw materials, production equipment and product/process specifications	No	0.29
	Customer complaint rate	Number of justified complaints as a percentage of all customer orders delivered	%	0.03
	Service level to customer	Percentage of orders shipped in time from the site and in the right quantity and right quality to your customer	%	0.18
	Quality cost	Overall costs for quality control and quality assurance at the plant	US$	0.25
Productivity	Overall equipment effectiveness	OEE = ((Scheduled time – Downtime)/ Scheduled time) × ((Amount produced × Ideal cycle time)/ Available time) × ((Input – defects)/ Input)	%	0.62[a]
	Yield	The difference between ideal and real achieved output due to material losses, etc	%	0.21
	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance	%	0.52[a]
	Maintenance cost	Overall costs for maintenance at the plant	US$	0.19
Inventory	Inventory days on hand	Days per month in which requested products from your customer are available at your warehouse	Days	0.19
Inventory	Finished goods turns	Annual cost of goods sold divided by the average finished goods inventory	No	0.08
	Raw material turns	Annual cost of raw materials purchased divided by the average raw material inventory	No	0.53[a]
Speed	Order lead time	The time between the order placing by the customer and receiving delivery	Days	0.03
	Production lead time	Average total lead time from raw material to finished goods including all kinds of process steps	Days	0.19
	Changeover time	Total time spent per change between different products for setting up and cleaning the equipment	Hours	0.58[a]
	Quality release time	Time from sample to material release for finished goods	Days	0.27
	Replacement time to customer	Response time for short-term delivery to the customer for goods not on stock (delivery time supplier + production time)	Days	0.16

[a]Significant positive correlation

(CI). The model used 17 metric-scaled key performance indicators including effectiveness-related indicators (e.g., rejected batches, yield) and efficiency-related indicators (e.g., quality cost, maintenance cost). The table also includes the Pearson correlation coefficients of the complexity index with each of the single key performance indicators.

The correlations show that certain key operational performance indicators are significantly impacted by the complexity level at the production plant, such as:

- The number of rejected batches,
- Overall equipment effectiveness
- The percentage of unplanned maintenance
- The number of raw material turns
- The changeover time.

According to the dataset of 158 production plants, overall complexity as measured by the CI, does not significantly impact complaint rates, finished goods turns, or order lead times.

Two Clusters in Comparison: True Masters Versus Laggards

The cluster analysis is based on differentiation between external and internal complexity. For both scopes (external and internal complexity), the index is calculated for each of the 158 production plants. Two main clusters are identified based on the external and internal complexity index calculation:

1. Production plants which are able to transfer a high level of external complexity into a low level of internal complexity
2. Production plants which are not able to make this transfer

The second part applied an additional filter to the clusters, specifically, the overall operational performance scores of the plants. The purpose of this additional filter was to identify plants which are able to transfer a high level of external complexity into a low level of internal complexity and, additionally, to achieve high plant operational performance. Similar to the calculation of the overall complexity index, the overall plant operational performance scores are calculated with equal weighting of the key performance indicators listed in Table 19.2 and normalized on a 0–100% range. Plants with a performance above 65 % are considered *high performers*.

Figure 19.3 shows the scatter plot for the identification of the clusters. The internal complexity index (CI) consists of the indicators in the products, processes and people dimensions. The external complexity index (CI) is calculated with the indicators in the market/customers and supply dimensions. The plot reveals that among the 151 production plants (seven of the 158 plant did not provide the complete set of key performance indicators), ten plants are able to achieve low internal complexity even with high external complexity (e.g., *complexity transfer)*

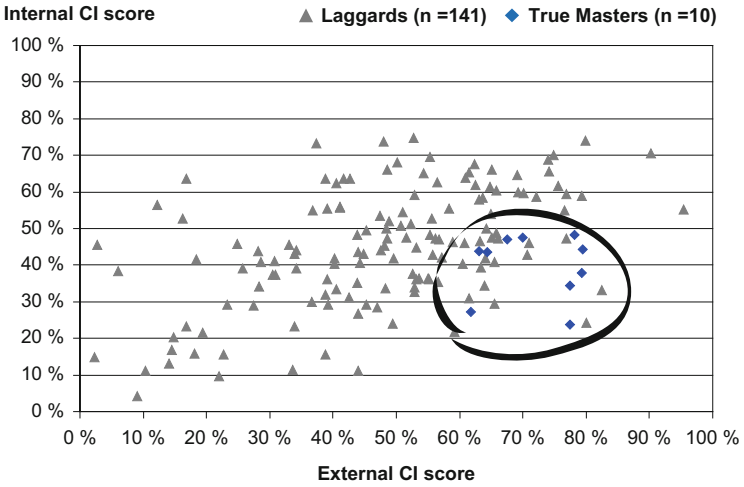


Fig. 19.3 Two clusters based on external and internal complexity and performance

and are achieving high performance. This cluster is called "True Masters". The remaining sites in the samples are identified as "Laggards" for this model.

The analysis of the two clusters shows that True Masters achieve better overall performance in the major performance categories of quality, productivity, inventory and speed, as well as in individual performance indicators.

In the quality category (see Table 19.2 for detailed definitions), major differences are revealed in the percentage of rejected batches and the cost of quality (in this case calculated as a ratio to the overall number of full-time employees in quality). In the productivity category, True Masters achieve better results in overall equipment effectiveness (OEE), unplanned maintenance, and maintenance cost per maintenance/engineering full-time employee (FTE). In the inventory category, the inventory days-on-hand in particular, is much lower at True Master plants. Minor differences in the turns of raw material and finished goods are also observed. In the speed category, production lead time, changeover time, and replacement time to customer shows major advantages by the True Masters compared to the larger Laggards cluster.

Figure 19.4 illustrates and highlights the main performance differences between True Masters and Laggards using this complexity model. In summary, the correlation analysis indicates that specific performance indicators at the plant level are impacted by the level of complexity. However, there are production plants which are able to manage a high level of external complexity with lower levels of internal complexity. In fact, certain plants are able to transfer high external complexity into a low level of internal complexity and achieve high performance.

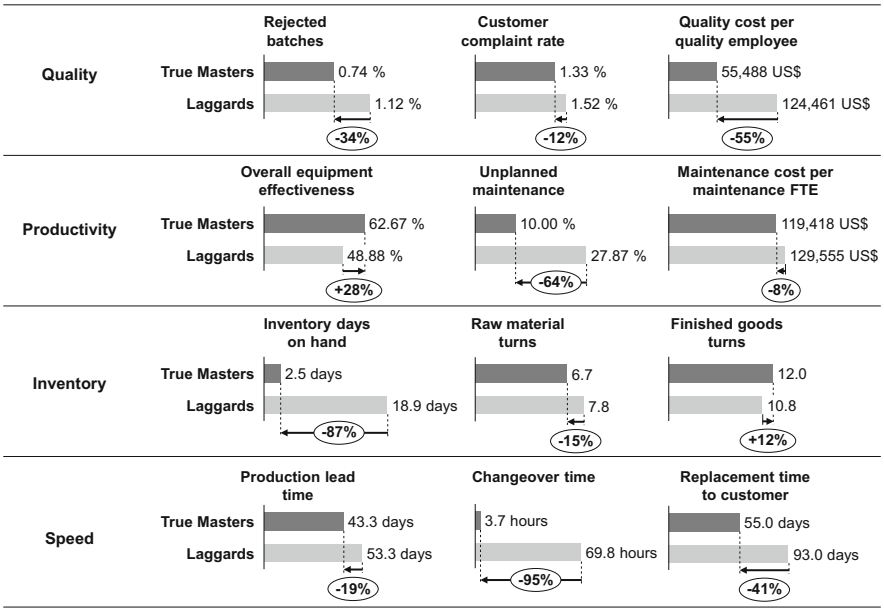


Fig. 19.4 Performance differences between True Masters and Laggards

However, the over-average performance of the true master plants is not achieved coincidentally. A further analysis correlating the degree of implementation of selected operational excellence (OPEX) categories (e.g., TPM, TQM, Lean) reveals that the true masters show better implementation along each of the OPEX enabler practices. While some laggards have been noted as having overall higher implementation of OPEX practices, the correlation with the True Masters indicates that appropriate and sustainable application of these practices support better complexity management and higher operational performance.

Deriving Consequences for Pfizer on Plant and on Network Level

Based on the outcomes of the described analysis, the data of three selected Pfizer plants were compared to the complexity masters to determine if the complexity model was applicable to the Pfizer manufacturing network. In addition to verifying the model, Pfizer was also looking to identify complexity factors at these sites that can be managed locally to improve performance. Furthermore, knowledge gained from these locations can be used to develop potential broader complexity strategies at a manufacturing network level.

The three plants selected represented different areas and technologies within Pfizer's manufacturing network, specifically, traditional small molecule manufacturing, manufacturing of over-the-counter consumer products, and biotech manufacturing. For the three Pfizer manufacturing plants in the study, the complexity modeling results were consistent with the analysis of the larger empirical data set of 158 plants. All three of the Pfizer facilities were in the "laggard" grouping based on the external and internal complexity relationship (see Fig. 19.3) and external complexity was not transferred to a "true master" (low level) of internal complexity. The overall operational performance index was typical of the empirical data set average for two of the plants.

One of the three Pfizer plants is, however, nearing true master levels of external complexity. This plant was able to transition internal complexity to a level approaching the true masters and with an operational performance nearing true master performance as well, even though the site had recently increased production levels with product lines new to the site.

Of note, this plant had an OPEX implementation score at the true master level. This resulting observation linking high levels of OPEX implementation to higher levels of complexity management and higher levels of operational performance is consistent with the observations from the larger empirical data set.

Key observations regarding "*true master*" plants in relation to the small sample number of Pfizer sites tested in the model were also consistent with the results from the larger empirical data set of 158 pharmaceutical plants. Specifically,

- The true master plants are more *specialized externally*. They serve fewer geographic regions, but still manage a larger number of customers. The true masters also have a higher degree of forecast accuracy than the other sites in the data base.
- True masters are also more specialized internally. They have a less diverse final product mix and a higher percentage of dedicated equipment, resulting in fewer changeovers.
- From an effectiveness standpoint, true masters have higher equipment utilization and less unplanned maintenance.
- Form an efficiency standpoint, true masters have lower costs for quality and maintenance, without impacting overall performance in these areas (e.g. right first time, amount of unplanned downtime).

Using these key observations as potential levers for improving complexity management and operational performance at the individual plant and manufacturing network level were important outcomes of the complexity analysis. The analysis provided insight into specific complexity factors that had high correlation, and therefore potentially high impact, on plant operational performance. From the empirical model using the 158 plants and the specific model testing with three Pfizer locations, Pfizer was able to make the impact of a number of complexity factors, particularly those beyond the more traditional portfolio complexity factors, transparent to the plants that participated in the analysis and can apply them to the broader manufacturing network.

The transparency and identification of key complexity factors impacting performance have resulted in a number of strategies at the plant and network level including:

- Continued implementation of appropriate OPEX practices at the plant level that not only support effectiveness and efficiencies, but also build sustainable capabilities. This analysis helps confirm that OPEX implementation is a critical success factor in managing complexity as well.
- A comprehensive deep-dive analysis of maintenance practices and processes and the impact of complexity on maintenance and asset performance (e.g., cost of maintenance, percentage of unplanned maintenance, overall equipment effectiveness (OEE))
- A comprehensive review of quality processes and the impact of complexity on the cost of quality, while still maintaining high quality products expected by the customer

Conclusions

The described complexity analysis results in five major propositions:

1. A baseline metric of complexity on plant level is a multifaceted concept and should include a number of different indicators, not just portfolio complexity.
2. Overall complexity levels at production plants significantly impact single key performance indicators at the plant level.
3. There are pharmaceutical plants which are able to transfer a high level of external complexity into a low level of internal complexity and also achieve an over-average operational performance in comparison to the production plants which are not able make this complexity transfer.
4. Part of the explanation for the high performance of the complexity masters is an above average, appropriately applied, and sustainable degree of OPEX enabler implementation.
5. An analysis of a single plant, or even a plant network, from the complexity perspective can be a valuable addition to traditional portfolio focused and cost-driven inquiries. An understanding of the importance of capabilities to manage complexity will be crucial in a pharmaceutical environment that continues to be more and more complex.

The result of the described project also contributes to the broader literature on complexity management in manufacturing environments. It presents a comprehensive complexity index for assessing complexity levels at production plants which is supported by the analysis of empirical data from 158 production plants. Further, it identifies two clusters based on complexity and performance levels within the dataset and reveals performance differences between them.

References

Cargille B, Fry C, Raphel A (2005) Managing product line complexity. OR/MS Today 32(3):1–9
Child P, Diederichs R, Sanders F, Wisniowski S (1991) The management of complexity. McKinsey Quart 4:52–68
Cooper R, Kaplan RS (1988a) Measure costs right: make the right decisions. Harv Bus Rev 66 (5):96–103
Cooper R, Kaplan RS (1988b) How cost accounting distorts product costs. Manag Account 20–27
Fisher M, Jain A, MacDuffie JP (1995) Strategies for product variety: lessons from the auto industry. In: Bowman E, Kogut B (eds) Redesigning the firm. Oxford University Press, Oxford/ New York, pp 116–154
Gottfredson M, Schwedel A (2008) Cut complexity – and costs. Harvard Manag Update
Jacobs MA, Swink M (2011) Product portfolio architectural complexity and operational performance: incorporating the roles of learning and fixed assets. J Oper Manag 29(7–8):677–691
Klingebiel K, da Cunha Reis A, Scavarda LF, Schaffer J, Brafman S (2011) Product diversity management within a supply chain perspective: lessons from an empirical study. In: Proceedings of the EurOMA conference, Cambridge, 3–6 July 2011
Kreimeyer M, Lindemann U (2011) Complexity metrics in engineering design – managing the structure of design processes, media. Springer-Verlag, Berlin/Heidelberg
Lechner A, Klingebiel K, Wagenitz A (2011) Evaluation of product variant-driven complexity costs and performance impacts in the automotive logistics with variety-driven activity-based costing. In: Proceedings of the international multiconference of engineers and computer scientists. Hong Kong, 16–18 Mar 2011
MacDuffie JP, Sethuraman K, Fisher ML (1996) Product variety and manufacturing from study the performance: evidence international automotive assembly plant. Manag Sci 42(3):350–369
Martin MV, Ishii K (1997) Design for variety: development of complexity indices and design charts. In: Proceedings of 1997 ASME design engineering technical conferences. Sacramento, 14–17 Sept
Orfi N, Terpenny J, Sahin-Sariisik A (2011) Harnessing product complexity: step 1 – establishing product complexity dimensions and indicators. Eng Econ 56(1):59–79, Taylor & Francis
Pil FK, Holweg M (2004) Linking product variety to order-fulfillment strategies. Interfaces 34 (5):394–403
Ramdas K, Sawhney MS (2001) Cross-functional approach to evaluating multiple line extensions for assembled products. Manage Rev 47(1):22–36
Scavarda LF, Schaffer J, Scavarda AJ, da Cunha Reis A, Schleich H (2009) Product variety: an auto industry analysis and a benchmarking study. Benchmark Int J 16(3):387–400
Schuh G, Schwenk U (2001) Produktkomplexität managen – Strategien, Methoden, Tools. Carl Hanser Verlag, München/Wien
Sivadasan S, Efstathiou J, Calinescu A, Schirn J, Nielson F (1993) The costs of complexity. Manuf Eng 79(3):109–114
Staeblein T, Aoki K, Tomino T (2011) External product variety, mass customization and order fulfilment in the automotive industry: a comparison between German and Japanese cases. In: Proceedings of the EurOMA conference. Cambridge, 3–6 July 2011

Chapter 20
Knowledge Exchange in Production Networks: Operational Excellence Multiplied

Simone Thomas, Fabian Liebetrau, and Thomas Friedli

Introduction: Importance of Knowledge Management in Manufacturing Networks

Ikujiro Nonaka, one of the most influential researchers in knowledge management, once stated that "[i]n an economy where the only certainty is uncertainty, the one sure source of lasting competitive advantage is knowledge. When markets shift, technologies proliferate, competitors multiply, and products become obsolete almost overnight, successful companies are those that consistently create new knowledge, disseminate it widely throughout the organization, and quickly embody it in new technologies and products." (Nonaka 1991, p. 96) Thus, manufacturing network managers have to focus their attention not only on the management of the physical flow of goods but also on the management of the intangible flow of knowledge (Chew et al. 1990). This applies to all kinds of industries: The strength of an international manufacturing company today is to a large degree dependent on its ability to exploit the knowledge that is available somewhere within its network or in its boundaries. To achieve this, network management has to be aware of the knowledge available at each site, generated, e.g., through Operational Excellence programs. It further has to trigger the distribution of process innovations and successful practices within the network (De Meyer and Vereecke 2009). However, many attempts to foster the exchange of knowledge in the network fall short of expectations. Popular examples are idle databases or lacking exchange of successful practices. Competition between manufacturing sites adds further barriers to the sharing of knowledge.

To overcome existing shortcomings and obstacles, a structured approach is needed which takes the network's structure and the specificity of knowledge into

S. Thomas (✉) • F. Liebetrau • T. Friedli
University of St.Gallen, Institute of Technology Management, Dufourstr. 40a 9000, St.Gallen, Switzerland
e-mail: simone.thomas@unisg.ch; fabian.liebetrau@unisg.ch; thomas.friedli@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_20,

account and thus enables the OPEX organization to actively steer the flow of knowledge in the production network.

In the following sections, we first address how knowledge is created in an organization. We then proceed with a discussion of the aspired exchange structure and degree of transparency which together form the basis of knowledge management within the network. Afterwards, we introduce different exchange mechanisms. The chapter concludes with a summary of incentive systems, which reinforce the knowledge management efforts. Practical examples enrich the theoretical framework.

Creating Knowledge Within a Global Manufacturing Network

The creation of new knowledge always starts with individual learning (Nonaka 1991). Only when this individual knowledge is shared and accumulated within the company, it becomes organizational knowledge (Foss et al. 2010). In this endeavor, the ease of knowledge sharing mainly depends on the type of knowledge: Whereas explicit knowledge is highly codified and thus may be easily shared (e.g., the knowledge of how to use a DVD player is easily shared by means of a user manual), tacit knowledge is highly personal, context-specific, mainly embedded in actions and thus difficult to communicate (e.g., the ability to ride a bicycle cannot easily be communicated) (Nonaka 1991). Thus, with tacit knowledge individuals seem to know more than they can tell (Polanyi 1966). That is, individuals learn on the job, acquire practical expertise, but are unable "to describe [the tacit knowledge] in a way that is helpful" (Szulanski and Winter 2002, p. 64). According to Nonaka and Takeuchi (1995), knowledge is created through a conversion of tacit into explicit knowledge while proceeding in a spiraling process from the individual to the organizational level (Nonaka and Takeuchi 1995; Fig. 20.1). The authors distinguish four modes of knowledge conversion: (1) from tacit to tacit knowledge, i.e. socialization, (2) from tacit to explicit knowledge, i.e. externalization, (3) from explicit to explicit knowledge, i.e. combination, and (4) from explicit to implicit knowledge, i.e. internalization (Nonaka and Takeuchi 1995).

First, socialization describes the process of knowledge creation through shared experiences between individuals (Nonaka 1994). This involves primarily learning through observation, imitation, and practice (Nonaka 1994). A common principle used in companies to spread tacit knowledge is on-the-job training. Second, the process of externalization comprises the conversion of tacit knowledge into explicit knowledge. It usually takes place within the context of concept development. As tacit knowledge cannot directly be grasped, it needs room for interpretation. This is realized by use of metaphors or analogies, e.g., within the scope of product development. Third, knowledge creation through combination covers the creation of new (explicit) knowledge through a reconfiguration of existing explicit

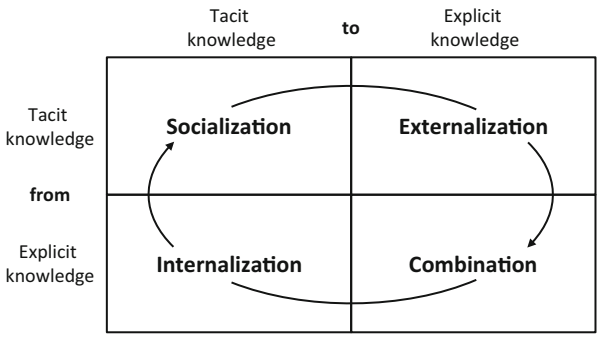


Fig. 20.1 The knowledge spiral (Adapted from Nonaka and Takeuchi 1995)

knowledge. It is based on an exchange of knowledge through documents, meetings, telephone calls or data bases and involves sorting, reorganizing, and adding of existing knowledge. Finally, internalization depicts the conversion of explicit knowledge into tacit knowledge. It is similar to the practice of learning-by-doing. Documentation may provide a useful basis for the process of internalization. (Nonaka and Takeuchi 1995)

Summarizing, knowledge creation is achieved in different ways with different underlying conditions and the application of different exchange mechanisms. To advance knowledge creation within a global manufacturing network, the conditions should be set appropriately to support the different modes of knowledge conversion.

Determining the Exchange Structure and the Degree of Transparency

The two main dimensions that describe the basic conditions for knowledge creation and dissemination in a network are the structure and the transparency of knowledge exchange (Mundt 2012). The exchange structure defines the degree of centralization of knowledge exchange (Mundt 2012). It range from complete decentralization, focused on a direct exchange between sites with little or only indirect central guidance, to full centralization, with knowledge being centrally provided from the headquarters to the plants (Chew et al. 1990). Additionally, a mixture between a decentralized and a centralized structure may occur which allows a certain degree of direct exchange between sites while still having a central steering in place. Progressing towards a more centralized structure, knowledge exchange may also be centrally coordinated by a hub that collects and distributes knowledge within the network (Mundt 2012). The prevalent exchange structure strongly influences the channels, through which knowledge is collected, processed, and distributed (Mundt 2012).

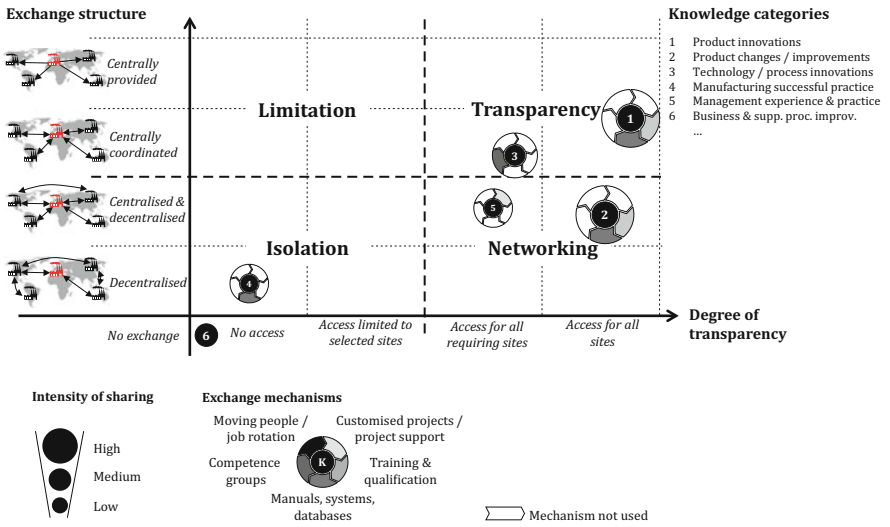


Fig. 20.2 Knowledge sharing framework (Adapted from Mundt 2012)

The second dimension comprises the degree of transparency, i.e. the sites' accessibility to the available knowledge (Mundt 2012). It ranges from fully accessible to fully restricted. In case of the latter, managers with network-wide responsibilities have the opportunity to control the exchange of knowledge and steer the sites by granting or restricting the access to knowledge. This may either involve certain sites or certain pieces of knowledge (Mundt 2012).

Figure 20.2 visualizes the two dimensions in the knowledge sharing framework.

The framework reveals four generic positions for knowledge sharing (Mundt 2012):

1. The isolation position is based on a decentralized structure with restricted access to knowledge. This position is usually owed to highly autonomous sites acting independently and lacking a platform for knowledge exchange.
2. The networking position is also built on a decentralized structure, but involves a high degree of transparency. This position occurs when sites are actively engaged in knowledge exchange, thus perceiving themselves as "team members" within the network.
3. The transparency position is characterized by a central exchange structure and a high degree of transparency. Typically, headquarters or a leading site in the network are steering the knowledge exchange, being responsible either for the creation and provision, or the collection, processing, and transfer of knowledge.
4. The limitation position is also based on a centralized structure, but characterized by a low degree of transparency. The sites are hence restricted in their access to knowledge. This may either be due to strategic targets of the central steering unit, e.g., conscious limiting of the sites' access to knowledge, or due to a selective allocation of knowledge.

The cases of two global non-pharma manufacturing companies illustrate the implications of the knowledge sharing framework. In the case of a mechanical seals manufacturer, the network management was struggling with knowledge sharing. It found itself locked in the isolation position with the autonomous sites being reluctant to share their knowledge with each other. Only financial information "which was collected centrally" and knowledge on product innovations from the central R&D function were exchanged throughout the whole network. Local product adaptions as well as local innovations in technologies and processes remained undisclosed from network management. This in turn hindered the achievement of a common global product quality standard and process standardization. In order to counteract the adverse effects, network management had to actively engage in knowledge management. Measures inducing a change and a move towards the transparency position included a centralization of product- and process-related knowledge sharing. This again demanded a harmonization of the various existing product data management systems to create a platform for a transparent knowledge exchange.

The second case of a chemical engineering company in the dental industry illustrates how the company succeeded in reaching the networking position. The first step to get the manufacturing sites working closer together was achieved by a comprehensive overhaul of the organizational structure, which led to the creation of a central production function. This reduced the existing organizational barriers and competition between the manufacturing sites. However, one of the main success factors was the personal commitment of the network manager who not only created dense ties to each of the sites but also between them. He did so by establishing a structured exchange which included regular meetings on different hierarchical levels, within functions, as well as cross-functional.

In the next section we will concentrate on the different types of knowledge exchange mechanisms and their application in the network.

Examining the Different Types of Knowledge and Deriving Appropriate Exchange Mechanisms

Choosing the appropriate mechanisms to generate and distribute knowledge within the network is another prerequisite for successful knowledge management. The right mechanism for the transfer of knowledge depends on the type of knowledge that has to be transferred. Ferdows (2006) provides a framework that builds upon the distinction between tacit and explicit knowledge and the speed with which the knowledge changes (Fig. 20.3). For explicit knowledge, codification is a key mechanism to transfer knowledge (Ferdows 2006). New knowledge is mainly collected centrally and then codified in operations manuals or systems (Ferdows 2006). Requiring employees or units may then be taught how to apply the new knowledge. When, however, production knowledge is tacit, it has to be transferred

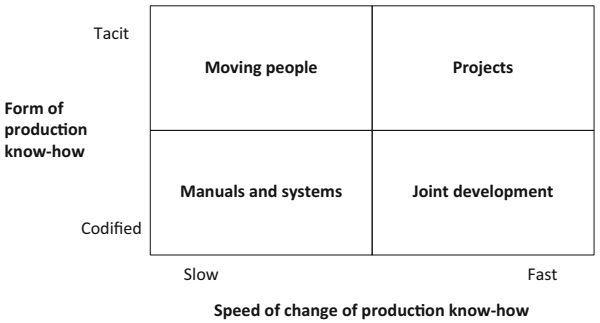


Fig. 20.3 Exchange mechanisms (Adapted from Ferdows 2006)

face-to-face (Ferdows 2006). In this case, network management should consider moving people to spread the new knowledge within the network (Ferdows 2006). Furthermore, regardless of whether the knowledge is explicit or tacit in its nature, if it is changing quickly, a critical mass of experts is needed to participate in the creation of new knowledge (Ferdows 2006). The use of experts also allows for a fast implementation of new production methods and transfer of the knowledge in time to other employees or units (Ferdows 2006). In the case of quickly changing tacit knowledge, the experts should participate in projects to directly contribute their knowledge and expertise. In the case of quickly changing production knowledge that can be codified, joint development between the central unit and the manufacturing sites is an appropriate mechanism to generate and distribute new knowledge.

The relation between the type of knowledge and the use of exchange mechanisms is illustrated by several practical examples. A leading producer of private label pet food, for example, has implemented so-called centers of expertise (CoE), which support the company's strategic target of being a quick follower. The CoEs consist of experts in a certain field of operations, e.g., they are related to a specific production technology or to product development for a particular product group. All experts belonging to a CoE are centrally assigned and their role is clearly communicated in the network to achieve a high degree of transparency. Main tasks of the CoEs comprise support for the producing plants and further development of the CoE's specific field of expertise within the whole network. Thereby, the experts are both engaged in documentation of existing knowledge and sharing of their expertise in joint development projects. Thus, the CoEs are the basis for the company's ability to quickly launch new products and expand production to several sites of the network within a short period of time.

In the network of a polymer processing company, a central unit steers the exchange of knowledge. It is primarily responsible to ensure global adherence to the standardized production process. Consequently, it is not only engaged in the process control system but also in the documentation of the target process, and accomplishment of process audits. Where applicable, information and knowledge are codified and stored in a database. The sites may access the information, but are not able to make any changes to the standard process. Requests for changes always have to be directed to the central unit which then checks if a modification of the

standardized process is necessary. If modifications are made, the central unit sends its experts to the sites to introduce the changes. Usually, the experts support the modification of one production line; modifications of the other lines are done by the site itself. Thus, the experts transfer their knowledge to the dispersed sites but, due to supporting the modification of the different sites' production lines, also acquire new knowledge.

In the case of a producer of domestic appliances, the choice of appropriate exchange mechanisms was crucial to the establishment of cooperation between China and Europe. Cultural differences represented major barriers to an exchange of knowledge, which could not be overcome by conventional communication channels such as e-mail and telephone calls. Hence, in a first step network management introduced regular video-conference meetings which were less and allowed for a more personal communication. In a second step, an exchange of employees was initialized to strengthen the tenuous ties. Thereby, the exchange not only involved the management level but was enlarged to comprise also functional layers. By this means, the network management succeeded in creating a mutual understanding and could identify ties between the European and the Chinese sites. Today, the plants work closely together and knowledge is exchanged frequently. The mechanisms used today also comprise e-mail and telephone calls, as the employees now draw on a closer relationship based on common projects, discussions, and meetings (Mundt 2012).

Incentive System: Reinforcing Knowledge Management

After having defined the basic structure of knowledge exchange, the degree of transparency, and the appropriate exchange mechanisms, another crucial task of network management is to embed the sharing of knowledge in the network. This must of course involve the dispersed sites. Thereby, the targets of the sites, e.g., increasing their own knowledge base to strengthen their position in the network, may be contrary to the targets of network management, e.g., sharing of successful practices to enhance product and process quality throughout the network. Thus, it is important to set the right incentives. According to Mundt, "[i]ncentive systems provide mechanisms to motivate an intended behavior by facilitating desirable or restricting unwanted actions." (Mundt 2012, p. 91) The definition of network- or site-specific targets and the related allocation of rewards provide network managers with a means to steer the sites along the network's goals. If targets are set for individual sites, this may foster competition, whereas setting targets for the whole network may intensify collaboration between sites (Bartol and Srivastava 2002). The allocation of rewards further affects the interaction between sites: If rewards are solely based on each site's individual contribution, e.g., connecting the site manager's bonus payment to the site's performance, this is likely to fuel competition. On the other hand, if rewards are equally allocated between sites, this may strengthen cooperation between them (Mundt 2012).

Conclusion

In this chapter we provided an overview of our structured approach to foster the exchange of knowledge in a global network. We illustrated how knowledge is created within an organization, i.e. with individual learning always standing at the beginning of knowledge creation. It then comes to determine an appropriate structure for knowledge exchange. On the one hand, strong centralization gives headquarters a comprehensive overview of existing knowledge and might, in combination with a limited access to knowledge, be used as a means to control the flow of knowledge. On the other hand, a centralized structure together with free access to knowledge may foster networking within the organization. Knowledge exchange may further be supported by applying suitable exchange mechanisms. These are dependent on the type of knowledge. Especially for organizations which have to keep up with fast-changing production know how, mere documentation will not suffice to spread knowledge between sites. Finally, we claim that the implemented knowledge exchange system should be supported by an appropriate incentive system.

The structured approach to knowledge management allows the network function to actively steer the exchange of knowledge in the production network. The OPEX organization with network-wide responsibilities is thus in the pole position to drive knowledge exchange in the network and multiply the benefits achieved at the single sites.

References

Bartol KM, Srivastava A (2002) Encouraging knowledge sharing: the role of organizational reward systems. J Leadersh Organ Stud 9(1):64–76

Chew WB, Bresnahan TF, Clark KB (1990) Measurement, coordination, and learning in a multiplant network. In: Kaplan RS (ed) Measures for manufacturing excellence. Harvard Business School Press, Boston, pp 129–162

De Meyer A, Vereecke A (2009) How to optimize knowledge sharing in a factory network. McKinsey Quart 3:1–7

Ferdows K (2006) Transfer of changing production know-how. Prod Oper Manag 15(1):1–9

Foss NJ, Husted K, Michailova S (2010) Governing knowledge sharing in organizations: levels of analysis, governance mechanisms, and research directions. J Manag Stud 47(3):455–482

Mundt A (2012) The architecture of manufacturing networks. Integrating the coordination perspective, Doctoral Thesis University of St.Gallen, St.Gallen

Nonaka I (1991) The knowledge-creating company. Harv Bus Rev 69(6):96–104

Nonaka I (1994) A dynamic theory of organizational knowledge creation. Organ Sci 5(1):14–37

Nonaka I, Takeuchi H (1995) The knowledge-creating company: how Japanese companies create the dynamics of innovation. Oxford University Press, New York

Polanyi M (1966) The tacit dimensions. Routledge & Kegan Paul, London

Szulanski G, Winter S (2002) Getting it right the second time. Harv Bus Rev 80(1):62–69

Part III
Leading Operational Excellence: Outstanding Leadership

"Day by day, from April 1864 to April 1865, Grant fought Lee's Army . . . head-on . . . He would not retreat . . ., "I intend to fight it out on this line if it takes all summer.-"[1]

""Ike", she remembered, "got out and just started walking among the men. When they realized who it was, the word went from group to group like the wind blowing across a meadow, and then everyone went crazy – the roar was unbelievable . . . I stood by the car and watched as the General walked among them. . . . He went from group to group and shook hands with as many men as he could. He spoke a few words to every man as he shook his hand, and he looked the man in the eye as he wished him success. . . ."[2]

Good leadership requires true dedication, persistency and to care about people. In this part of the book, we summarize various challenges to leadership, and ways to overcome them. After some theoretical considerations, we leave the stage to colleagues who have personally experienced such challenges, either by having led themselves, or by having closely observed leaders in their work. First, we provide some insights into transformational leadership based on a first-hand account from Pfizer. Next, we describe why and how to involve all organizational levels in the journey to Operational Excellence – including the middle management, which is often neglected yet vital for the success of an OPEX initiative. This is further emphasized by providing an insight into the true meaning and impact of HoshinKanri. The remaining parts examine characteristics of a good OPEX leader, and the leadership of OPEX on all company levels – from the global, over the regional to site responsibility. Together, these chapters clearly evidence the importance of leadership.

[1] Korda M (2007) Ike – An American Hero. New York, p. 433.

[2] Kay Summersby (General Eisenhower's driver) about a visit of Eisenhower to the 101st Airborne division the day before D-Day, cited from Korda, M. (2007): Ike – An American Hero, New York, p. 54f.

Chapter 21
Leadership Principles & Operational Excellence

Thomas Friedli and Jürgen Werani

Loyalty is the big thing, the greatest battle asset of all. But no man ever wins the loyalty of troops by preaching loyalty. It is given to him as he proves his possession of the other virtues.
Brigadier General S. L. A. Marshall (1947) (Men Against Fire)

If he had thought that he was sent to perform an impossibility with the means given him, he would probably have informed the authorities of his opinion and left them to determine what should be done. If the judgment was against him he would have gone on and done the best he could with the means at hand without parading his grievance before the public. No soldier could face either danger or responsibility more calmly than he. These are qualities more rarely found than genius or physical courage.
Smith (2002) U.S. Grant on General Taylor

We had been fighting since Yom Kippur, almost two straight weeks. Since then, no one in the division had gotten any real sleep. Men dozed off in their positions during the occasional lulls or tried to catch an hour or two at night on the warm engines of tanks and armored personnel carriers. The entire previous night I had spent at our forward posts staring into a Starlight scope toward Ismailia, looking for signs of Egyptian movement. Now, despite the shelling, I couldn't keep my eyes open. Wrapping my coat around me, I lay down in the sand next to my command APC. Already half asleep, I felt someone pull a blanket over me. Nearby a voice was shouting something, and I heard a soldier whisper hoarsely, Be quiet, Arik's tired. Let him sleep.
Sharon and Chanoff, A., 2001: Warrior: An Autobiography

T. Friedli (✉)
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch

J. Werani
Schuh & Co, Komplexitätsmanagement AG, Langgasse 13, St.Gallen 9008, St.Gallen, Switzerland
e-mail: juergen.werani@schuh-group.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_21, © Springer-Verlag Berlin Heidelberg 2013

For a long time, pharmaceutical companies mostly laid stress on the training of specialists and technical aspects in their pursuit of Operational Excellence. This focus on methods and tools somewhat distracted from one of the most important success factors for a sustainable implementation: leadership. The importance of leadership has been notoriously underestimated. We will start this chapter with a short introduction to leadership, and then highlight the importance of leading the "right way" at all levels of an organization: from the OPEX specialists, over the OPEX leader in a plant and the plant leader himself to the responsible person for OPEX at a corporate level and the Top Management. We will build a leadership model helping us to put leading in an OPEX context, and will then discuss what kind of leadership is the most appropriate for a sustainable implementation of OPEX.

Leadership: An Introduction

Wunderer and Kuhn (1993) defines leadership as "target-oriented social influence to fulfill joint tasks in respectively with a structured working situation" (Wunderer and Kuhn 1993, p. 24). Based on this definition, Wunderer states that there is a direct form of leadership that manifests in interactions, as well as an indirect form based on shaping structures, culture and strategies. Leadership theories are therefore quite diverse and highlight different aspects. We do not intend to give an overview of all possible existing leadership theories, but will limit our discussion to the more promising perspectives with regards to OPEX. Pavur (2012) states that "... the fundamental purpose of the manager's position is to help the organization to become more successful" (Pavur 2012, p. 270). Leadership is therefore not an end in itself, but an enabler for success. Typically discussed categories of leadership are production (initiation of structure), people (concern for the welfare, needs, and aspirations of employees, vendors, and customers) and change (cf. Pavur 2012). On the one hand, OPEX deals with all of these categories; on the other hand, the impacts on these categories are quite diverse over the different management levers that are involved (and needed) in today´s OPEX initiatives. Our model will therefore have to differentiate between these levers to be meaningful. Based on the above-mentioned categories, Pavur (2012) derived a taxonomy of general management (Fig. 21.1).

We will come back to this taxonomy when we discuss the requirements for leading OPEX.

The Nature of OPEX Initiatives

Operational Excellence is about change. In this book, we define change as its underlying philosophy, driving continuous improvement throughout the organization, and becoming part of the mindset of every single employee (cf. Chap. 2 and Chap. 7). And yet, OPEX is also about stability, consistency and sustainability.

Skills and Activities	*Functions*	*Broad Categories*
Clarifying	Plan, Organize, Command, Coordinate, Control (Fayol, 1917) Organize, Improve, Monitor (Taylor, 1911)	Initiation of Structure (Stogdill, 1974)
Planning & Organizing		
Problem Solving		
Informing		
Monitoring Results		
Supporting	Participation, Motivation, Support	Consideration (Stogdill, 1974)
Consulting		
Delegating		
Recognizing		
Rewarding		
Developing, Empowering, Motivating		
Managing Conflict, Building Teams	Achievement, Constructive conflict (Follett, 1941)	
Developing Teams		
Representing	External Liaison Anticipating Future Needs Adjusting to New Conditions	Adapting in Open Systems (Von Bertalanffy, 1950) Understanding the Environment (Emery & Trist, 1965) Change (Ekvall & Arvonen, 1991; Yukl, Gordon, & Taber, 2002)
Networking, Interfacing		
Communicating a Vision of the Future		
Taking Risks for the Organization		
Promoting Open Systems Analysis		
Enviromental Scanning		
Making System Decisions as a Team		

Fig. 21.1 Leadership skills and activities: a taxonomy of general management (Pavur (2012), p. 272)

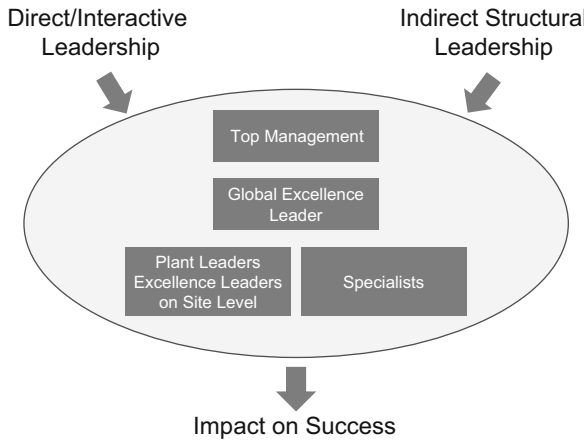


Fig. 21.2 The OPEX leadership model

This makes its leadership challenging. Leading OPEX is not only about creating a vision and a sense of urgency. Following Kotter (1995, p. 99), there is more to it – leading is like forming a powerful coalition, it is communicating a vision, empowering others to act on that vision, planning for and creating short-term wins, consolidating improvement while producing still more change and institutionalizing the new approaches. To achieve long-term success and impact, it is essential to avoid what Kotter lists as failure number 8 in change initiatives: "not anchoring changes in the corporate culture" (Kotter 1995, p. 103). Again, this requires communication, and OPEX has to become visible in structures, activities, incentive systems, etc. To some degree, OPEX has to become a routine operation, even if it will continue to be about change. It is both, fostering change and ensuring stability, what is required from leadership, and these two perspectives on OPEX together define the basic requirements for leaders: establishing structures, planning for improvements, organizing activities, establishing routines but also being present where the action is, caring about people, communicating, coaching, supporting and motivating employees. An appropriate model for leading OPEX has to reflect all of this.

A Model for Thinking About Leading in OPEX Activities

Based on the discussions so far, we introduce a framework for thinking about leadership. This framework is shown in Fig. 21.2.

Some of the discussed requirements can be addressed by indirect/structural leadership measures, i.e. they can become part of the strategy, structure and, ultimately, culture of the company. We have described an ideal structure for an OPEX initiative in Chap. 16, also suggesting to change this structure over the lifecycle of the program. We believe that this part of leadership has the strongest

impact on the stability and long-term impact of the initiative. Structures that come with resources communicate to the whole organization that an initiative is intended to last and is not meant as one-time exercise with a short-term impact. The difficult decisions to take is to decide when to give more power and responsibility to the decentralized parts of the OPEX organization; this is to ensure that the initiative has a chance to get embedded in daily operations, thereby becoming part of the mental model of every single employee. Unless this step is taken, there will always be the danger that people see OPEX as something external, unrelated to their daily concerns and responsibility.

In the remaining part of this chapter, we will focus on the leadership skills and capabilities each OPEX leader has to have deeply ingrained. Our model differentiates between the hierarchical levels of managers dealing with OPEX. Like in other important strategic initiatives, the top management, too, will have its role in making OPEX part of daily operations, and this role is a crucial one. The main driver of the program has to be the global OPEX leader, who will be the main point of identification for OPEX within the organization. His or her very character and example will decide about the acceptance of OPEX. As the main activities will have to take place at site level, this is the real battleground on which the war is won or lost. The level of the plant leaders and OPEX leaders at plant level is decisive. We have experienced that without visible commitment of the plant leader, any initiative is doomed to fail. We now come back to the leadership capabilities and skills shown in Fig. 21.1 and determine their importance for OPEX while differentiating the crucial roles identified in Fig. 21.2.

Figure 21.3 makes several points transparent:

1. Leading OPEX is a complex task with highly interdependent management levels involved
2. Especially for the day-to-day interaction, the plant leader and the OPEX leader on this level become crucial. On the one hand, they have to understand the vision and the objectives for the program in general, on the other hand, they have to translate this vision into a shop floor reality.
3. The global OPEX Leader has its main responsibility in ensuring that the preconditions for success are in place. He is the one who has access to Top Management. He will be the one to define and communicate a vision. He will be the one to make sure that OPEX remains a priority in the company. To be able to achieve all of these things, he has to understand the challenges of the plant leaders and the agenda of the Top Managers.
4. There are two leadership roles that are often underestimated in relation to the success of OPEX: the role of Top Management and the role of the specialists. Based on 10 years of experiences in striving for OPEX, the importance of the plant leaders and the global OPEX people in charge became evident but not of the top management and the specialists Top Management only recently became part of considerations in OPEX trainings, as companies realized that without an understanding of OPEX, and a visible support for OPEX at the Top Management level, there is no chance of a long-term impact of these programs. The specialists

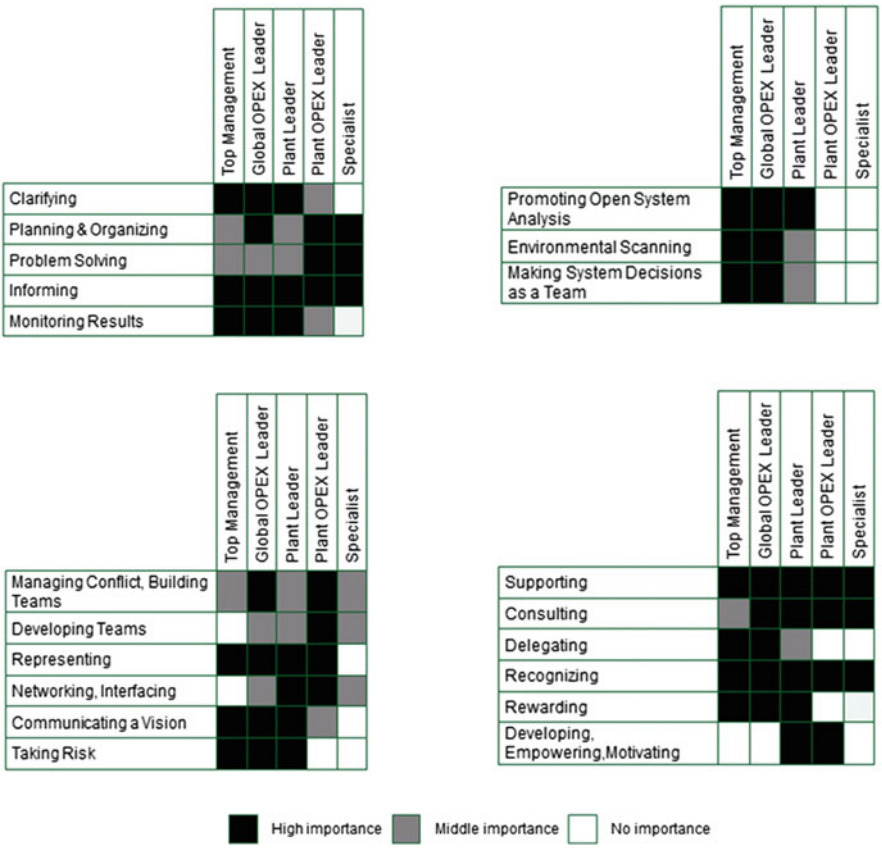


Fig. 21.3 Roles and leadership skills/capabilities

and the training of the specialists were rather seen as a technical than as a cultural challenge. A lot of the trained resources never managed more than one or two improvement projects, as they were re-integrated in the line functions. Yet, these specialists are in the center of the activities, they too become role models for the shop floor workers. Therefore, it is crucial to pay attention to them and to make sure that they, too, have leadership skills or leadership potential before they are selected!

Conclusions and Summary

In OPEX-advanced companies, the focus of activities more and more shifts towards leadership. Clear signs for this shift are increased efforts to train leaders, introducing new ways of leading and coaching and sensitizing Top Management

for OPEX and its requirements. Leading is more than managing. We have shown that OPEX requires both managing and leading, but depending on the management level organizing or "real" leading becomes more important. We know from military history that true leaders lead from the front – their position is where they have the biggest impact on the battle. In today´s pharmaceutical companies, this is the shop floor. This means that the next generation of managers has to be (willing to be) trained to go exactly there, leaving their air-conditioned offices in the administration building near-by behind for the real production environment. The requirements for this kind of new managers are high: Besides having good organizational skills, they will have to have a motivational appearance and a true commitment to and passion for the cause of OPEX. Unless people feel that their leaders believe in what they are doing, unless they become to role models for OPEX themselves, people will not follow. The hardest but most important characteristic of such a new generation of leaders is to additionally have a noble and incorruptible character. That said, it becomes clear that the selecting the right leader is key for success.

We have also mentioned the long-term and stability-related character of every promising OPEX initiative. To ensure this stability, we have emphasized the importance of the structural/indirect part of leadership. Embedding OPEX into the organizational structures is the easiest way to make sure that it will be taken seriously throughout the company.

References

Ekvall G, Arvonen J (1991) Change centered leadership. An extension of the two-dimensional model. Scand J Manag 7(1):17–26

Emery F, Trist E (1965) The causal texture of organizational environments. Hum Relations 18:21–32

Fayol H (1917) Préface à Administration industrielle et générale. Dunod and Pinat eds, Paris

Follett MP (1941) Dynamic administration: the collected papers of Mary Parker Follett edited by Henry Metcalf and Lionel Urwick. Pitman, London

Kotter JP (1995) Leading change. Harvard Business School Press, Boston

Marshall SLA (1947) Men against fire; the problem of battle command in future war. Infantry Journal/William Morrow & Co, Washington, DC/New York

Pavur EJ (2012) Leadership for managers. Psychol Manager J 15(4):269–274

Sharon A, Chanoff D (2001) Warrior: an autobiography, 2 Sub edition. Simon & Schuster, New York

Smith JE (2002) Grant, first edition. Simon & Schuster, New York

Stogdill RM (1974) Handbook of leadership: a survey of theory and research. Free Press, New York

Taylor FW (1911) The principles of scientific management. Harper & Brothers, London

van Bertanlanffy L (1950) The theory of open systems in physics and biology. Science 111:23–29

Wunderer R, Kuhn T (1993) Unternehmerisches Personalmanagement: Konzepte, Prognosen und Strategien für das Jahr 2000. Luchterhand, Frankfurt

Yukl G, Gordon A, Taber T (2002) A hierarchical taxonomy of leadership behavior: integrating a half century of behavior research. J Leadersh Organ Stud 9:15–32

Chapter 22
Transformational Leadership - Shaping the Future of the Biopharmaceutical Industry

Andy Crossman

The biopharmaceutical industry is undergoing deep structural changes in the marketplace as is the legacy business model that supports it. To succeed in this turbulent climate, organizations will need "transformational" leaders, at all levels, skilled at adapting to rapid socio-technical change, anticipating disruptive events in the marketplace, and setting a shared inspirational vision for all colleagues.

These leaders already exist today in "pockets" of innovation around the globe. They are creating a virtuous cycle of sustained continuous improvement and breakthrough performance that is distinctive in their organizations proving that "leadership matters". This chapter captures some of the key elements of "Transformational Leadership" and provides insights into developing this needed leadership at the macro and micro level. The hypothesis is that the needed transformational leadership skills can largely be learned and developed.

> To distinguish leadership from management, one can argue that leaders create and change cultures, while managers live within them. (Edgar Schein)

Superior management is vital for today's biopharmaceutical companies to succeed, but it is just an entry ticket to be in the "game". In this new environment, it is not enough to compete and succeed. Based on current information, operational performance improves, on average, 5–7 % annually across the biopharmaceutical industry. This suggests that incremental improvement, even using today's best-in-class targets, will only allow companies to stay level with its competitors, but fall behind the pacesetters, as they too will have improved over time. Transformational changes in operational performance require radically different action and thinking. The ability to inspire and align an entire organization around a shared vision, to create urgency where there may be none, to create the environment for innovation and the engaged workforce to thrive in the face of uncertainty and then execute their plans, requires the skills of a "transformational leader".

A. Crossman (✉)
Pfizer Network Performance Strategy, Rouse's Point, NY, USA
e-mail: Andy.Crossman@pfizer.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_22, © Springer-Verlag Berlin Heidelberg 2013

Overlaying organizational transformation, the introduction of new models in supply chain management and enterprise technology are also rapidly changing the way companies work and the results they are capable of producing. Pfizer's Jim Cafone, Supply Network VP, sees a macro vision of transformation creating whole new markets and customer-focused systems that did not previously exist. This macro level of leadership can be translated down to a micro level where innovative new ways of supporting the customer cumulatively transform an organization and produce transformational change in performance outcomes. Cafone states that "Innovation begins with the understanding that governments and customers will not pay for commoditized manufacturing technology. They will pay for innovation in both the product and the supply system". This cannot be achieved without clear vision and execution. In other words, it is not enough to just be a superior, best in class manufacturing organization. Rather we will need to master and exploit opportunities in the larger "end-to-end" supply chain. A strong and interdependent commercial linkage to manufacturing capabilities will be the winning combination for transformational industry leadership.

The Role of Leadership in Transforming the Biopharmaceutical Industry

Together with excellent management, transformational leadership is key to future success. Transformational leaders are rare, and for that reason highly valued. For some the skills come naturally, but for many, these skills are acquired during a lifetime of personal learning and experience. The process takes tremendous will, self-reflection, personal courage, and a choice-to-change over time.

It takes transformational leadership to carry an organization into an uncertain future where change is accelerating, exploiting previously unseen opportunities, and shaping a culture of continuous improvement. Pfizer Global Supply Andover, Massachusetts plant Site Leader Ken Bradley, states that "technology can be quickly replicated or reverse engineered by competitors, but an organization that has a continuous improvement culture creates a true competitive advantage – and that can't be easily replicated! We need to develop agile organizations that can respond to a changing business environment – linked in a partnership that creates value for our customers". Transformational leaders see the creation and nurturing of that culture as their primary responsibility.

In biopharma, we are challenged by an environment and culture that is often risk averse, where companies struggle with change and often create self-imposed complexity. What is required is a passion for creating better and more efficient work methods and practices while keeping the highest level of quality. This may mean a radical shift in how people look at their work and their ownership of change, understanding that they are in control and not simply passive observers. There is significant potential for improvement and learning that the industry is only beginning to understand – this may be the next great productivity frontier in biopharma.

To begin understanding the transformational leadership role, we must first develop a common understanding of what transformation is:

Transformation Definition

A conscious transition to a sustainable way of working at a significantly higher level of performance and health based on fundamental shifts in:

- Ambition and a will to win
- Collective self-beliefs and forward looking organizational culture
- Underlying capabilities, systems, and processes
- Innovation Culture of products, processes and systems

(Andy Crossman- adapted from McKinsey Transformation Definition)

The definition has implications that are far reaching and requires strong leadership to be realized. Notably they are mostly behavioral and start with the leadership itself setting the example. If the industry performance average rate of improvement is 5–7 % annually like stated in the introduction, to be transformational, a company may need to be improving at double the industry rate to move to the front. This rapid improvement cannot be achieved with incremental thinking and action; it can only be met with a transformational mindset and focused programs to deliver sustained results.

Additionally, there is a need to broaden the limited view of "leadership" from positional hierarchal managers, to developing transformational leaders at all levels. Transformation is about changing "the way the majority of colleagues work on a day-to-day basis", not just a narrow project scope or incremental approach.

Making transformation personal and reflecting on the different roles and behaviors is perhaps the most difficult challenge facing leaders today. Most transformational leaders point to the value of having trusted counselors and unbiased external observers provide them with feedback about their unconscious behaviors and communication styles. Trying to do this on one's own, without outside neutral perspective is extremely difficult, especially when trying to undo a lifetime of managerial habits.

At its heart, transformational leadership is about culture and systemic step change in results, delivering long term improvements for customers, colleagues, and shareholders. According to organizational change expert John Kotter, author of "Leading Change" the majority of transformational change efforts fail not because of technical challenges or lack of resources, but misaligned leadership behaviors and failure to engage all colleagues in the change.

Analysis of successful transformation efforts in the biopharmaceutical industry points to this cultural shift as the key to unlocking a wave of productivity improvement all while maintaining the highest levels of compliance and quality. The role of the leader in this context is to coach others to be successful and to achieve their full potential. Furthermore, these leaders are using the current difficulties and challenges as a catalyst to deliver more efficient ways to deliver needed products to the customer. They are redefining "what great looks like" for their organizations, and their followers are rising to meet that challenging vision.

Seven transformation success factors are all notably controlled by leaders at key levels of the organization:

1. Setting stretch aspirations and new expectations for performance with a clear view of "what great looks like"
2. Aligning everyone to the future state and building energy behind it
3. Communicating openly and honestly, using a compelling "Change Story"
4. Leaders make the change personal by modifying their own behaviors
5. Focus and intolerance of losses (e.g. waste, variability, inflexibility)
6. Demonstrated focus on "narrow but deep" transformation with a clear structure for change
7. Innovation for purpose that is behavioral based with an understanding of strategic business opportunities

Pfizer Specialty Biotech Operating Unit Leader Mike McDermott described the role of leadership as taking people out of their "comfort zone" and to stay ahead of the expected change. He believes aspirational stretch goals can produce leaps in operational performance and personal growth. He had experienced that himself as a former site leader. His favorite Southwest Airlines maxim for an organization is "always have a challenge" and foster the "warrior mentality" to keep it sharp and moving forward.

For Germain Morin, Pfizer Consumer Healthcare Strategy lead, the leader's role is to "find a reason for the organization to win a game every day and make a difference". The leader "keeps the burning platform alive, celebrating small victories and building the culture and capabilities that will last".

Sometimes leaders must leave behind the things that made them successful previously in their careers. Mike McDermott describes how he had been recognized, promoted, and rewarded for being a quick thinker and problem solver. As a new site leader his staff had the courage to tell him that his leadership style was actually hindering his organizations' initiative and inhibiting a culture of experimentation. "I had to change my leadership style to create the environment I wanted".

Suzhou, China site leader, Sui Jinguo compared his 5 year transformation journey to "a high speed train that never stops". His legacy is a culture that embraces change and sets ambitious "impossible goals" that are regularly achieved. He shifted his focus from equipment and products, to developing and engaging people and capabilities with significant productivity gains as the result. The Suzhou site measures colleague engagement and participation on regular basis, and sets ambitious targets that require everyone on the site to be part of continuous improvement. This approach has dramatically improved people engagement while improving productivity. The Suzhou plant uses benchmarking to gage its progress not only for internal comparison, but against external companies in industries considered to be more mature in their lean journey than the biopharmaceutical sector.

Pfizer Global Supply Andover, Massachusetts Site Leader Ken Bradley highlighted the need for leaders to encourage colleague efforts to be "in control

of their work". He believes that up to 90 % of problems in the workplace could be resolved by use of powerful six sigma and lean tools such as DMAIC problem solving and standard work, supported by leadership and guided by a strong core set of values and behaviors.

Right People, Right Place, Driving Change, and Building Capabilities

Understanding who your best people are (performance, potential, and values) at all levels of the organization is key to developing organizational capability. Transformational leaders deliberately identify, develop, and reward change leaders in their organization. Pfizer Specialty Biotech Operating Unit Leader Mike McDermott allocates 25 % of his leadership team's agenda to people development. The results over time have been impressive, with key leaders moving to other leader roles in the organization and talent seeking to join his organization knowing they will benefit from planned experiences and opportunities.

High performing leaders should not expect to be in the same role for significant tenures, but rather, be exposed to a variety of roles and skills that will broaden their contribution and personal growth. McDermott also expects his leadership team members to continue their own growth and development, pushing them to learn about new ways of working and looking outside their plant boundaries and the biopharma industry for innovative practices and technologies.

In the Pfizer Consumer Healthcare and Specialty Biotech unit, each year a group of high performing colleagues are selected to tackle one of the biggest strategic challenges or opportunities facing the business. Learning as a team, they develop and execute specific actions that will "move the needle" for the business, while developing their own transformational leadership skill sets.

Change Story - Broadening Ownership and Open Communication

One of the most powerful tools leaders can use in developing urgency and commitment is the "Change Story". It is an oral description of the organization, reflecting real conditions and the urgent need for change. It speaks to the emotional side of change for individuals, as well as to the unspoken "realities" in an organization. It helps build the "burning platform" for change (Fig. 22.1).

The Change Story requires personal transparency on the leader's part to help people get past fear and moves them to personal commitment. Leaders who challenge their organization to take the change story and personalize it, enable a transformational shift in ownership to everyone in the organization. Most

Fig. 22.1 Telling the change story and making the story personal

successful change stories can be told quickly (i.e., in minutes) and include a powerful and emotional "hook" that clarifies purpose and meaning in the organization's work. While the core remains constant, each person is encouraged to personalize their change story.

Change stories facilitate alignment of all colleagues and build excitement and understanding of the need for change. They are most effective when they engage people at the emotional level. Andover Site Leader Ken Bradley frequently uses storytelling and humor in the workplace to influence colleague's mindsets and awareness. For instance, his belief that zero workplace injuries are possible inspired colleagues to create a humorous change story about "the safest man in the world" that has significantly impacted and transformed the workplace safety consciousness and mindset at his site and had a "viral" impact on other facilities in the Pfizer global supply network. The stories are shared in a series of short videos with the "safest man in the world" reviewing a simple safety topic such as holding onto the hand-rails when using stairs. The video message is straightforward, engaging, memorable, and effective.

Germain Morin states that transformation is not just about "cost cutting". Reduced cost is only one outcome. Transformation "should help us face the future, in a more globally competitive, fast moving environment." This requires leaders to provide a positive and inspiring vision or Change Story to explain "where you are going and why". Morin's experience is that that vision needs to be constantly revisited and "repeated" to become part of a colleague's mindsets, while simultaneously bringing them together in a shared vision (Fig. 22.2).

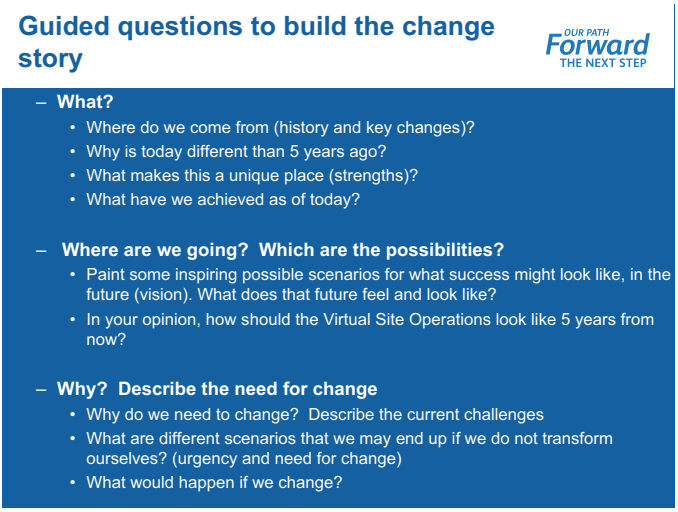


Fig. 22.2 Guidance on developing the change story

Creating Culture Through Mindsets and Behaviors

Many leaders have been promoted based on technical abilities but have limited exposure to techniques or development of soft skills such as time management, coaching, change management, building organizational trust, and accountability that require practice and feedback. Coaching in mindsets & behaviors becomes a priority of the transformational leader (Fig. 22.3).

Sui Jinguo, Suzhou China's site leader, noted that the biggest change for his site transformation was the change in mindset, while maintaining the highest levels of quality and efficiency, and having been recognized for their performance by the company and external organizations. The site has seen dramatic improvement in overall people capabilities through their transformation. The cultural shift has been dramatic according to Sui who noted that "in China we ran the plant as pure engineers, now we have shifted to a people and customer focused organization". Leaders must set the tone by "knowing the way, seeing the way, and showing the way".

Shared Leadership

Research shows that shared leadership is more realistic and potentially more impactful than the single leader as "heroic figure" model. Because of the many needed leadership behaviors, it is nearly impossible for a single person to fulfill. Therefore members of the group must also step up into these leadership "gaps" in

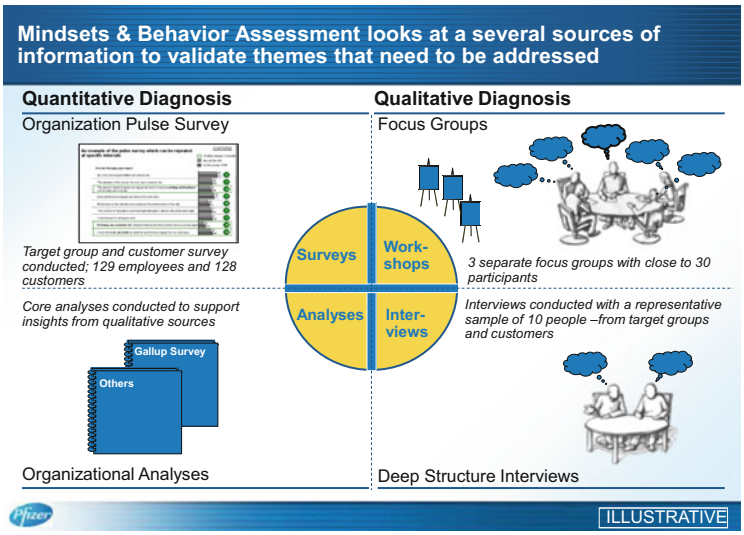


Fig. 22.3 Mindsets and behavior assessment overview

order for the team to be successful. This also promotes greater accountability and team unity. The leader's purpose or role is then to make sure there is leadership being exercised- around key activities: shared purpose, action, progress, results, teamwork and individual attention.

While leadership can be shared, the ultimate responsibility that leadership is exercised still rests with the leader. Mike McDermott states that the entire leadership team, or at least its core, must act and behave differently for transformation to take hold. It cannot be delegated. This can require difficult conversations with "blockers" even at the senior level. Some senior managers cannot make the transition to this environment.

External Supply Operations leader Jerry Mujica believes that "high performing organizations need to have mutual accountability, which means shared objectives. This provides a solid foundation to build customer facing organization that cares more about the customer, than protecting its own rules and structures". Several leaders stated that they had to replace members of their leadership teams or middle management ranks, who were unable to operate in a more open, dynamic, and transformational culture. This action also sent a powerful message to the organization that the culture had changed and would not be going back. Failing to address behaviors contrary to a transformational culture will almost certainly lead to failure.

Some of the most dedicated transformational leaders have also demonstrated their willingness to learn alongside colleagues at all levels by direct participation. Done appropriately this builds an incredible sense of trust and connection across the organization levels and models what is expected of others.

Organizing for Transformation

Successful transformation requires an organized and planned structure to support it. As a starting point, first begin with the question "what does the business need?" and then focus on those areas with greatest impact. In organizing supporting resources, it is important not to overly rely on technical experts (e.g. Belts, lean experts), and be intentional about having skilled facilitators build capability in the line leadership through coaching, mentoring, and skill building. Embedding new skills in the line-leaders is one of the foundations of transformational efforts. The importance of this line-leader ownership must be emphasized repeatedly by leadership. Project leadership should be drawn from the best talent in the organization regardless of where it exists.

At the Pfizer Puurs, Belgium plant, which has been recognized as a transformational model, the site has invested in one extra colleague per shift to help drive their lean transformation process. Transformation leader's experience suggests that organizations may need to allocate at least 2–3 % of the total workforce to operational excellence to truly drive transformational change. Given the importance of "soft" change management skills in transformational activities, at least 1 % of the workforce may need to be dedicated to coaching, change management, communication, and mindset & behaviors training. Even then, organizations need to embed these skills and capabilities within their functions, including rotating colleagues between line operations and operational excellence (OPEX) roles, for both organizational and personal development. This ensures a strong business connection and understanding between OPEX activities and operations. Bypassing this investment in organizational change often leads to suboptimal results or non-sustainable improvement.

Several leaders emphasized the importance of bringing in external expertise to help jump start their transformation journey. In Pfizer's Consumer Healthcare Operating Unit, there is an intensive effort to use "pull forwards" from other sites and functions to infuse new thinking and knowledge transfer across the network. In Suzhou China, transformation has been a multi-year, phased approach, with all areas of the plant ultimately involved. This allows for total organization understanding and alignment to transformational breakthrough improvement.

A clear governance structure with a portfolio approach to managing transformation initiatives has been identified as central to successful change efforts. The Boston Consulting Group (BCG) research has shown significantly higher rates of success when these elements are integrated in a holistic program of improvement (Fig. 22.4).

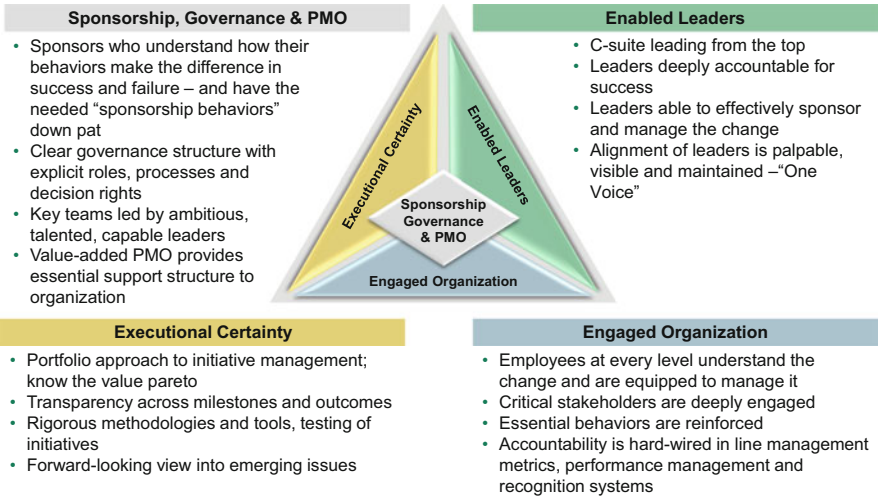


Fig. 22.4 Elements for managing transformation change

How Do Transformational Leaders Spend Their Time and Energy?

The difference between managers and leaders can be observed by learning how they spend their time and energy. One model used to categorize leader's time is noted below and focuses on daily management, continuous improvement, and breakthrough improvements. Transformational leaders may need to focus at least 75 % of their time in the continuous improvement and breakthrough improvement areas with particular emphasis on people development and coaching (Fig. 22.5).

Specialty Biotech OpU leader Mike McDermott believes that transformational leaders should not be spending as much time on execution and tactics. Rather they should be focused on strategy, innovation, people development, being a "differentiator, and going beyond the expectations of the customer". For McDermott, a key example is implementing a Supply Model Transformation strategy which is moving beyond an asset based cost view, to a more efficient and responsive total supply chain model.

For Pfizer Global Supply Network VP Jim Cafone, transformational leadership "may mean giving up what you loved and were good at", for example moving from managing a technical asset-based organization to a supply model organization. This transformation change requires overcoming fear of the unknown and new learning for leaders. Personal awareness and growth a key for change leaders.

A frequent practice of transformational leaders is to ask "the difficult question". Ken Bradley, Andover Site Leader tries to ask all colleagues "how are you improving your work every day?" He also notes that just 10 years ago, customer needs did not change very much, now they are changing in just 6–12 months. One of

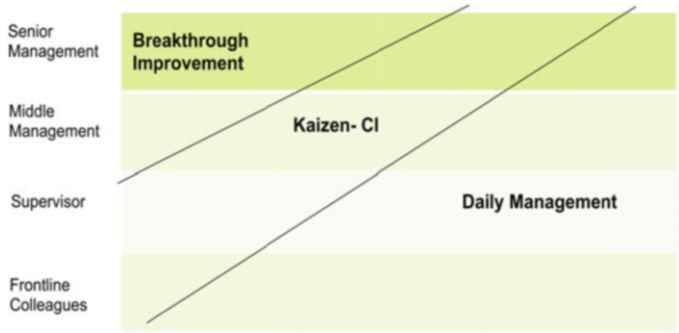


Fig. 22.5 Transformational leaders spend up to 60 % of their time on breakthrough improvements, communication, coaching and developing talent

his techniques for bringing other leaders on board with change is to provide experiences at other companies or facilities where staff can "go and see for themselves". This practice has helped colleagues to see things differently and offered new possibilities for excellence.

Commitment to the Long Term Transformational Strategy

Commitment by leadership to the long term strategy is a key element for successful transformation. Transformation requires commitment to capability building and leader development not just "quick win" solutions. Leaders need to be able to prioritize key elements of the transformation while providing the vision for change over the long term (Fig. 22.6).

One plant solved its ongoing struggle with prioritizing too many objectives for the available resources with the use of Hoshin-strategy deployment. The use of high level 12–18 month single-page "Transformation Roadmaps" ensure a planned execution of strategically important projects, kaizens, and training, that is aligned with business activities and objectives. For example, green belts attending training will already have a pipeline of strategically selected projects assigned to them for real time application of learning concepts (Fig. 22.7).

Diagnostics, which are usually 1–3 weeks in length provide the initial "opportunity-scoping" and framework for later intensive "mini-transformation" projects which can last anywhere from 6 to 14 weeks. Longer projects tend to lose momentum and focus, and may be more effective by being broken into more manageable units of time.

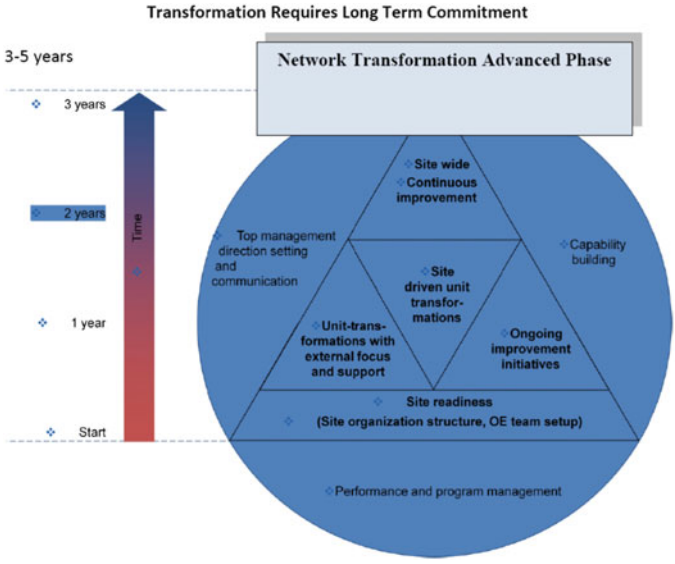


Fig. 22.6 The commitment to transformation requires long term vision and capability building

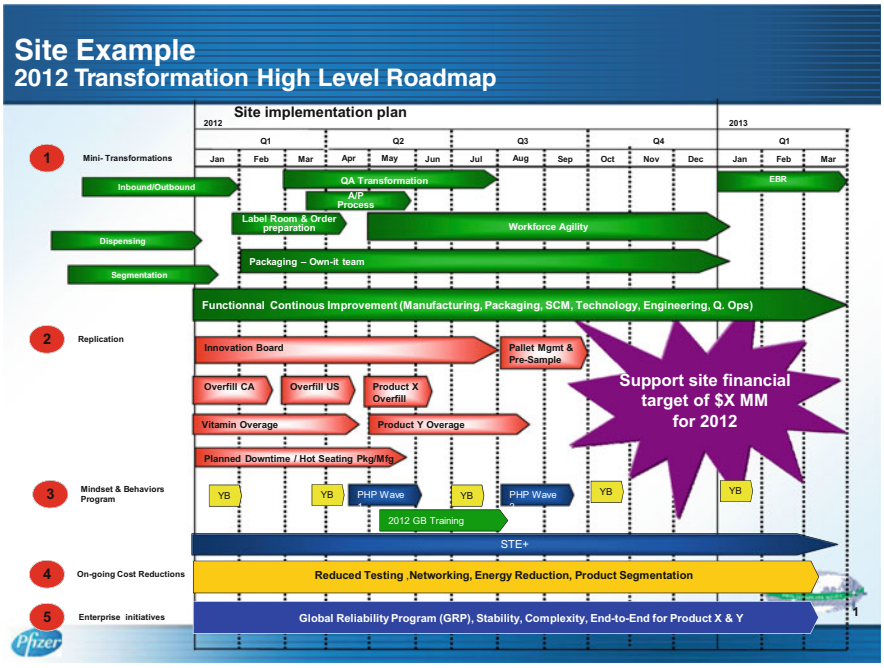


Fig. 22.7 Transformational roadmaps provide visibility into the execution plan

Conclusion

Transformational leaders are at the front of the change curve in the biopharmaceutical industry. They recognize that they are on a journey of personal discovery and growth, and that their learning in this environment never stands still. Simply holding in position at 5–7 % annual growth in productivity will not be enough to survive the winds of change. Their goals are much higher, and while described in language such as capability, mindsets and behaviors, organizational trust, set the foundation for 10–15 % or greater annual gains in productivity and performance. Conversely, leaders and organizations who can deliver step improvement changes will quickly find themselves as leaders in the industry, with bright prospects for the future. This journey requires courageous choices, but that is the hallmark of the transformational leader.

1. The DMAIC project methodology has five phases: ***D****efine* the problem, the voice of the customer, and the project goals, specifically. ***M****easure* key aspects of the current process and collect relevant data. ***A****nalyze* the data to investigate and verify cause-and-effect relationships. Determine what the relationships are, and attempt to ensure that all factors have been considered. Seek out root cause of the defect under investigation. ***I****mprove* or optimize the current process based upon data analysis using techniques such as design of experiments, poka yoke or mistake proofing, and standard work to create a new, future state process. Set up pilot runs to establish process capability. ***C****ontrol* the future state process to ensure that any deviations from target are corrected before they result in defects. Implement control systems such as statistical process control, production boards, visual workplaces, and continuously monitor the process. From De Feo JA, Barnard W (2005). JURAN Institute's Six Sigma breakthrough and beyond – quality performance breakthrough methods. Tata McGraw-Hill. ISBN 0-07-059881-9
2. Standard Work is having documented visual processes for every task that is done inside the factory from: Shigeo Shingo: A study of the Toyota production system. Productivity Press, 1981 **(Japanese)**, 1989 **(English)**, ISBN 0-915299-17-8
3. Change Delta Model- Boston Consulting Group
4. Schein E (1985) Organizational culture and leadership. Josey-Bass, San Francisco
5. Kotter J (1996) Leading change. Harvard Business School Press

Chapter 23
Making Operational Excellence a Priority at Every Level

David Hampton

Operational Excellence programs do not come with a guarantee of success. Many reasons have been given for failures, one of the most common being the 'layer of clay' in middle management levels who are resistant to change. However, inertia, complacency and resistance are key challenges at the level of individual contributors and senior executives as well as middle management.

This chapter addresses the key factors affecting motivation for the program at all three levels, defining the key issues and presenting powerful approaches to creating commitment throughout the organisation, with case studies from the industry.

How Top Leadership Influences Motivation for Operational Excellence

Defining the Goal of Operational Excellence

The first and most important step in launching an Operational Excellence program is to define the business goals that it will support.

A common mistake is to define the goal too generally, as 'cost reduction' or 'improve our processes'. These are too broad to give any sense of direction as to how the goal is to be achieved. When a business chooses to invest in a new piece of manufacturing equipment or launch a new product, it will not simply be because the decision offers an attractive ROI – there will be an underlying plan (breaking a bottleneck or entering a segment that offers high growth potential) that enables the right business choices to be made. Similarly, the goal of an Operational Excellence

D. Hampton (✉)
SSA&Company, Sevenoaks, UK
e-mail: dhampton@ssaandco.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_23,

program needs to be specific enough to help guide decision-making in project selection.

- In Pharmaceutical Manufacturing, the goal of an Operational Excellence deployment is typically clear to the business – to improve process robustness or service levels, for example.
- In Clinical Development the goal is typically lead time, but there is an increasing focus on compliance and patient safety. In Pfizer, the Operational Excellence program was greatly strengthened by a decision to focus it specifically on reducing the risks in clinical development. The re-energised program was called Clinical Trials Excellence[1] and involved an ambitious end-to-end study of risk and fragility in the design, conduct and reporting of clinical trials, creating a unifying sense of direction that lasted long after the initial analysis was carried out.
- For Research, the goal will be to reduce attrition and overall lead times. Like cost reduction, these goals are generally too broad as they stand, because of the complex interconnections with other parts of the business. For example:
  - Understanding manufacturing feasibility and the cost-benefit trade-offs of Quality by Design require close coordination with Manufacturing.
  - Where new drugs are aimed at indications with existing treatments, it is important to set targets for therapeutic advantage in order to ensure reimbursement – which requires Research, Clinical Development and the Marketing function to work effectively together.

  A more holistic approach is therefore needed when setting goals for operations improvement in R&D, considering the broader business needs.

Where the goal has not been sufficiently well defined, a formal assessment is required and should encompass the business or site as a whole rather than individual Value Streams. This requires a Business Relationship Map (BRM), taking an organisation-wide view encompassing all the key value streams of the business. It enables executives to look across organisational boundaries to see the overall improvement priorities, in much the same way that a Value Stream Map helps users see the broader picture for a specific value stream. The form of the BRM varies from case to case, but its key feature is its ability to see the operation of a business as a system, highlighting performance constraints such as communications issues, excessive non-value adding work and poorly aligned business metrics.

[1] Pfizer Annual Review 2010, 2011.

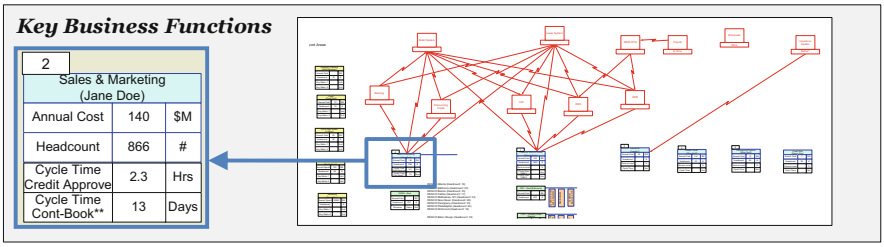


Figure: Illustrative business relationship map

How Do Leaders Communicate Their Priorities?

One of the key benefits of having a well-defined goal for the Operational Excellence program is that it increases support from the leadership team by enabling them to understand the business value of the effort. The way they communicate their support will, however, be critical to the way the message is received. Whether through a conscious effort or unconsciously, business leaders continually send signals about their priorities, and frequently overestimate the power of formal channels. Employees at all levels are used to blogs, articles, videos and other scripted media, and typically interpret them as being primarily the words of communications specialists rather than the individual leaders. So, although these remain a necessary part of the mix, the signals that convey what leaders truly feel come more from how they use their most valuable resources, such as their most talented people and their own time.

In Pfizer Manufacturing, Nat Ricciardi, President of Pfizer Global Supply, sent a personal congratulatory email to every Green Belt or Black Belt that completed a project, and insisted on writing the email himself, with comments that showed he had read the storyboard. This was not limited to initial certification – every project received this treatment, to ensure that follow-on projects were properly encouraged. When Nat retired his successor, Anthony Maddaluna, continued the practice – an exceptionally powerful way for a leader to communicate that there would be no let-up in the drive behind the program. Actions like this are time-consuming and it might be expected that a member of Pfizer's Executive Leadership Team such as Nat or Anthony would delegate the task rather than give up the (mostly weekend) time that this commitment required. But employees can tell the difference between pre-scripted communications and genuine passion, and word gets out about the effort that is being made. This is how they know how much interest a senior executive really has in the program.

Similarly, the selection of the most able candidates for roles such as Black Belts and Kaizen Specialists is important not only for effective execution of the work but also for the signal it sends about the organization's commitment to process improvement.

Attending report-outs or making time to personally review the project pipeline are also important activities for the CEO, as these meetings directly connect him to the progress of the Operational Excellence program. Project selection and delivery are critical to the success of Operational Excellence, and a wise CEO will want to 'go and see' for himself the results that are being achieved rather than rely on reports of numbers of projects completed.

While these actions do not directly communicate to a wide audience, they provide leverage for the CEO's time in a different way, by demonstrating genuine interest and ensuring that problems cannot be hidden for long. The informal communication channels are then remarkably effective in spreading this information.

Constancy of Purpose

The third challenge for business leaders is the need to maintain a stable program over a period of years. If the company has not developed a well-defined goal, this will be very difficult; it is common to see Executives in search of the 'Next Big Thing'. It is easy to underestimate the time required for employees to fully understand and support new initiatives, and people are normally reluctant to commit to a program they expect will be short-lived. So sticking with a program in the long term is essential for realising its full potential.

Even a well-defined and run program is difficult to maintain over an extended period of time; it requires discipline and conviction. In mature programs, there are three particularly common temptations:

- The belief that the war is won – the view is often expressed that Operational Excellence will become 'a way of life' and that a point will be reached where the structures needed to launch it and sustain the effort through the early years can be dismantled. It is very difficult to find examples where this has truly been achieved, but there are many cases where, perhaps because dismantling the infrastructure is seen as an indication that the company's priorities have moved on, this leads to the collapse of the program and the departure of the most experienced improvement specialists. Operational Excellence requires permanent, sustained effort. Though the size of the central team will be reduced after the first 2–3 years, if the team is not constantly moving the program forward and adapting it to the company's changing needs, it will slide into irrelevance.
- Reducing certification timelines – pressure tends to increase to accelerate the development of experts such as Lean Masters and Six Sigma Master Black Belts, who are able to pass on their skills to others once they are qualified. Short-cutting the qualification process brings rapid benefits in the improved availability of these experts, but at the risk of creating long-term damage that is very difficult to reverse once a lower qualification standard has become accepted. When these

specialists can no longer be relied on to win the trust and confidence of the leadership team, the program suffers a major setback.
- Believing the program remains healthy even as it is losing momentum – Operational Excellence is not a 'fix and forget' effort, but a permanent commitment to working in a better way that requires sustained effort. The individuals charged with the implementation of programs such as Lean Six Sigma have an inbuilt incentive to report good progress, for example by selective reporting of project results, even if the program is unravelling. Executives need to maintain a personal involvement in improvement projects as this is the only reliable way to both prevent and detect a reduction in effort over time.[2]

When Operational Excellence programs fail, they tend to do so slowly – so slowly that it is difficult to see whether the program has lost its effectiveness because leaders have lost interest or vice versa. But what is clear is that programs that are successful in the long-run invariably enjoy the long-term support of the senior leaders in the company. While there will be an evolution over time in the scope and purpose of the program, adherence to the disciplines of Operational Excellence need to remain fixed.

Motivating Middle-Management

Most of the literature on Operational Excellence focuses on issues for company leadership, deployment specialists and individual project leaders and their teams. It largely ignores the middle layer of management that frequently becomes a weak link in the overall effort. Not sufficiently senior to directly influence the program as a whole, yet (typically) considered too senior to attend training that may run to several weeks, they are expected to act as 'Champions' for projects with minimal training, and frequently seek to do the minimum necessary to be seen to be supportive. It is not surprising, therefore, that people in this position are frequently perceived to be underperforming in their Operational Excellence role.

Operational Excellence Needs a Broad Definition

Part of the problem is the limited exposure that managers have to formal training in Operational Excellence. This can result in an oversimplified perception of its purpose and methods: 'It's all about Green Belt projects', 'We have to hit targets for training and certification', 'It's about improving flow'.

[2] Where Process-Improvement Projects Go Wrong – Wall Street Journal, January 25, 2010 (Satya Chakravorty).

Such narrow interpretations of Operational Excellence can lead to pigeon-holing the concept with terms such as 'Lean Six Sigma', 'Risk Management' or 'Continuous Improvement'. In some businesses this is not a problem, because their challenge at a particular point in time may be relatively specific: 'make manufacturing processes more robust' for example. But in the long run, it is important to ensure that Operational Excellence does not become perceived as a narrow set of tools for a specific purpose in a specific part of the business, because such a narrow view will eventually make it seem irrelevant to other business challenges.

In reality, Operational Excellence has to span both core functions (Product Development, Demand Generation and Supply Chain) and supporting functions (Finance, Business Technology, HR and so on). Key themes should not be limited to process improvement but also include other aspects of the operation that effect performance, such as business architecture, cash management, business technology and customer focus. Most importantly, it needs to include organisational culture and people development, not just tools. It is not possible to sustain an improved way of working through tools alone, with employees merely cooperating with the effort. In this way, Operational Excellence can be shown to directly support management objectives – it is not just about conducting individual improvements (worthy though these are), but rather striving for the best way of managing every aspect of the business. Eventually, the goal should be that the Operational Excellence provides a template for the way people carry out their work day-to-day, with the key concepts of customer focus, using data effectively and continuous improvement established as part of the culture.

Creating 'Pull' for Operational Excellence

When Six Sigma was originally launched in GE, the approach was a top-down approach that carried a message 'we are introducing this methodology to make our business more competitive and everyone needs to get behind it'. This approach is sometimes referred to as 'Push' and fits a command-and-control model. 'Push' gets the program running quickly and works well if the leadership of the company is in a position to dictate not only the company's goals but also how to reach them, but has obvious weaknesses: it drives compliance rather than enthusiasm, and is difficult to sustain because it needs constant reinforcement from the top until employees at all levels see sufficient benefits from the program that they choose to support it.

An alternative approach which we shall refer to as 'Pull' involves setting the goal but not mandating the method by which it is to be achieved. Where 'Pull' is used in the launch of an Operational Excellence program, resources are made available to run (for example) Kaizen Workshops or Lean Six Sigma projects, but leaders have discretion in whether or not to use them. This is also problematic because the rate of adoption of the new methodology may be slow and highly variable across the organisation – so it is unlikely to make a significant impact.

The most effective approach seems to be to combine elements of Push and Pull, with elements of both mandating the program and working closely with leaders at all levels to ensure it supports them in meeting their specific business objectives. This is likely to lead to a more complex program (involving tailoring the methodology to meet the specific needs of different divisions, for example) but offers the best chance of engaging the management team by enabling them see Operational Excellence as a means to achieve their objectives. Some examples of the way organisations may be encouraged rather than compelled to adopt the Operational Excellence program include:

- Focusing on fast-cycle improvement projects in the early days. Tackling specific high-value opportunities and delivering sustainable results over execution cycles of 90 days or less enables a broader transformation to be kick-started by demonstrating results and communicating them. Generating an early positive financial return helps to overcome management scepticism, but requires the improvement targets to be carefully selected and scoped.
- Setting up pilots in areas that support the program enthusiastically, and then challenging other areas to replicate their results. This approach enables the benefits of the approach to be demonstrated quickly in a limited area, but some businesses may find that it takes too long to roll out broadly.
- Setting targets and expecting executives to reach these by whatever means they consider most effective – with the understanding that Operational Excellence is the preferred route, and resources for this are made freely available. The underlying message is that if an executive does not use the recommended approach, and also fails to meet his target, the resulting conversation will be an uncomfortable one. The risk here is that the metrics have to be chosen with great care, as described later – otherwise the system may be 'gamed' by achieving short-term results at the expense of long-term performance, or optimising one metric at the expense of another.

Project Selection

The selection of impactful projects is probably the single most important factor affecting the long-term success of the Operational Excellence program. Well-targeted projects help to reinforce the importance of the program to delivery of business objectives, and properly-scoped projects are much more likely to be completed.

Typically, in the early stages of a deployment (the first year or so), there will be a wealth of issues that have been waiting to be properly addressed, so it is not necessary to engage in a highly formal process for project selection – simple prioritisation based on a few key criteria is sufficient. In these early stages, extra emphasis should be placed on the effect the projects have on motivating staff, to keep building the momentum of the program. Projects that reduce non-value-added

work or rework should therefore be prioritised over those that reduce inventory or the cost of purchased goods, because they are more visible and have a noticeable effect on people's working lives. Equally important is the need to keep projects short, to establish an expectation that results should be delivered within 90 days – so careful scoping is important, with larger projects broken into smaller ones.

Within 12–18 months, however, it will be necessary to put a more formalised structure into place to ensure that projects are aligned to tackle the key business priorities. The successful completion of early projects is an important precursor to this step, as these enable the Operational Excellence program to gain credibility with the management team and become accepted as the means by which strategically important issues can be addressed.

There are several approaches to project selection that derive projects directly from business priorities, the choice depending on the priority area to be targeted. The most widely-used are:

- To strengthen manufacturing process robustness: carry out an analysis of the capability of each manufacturing process, with emphasis on Critical or Key Process Parameters and Quality Attributes. Target projects on the processes with the lowest process capability.
- To address lead times: use Business Relationship Mapping followed by Value Stream Mapping to identify steps in the manufacturing or research and development process that contribute most to inventory accumulation or delays. This approach involves a holistic analysis to ensure that improvements have the maximum leverage on the overall system performance. A short workshop (with sufficient preparation) is normally all that is needed to create a Current State Value Stream Map, after which a 'blue sky' Future State is developed. From this, a feasible version that can be delivered in 6–12 months is generated. By working back from an ambitious map, rather than generating the Future State directly, this approach delivers more creative ideas and can achieve breakthrough improvements.[3]
    - It is also interesting to note that a variant on this has been found to work well at Shire Pharmaceuticals, where it was noted that some issues were common to value streams of all product lines. Rather than optimising one Value Stream and leaving the others untouched, they identified high-leverage opportunities (for example, analytical testing or late stage customisation) and applied them across all product lines.[4]
- To derive projects from existing data: use business dashboards to monitor Key Process Indicators (KPIs). Priority areas can be developed from indicators that are trending downwards or below target, or from benchmarking between sites to

[3] Harvesting the Benefits of LEAN in Biopharmaceutical Manufacturing – Biopharm International, October 2009 (Thibaud S. Stoll, Jean-François Guilland).

[4] Interview with Paul Nelson, Leader, Operational Excellence and Transformational Change at Shire Pharmaceuticals.

see where there is an opportunity to improve. It is important to note that these tools should be used as far as possible for identifying improvement opportunities rather than for reward and punishment; this is discussed in more detail in the next section.

- To tackle infrequent but serious problems: use a structured Failure Mode and Effect Analysis to pool Subject Matter Expert knowledge on process vulnerabilities. This approach was used in the Pfizer Clinical Trials Excellence initiative described earlier, and was also successful in an aseptic manufacturing plant at Monsanto to reduce the risk of sterility failures. In the Monsanto case, multiple brainstorming approaches were used to think through the issue from different angles; potential failures were weighted by the number of batches that could be affected, expert judgement of likelihood and the controls already in place. Many solutions were found that were simple to implement, and the more complex solutions could be justified by the rigour of the FMEA methodology.[5]
- To align projects behind a specific improvement goal: use drill-down approaches such as Hoshin Kanri to translate high-level objectives to major themes, key challenges to deliver on these themes and, eventually, specific improvement initiatives that will enable these challenges to be met. This approach drives projects from the strategy to ensure that they have maximum impact on the things the leadership team cares about.
- To support the introduction of Quality by Design: before conducting designed experiments aimed at establishing appropriate operating tolerances for a new product, focus on reducing variability in the manufacturing processes or measurement systems that will be used. QbD work may also highlight issues with process variability that have to be resolved in order to control volume manufacturing.

The Impact of Measures on Behaviour

While the use of dashboards and balanced scorecards are well-understood, the way that measures should be used in practice, and the consequences of their misuse, is a much more challenging area. The problem is not so much that the wrong things are measured but rather that the metrics are used as targets or criteria for reward or punishment. A few examples will serve to illustrate what is, for most people, a familiar problem:

- A Site Leader's interest in the implementation of Lean manufacturing proved to be purely cosmetic because inventory was not one of the factors in his performance objectives

[5] Interview with Craig Alexander, Regulatory Process Improvement Lead at Monsanto.

- A Pharmaceutical Development organisation was tasked with training a certain percentage of employees in basic problem-solving, and achieved the goal while failing to provide any support or encouragement for those that had been trained, leading to them forgetting their skills over time
- A Research department was tasked with delivering a certain number of candidate drugs each year. Roughly one-third of the target was delivered in December, with predictable effects on the quality of the candidates.

Looking carefully at the effect of business metrics is a critical part of Operational Excellence, because if the use of metrics is driving the wrong behaviour then this will ultimately overcome the beneficial effects of improvement projects. Experienced managers who anticipate that their performance evaluation will largely be driven by achievement of targets can hardly be blamed for doing the wrong thing if their targets drive them in this way. So analysis of the current state needs to include a comprehensive understanding of the measures in place and the consequences to individuals if these are trending in the wrong direction. This should include not only factors that drive behaviours relating to the improvement goal but also those that affect motivation to continue the effort after the project has been completed.

The general principle to follow when establishing metrics is that only those metrics that fully capture the purpose of the process should be used to incentivise staff. For example, in sales the profit from new business is a better metric than the value of new business because it captures the profitability of new accounts, while a worse metric would be the number of new accounts, which ignores both value and profitability.

All other metrics – those that describe some component of the process – should be used for diagnosis only, or there is a risk that employees will work to optimise the metrics rather than performance as a whole. This form of compliance behaviour generally acts against overall process performance.

An example of a metric that fully captures the purpose of a process would be end-to-end lead time (or inventory). In manufacturing this means the time from production of raw materials through to dispensing of the drug in a pharmacy, which is likely to be very difficult to measure. It may be expedient to measure lead time within a specific manufacturing site, but this would not capture the entire value stream. Efforts to incentivise performance on just this one segment will lead to some level of damaging distortion – for example, measuring inventory at the end of each quarter, which typically leads to sites shipping all available materials to each other at the last minute. The amount of distortion and harm caused depends on the size of the incentives applied.

It should also be noted that cautious use of metrics needs to be applied to the Operational Excellence program itself as well. For example, targets that focus on the number of employees trained rather than the benefits they deliver to the business will encourage training rather than business benefit.

Engaging Individual Contributor Employees

If Operational Excellence is to become part of the culture of the business, then the way employees at all levels perceive the process of improving processes needs to be carefully addressed, and patterns of behaviour established and reinforced that will, over time, become the established way of working.

This section deals mostly with training and project work, because training is the essential first step to give employees the capability to do this work, and contribution to projects is the means by which they will become confident in applying the methodology.

Training Specialist Operational Excellence Experts

Every program will need its core of specialist experts, often referred to as Green Belts, Black Belts and Master Black Belts/Lean Masters, who have received extensive training in the methodology. These people provide the essential core of capability to tackle difficult problems, coach others as they execute projects and pass on their knowledge through training so that the system is capable of sustaining itself. Although this fundamental structure is still in wide use, 30 years after it was originally developed in Motorola, a number of important refinements have been adopted by many companies over the years in order to tailor the approach as closely as possible to the needs of the business. Key areas to consider are:

- How to integrate Lean with Six Sigma: there is no one best practice for this, though it is normal to find that experienced people have strong views that their way is the best. It is best to consider the strengths and weaknesses of different approaches and decide on which fits the business needs most closely:
  - Treating Six Sigma and Lean separately enables companies to maintain a clear focus on both quality and waste reduction. This approach has served Pfizer manufacturing well, with separate training and qualification routes for the two disciplines ensuring that improvements built on each other in a way that reflected the company's priorities – strengthen process capability first before removing waste. This may, however, be a slower approach because of the need to run separate training and projects.
  - Integrating Lean and Six Sigma into the same training gives companies the flexibility to direct projects to the challenges that are most pressing, and to have individual team leaders well-prepared for projects that change course (for example, a setup reduction project that is eventually scoped down to reducing quality problems in start-up). The risk here is that the depth of understanding, for Lean in particular, is normally not as complete as when the two methodologies are taught separately, and this may be particularly evident at the Lean Master/Master Black Belt level. To achieve sustainable

independence from consultants, it is essential to have colleagues whose capabilities are close to those of the consultants they will be replacing.

- Customising the training curriculum: manufacturing-oriented training courses have long ceased to be acceptable in other areas of the business, but there is a trade-off to be had between providing a good fit for each part of the business and over-complicating the range of course offerings. The most important distinction to draw is between technical and non-technical areas, and generally it is acceptable to participants to have a common set of materials within these two groups. This makes it possible to reserve the more complex tools and statistical software for the technical groups and using a much shorter course in non-technical areas, based around commonplace software such as Excel. By maximising consistency in this way, it is easier for internal Black Belts and Master Black Belts to operate cross-functionally and so provide support for smaller parts of the business, There is, however, no one accepted 'best practice' in this area and so each business must determine what makes most sense for their circumstances.
- Customising training materials: the more relevant materials are to the business' specific industry, the more easily participants will find it to grasp concepts. This can sometimes be a frustrating task because it is very time-consuming to create bespoke case studies and examples, and the resulting material may not be objectively better than the original 'generic' content, but the effect on participants' confidence and sense of ownership makes it well worth the effort. At Roche, this concept has been extended well beyond merely providing customised case studies – teams of specialists from global operations sat together in teams to assemble training modules that drew on the best of their collective ideas and experience. Techniques such as Total Productive Maintenance and Material Flow benefitted greatly from this customisation, as trainees perceived it as something specific to Roche and not 'off the shelf' – the benefit was not merely in classroom effectiveness but in the enthusiasm for the program back at the sites whose experts had contributed to the materials.[6]
- Incorporating change management: historically, change management training has been reserved for Black Belt or Master Black Belt/Lean Master curricula. Over time there has been recognition that acceptance of change is a critical component of any process improvement effort, and even short (1 week) curricula need to incorporate elements of this content. The training should be tailored to meet the specific needs of the business but will typically include concepts such as Stakeholder management, recognising and dealing with resistance, and influencing skills.

[6] Starting Up a Business Excellence Programme: The Roche Pharmaceutical Journey – PEx Network (Ernst Kasper).

Training for General Employees

When Six Sigma (and, later, Lean Six Sigma) was conceived, the emphasis was entirely on the specialists whose training is discussed above. It became clear in the mid-2000s that insufficient attention was being paid to the need to engage all employees in problem-solving and waste-reducing activities of one sort or another. This is key to maximising the impact of the program, as there are far more simple problems to be solved than complex ones, and it is also key to achieving a change in the organisational culture, because culture arises out of the habit of the majority of employees.

Biogen Idec's experience has shown that behaviour change is by far the most impactful part of their Operational Excellence program – considerably more important than the tools and analysis that are used.[7] For example, implementing a kanban system for supplies in Research Laboratories helped scientists to see that the goal of Lean is not to interfere with the science, but to free them from burdensome work that adds no value. Nevertheless, it required persistence and patience to reach a point where the system ran reliably.

Training needs for engaging employees who will not become Operational Excellence specialists need not be great. A 1-day or 2-day program is typical. The key is to make the training motivating, as the participants will not come to the course feeling as engaged as someone who has been specially selected to undertake a larger project. For this reason, such training should involve a great deal of interactivity, for example using a simulation, so that concepts can be explored and tools practiced before they are expected to be applied to real-world situations.

Key to the success of these all-employee programs is the application of newly-acquired knowledge to problems in employees' own area of work. Ideally this should involve individuals or teams working on small projects in their own work groups, because these have the greatest relevance and the best chance of leading to follow-on projects. Basic training may also be used to prepare employees for taking part in a workshop or supporting a larger project, but these activities are more likely to be seen as one-off events, after which the employee may feel they have 'done their bit'. While this will not immediately be recognised as a problem, one-off activities are not sufficient to establish a new way of thinking about improving processes – the key is to establish a pattern of repeating improvement efforts so that the skills become well-established, and process improvement activity is seen of part of regular work.

Another approach is to define a specific set of Operational Excellence skills that are need for each job role, incorporating these into the normal process of employee education and training. For example, a Production Engineer in an API plant might be trained in Setup Reduction, Failure Mode & Effect Analysis, Total Productive Maintenance and Overall Equipment Effectiveness in addition to existing GMP and company-specific training. This bespoke training in individual tools can be given on

[7] Interview with Rui Coelho, Associate Director, Operational Excellence at Biogen Idec.

a much broader basis than the more comprehensive Green Belt curriculum, and is another step towards implementing culture change by ensuring that each role has a defined set of core skills regarding Lean thinking, use of data, process analysis etc. Biogen Idec has carried out extensive training in the use of individual tools, to engage employees more quickly and easily into improvement activities. Although it is important to ensure that training with a limited set of tools does not lead to over-reliance on one or two, Biogen Idec's experience with this approach is that the problem rarely arises.[8]

Maintaining a Consistent Standard

As time goes on, pressure to reduce the cost of training programs generally increases. This is particularly common in deployments where the link to key business priorities has not been well established. Unfortunately, such pressures often come with little or no reference to the savings that improvement projects generate, and ignore the potential risk to effectiveness. The best protection is to demonstrate the value of improvement projects, but it is also important to be sure that training curricula are defined based on business needs so that unnecessary content is removed while the necessary content is protected.

The question then resolves into the best way of delivering this content. It should go without saying that a good internal instructor is preferable to a consultant, but if the internal certification process has been short-cut then the quality of internal trainers may be substandard, which is the start of a spiral of cuts and reductions in performance as described above.

Blended learning (combining face-to-face training with e-learning) should of course be considered, but with caution. It is cost-effective when it is not possible to adequately fill a classroom because there are too few trainees or they are widely dispersed geographically. It offers the convenience of taking the course in shorter sessions and in theory these can be taken 'just-in-time'. However the reality is often that trainees do not know what they need or when they need it, and need the instructor's immediate help to answer questions and correct mistakes in the use of statistical software. If the motivation for such changes is to provide more flexible and trainee-focused instruction, the revised program will likely involve at least as much instructor interaction overall as a traditional classroom-based curriculum; properly-used, blended learning is not a low-cost option.

Once training has become internalised, the cost involved should be only a small fraction of the benefit of the projects delivered. Given this, it is not rational to experiment with lower-cost training delivery approaches that could jeopardise

[8] Interview with Rui Coelho, Associate Director, Operational Excellence at Biogen Idec.

project success. It is therefore important to realistically assess the downside of reducing training content and run pilots that monitor the results carefully for training completion, project completion and follow-up project completion before committing to wholesale change.

Conclusion

We have reviewed the key areas that affect motivation for Operational Excellence at all levels in the business.

The first challenge is to execute the program effectively, and this chapter has focused on establishing and communicating a clear goal for the program that is driven by the needs of the business; selecting projects effectively to deliver results that help the organisation to execute its strategies; making appropriate use of metrics and engaging employees in general.

The second challenge is to sustain the effort, and this long-term commitment is something that many leadership teams find difficult to deliver. For this reason, some companies cycle between making intensive efforts to improve their performance, and focusing in other areas and allowing the gains to fade away, only to reach a point where the need to start again becomes pressing.

Setting up the program well creates the results that are needed – as a minimum – to enable the effort to be sustained. And once it is clear that Operational Excellence is truly a long-term commitment, many of the decisions regarding the scope of the program, project selection, training, certification and so on become considerably easier to make. The momentum behind Operational Excellence will develop over time as it becomes accepted as a permanent part of the culture, but this will only continue as long as the structures that support the effort are maintained.

Chapter 24
How Do We Create Leadership Pull for Operational Excellence?

Paul Docherty

The Paradox of Leadership Commitment

Several times a year, over the last decade, in multiple Operational Excellence (OPEX) focused conference workshops, we have asked the same question. What's the #1 obstacle to successfully deploy OPEX? The #1 answer has invariably remained "lack of top management commitment".

At a superficial level, at least, this answer doesn't seem to make sense. OPEX activity is in theory something that every business leader should actively want to support. OPEX promises to simultaneously improve quality and reduce costs – both of which are clear drivers for better business results. These are the same business results for which business leaders are directly rewarded and recognized. Additionally, there is significant, indisputable evidence that operational excellence programs have had a significant effect on the business results of not just tens, but hundreds of large private sector organizations (iSixSigma 2011). It seems obvious given this evidence and the direct link to what they get rewarded and recognized for that top management would naturally see OPEX as a priority.

The reality however is very different. Our research has shown that over 50 % of operational excellence pilots fail (Docherty 2006) and even highly successful programs suffer seismic shocks – we've seen top management in multiple companies inexplicably cancel OPEX programs generating hundreds of millions of dollars in savings – including, for example, BT's Wholesale Division Lean Six Sigma (LSS) program (stopped in 2005) and the decision by Network Rail (the UK Rail Operator) to disband their Operational Excellence program in 2007.

P. Docherty (✉)
i-nexus, George House, Herald Avenue, Coventry Business Park, Coventry, CV5 6UB, UK
e-mail: paul.docherty@i-nexus.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_24, © Springer-Verlag Berlin Heidelberg 2013

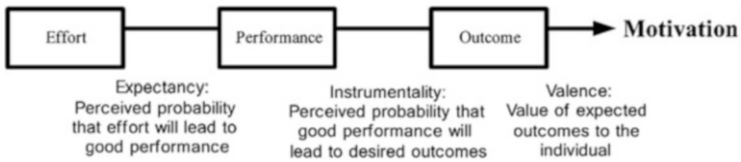


Fig. 24.1 Vroom expectancy motivation model

The Problem with the 'Push' Model

Clearly we have to look deeper under the surface to understand what's going on. Our simplistic assumption – that leaders will be motivated to support operational excellence – is based on the view that they will be motivated by the obvious link of OPEX benefits to the things they care about. The reality however, is that the link (particularly when OPEX is seen as a program) is often not that obvious, and in reality, motivation is based on more than just the belief that a link exists. A powerful model that helps us understand what drives motivation of individuals is Vroom's Expectancy motivation model (Bandura 1977). This model suggests for us to be motivated to do something we must believe at least 3 things (Fig. 24.1):

1. If we do something it will result in an outcome.
2. That the outcome that will result is personally valuable to the individual i.e. there is a clear WIIFM (what's in it for me) and;
3. That doing that thing (over all other things) will get to the desired outcome (that we will get rewarded for) faster/more effectively than all other potential things we could do to get to the outcome.

This model helps us understand both why leaders frequently don't throw their support and energy behind operational excellence and why this leads to the erosion of support for the concept and ultimately to the reason why OPEX programs fail.

Consider the following causal analysis which is based on the insights from Vroom's motivation model (Fig. 24.2). It links the 'symptoms' of lack of management commitment to OPEX programs to the consequences of these symptoms – effectively the death of the program by "1000 knives" and "chains back" to the potential causes of this lack of commitment.

Fundamentally this model suggests that there are three pre-requisites that need to be in place for leaders to be motivated to support operational excellence activity:

1. Leaders have got to believe that the operational excellence projects are directly aligned with their personal objectives i.e. that the project outcomes will directly contribute to achievements of the outcomes they get rewarded for.
2. Leaders have got to believe that applying operational excellence tools and approaches will fundamentally deliver results more quickly/effectively than alternative approaches.

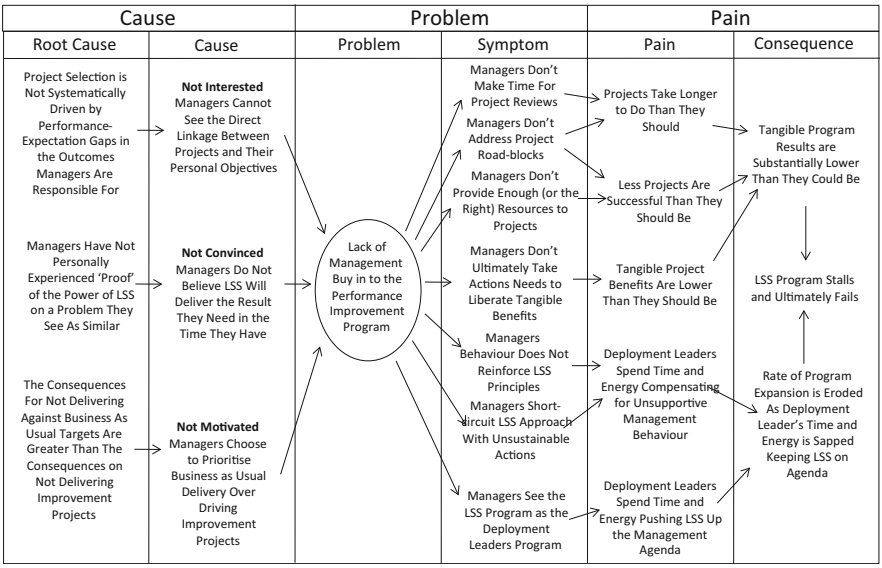


Fig. 24.2 Causal analysis of drivers for lack of management buy-in to OPEX programs

3. Leaders have got to believe that the consequences of not delivering improvement activity are greater than the consequences of not delivering the business as usual activity

With this insight it is clear why traditional "program driven" approaches to operational excellence often fail. Whilst, popular, the "deploy OPEX as a program" approach (as promoted by the initial adopters such as GE, Motorola and Honeywell and subsequently adopted by hundreds, if not thousands, of other companies) is based on some flawed assumptions. This approach, in which a corporate staff function – variously called Lean Six Sigma, Process Excellence, Business Excellence, or similar, is set-up to 'push' a training program in which high potential employees are taken out of the line roles and trained in waves to run improvement projects – can easily create a situation where leaders feel little or no ownership for the improvement projects. There are two principle reasons for this:

1. The first is the consequence of the widely adopted 'no project, no training' rule. This rule which is based on the apparently sound premise that training people without a way of directly applying that training is pointless, has led in the vast majority of organizations to many dubious projects being selected due to the combination of pressure to pick something to work on, and the lack of an easy way for operational managers, who tend to focus naturally on the day to day, to understand which would be the very best problem for their nominee to solve in the context of the organization's strategic goals. The consequence of this rule is in practice that there is typically a relatively poor alignment between the projects being initiated and the agenda of the top management – with the consequence

that whilst the managers often recognize the project as something worth doing it doesn't make their top 3–4 priorities – which ultimately govern what they spend their time and energy on.

2. The second is the consequence of the perception that naturally results from the act of creating a central Program Office to drive the OPEX program i.e. (a) That they (the operational line managers) don't own the OPEX program (it's "owned" by the head of the staff function that's leading the program) and (b) It is ultimately not their job to deliver the OPEX program benefits. This perception is reinforced by the fact that in most organizations operational managers are incentivized to deliver 'run the business' operational outcomes i.e. more outputs for less cost. These managers will understandably then prioritize those actions that they believe will lead to these operational outcomes at the cost of projects – particularly if they can't see a direct link to the outcomes they are rewarded for and/or if they believe there is a way to pull an alternative lever that will get results more quickly even if it's not sustainable. This helps explain, for example, why apparently sane managers would often rather shoot the alligators than drain the swamp e.g. throw people at chasing debt (quicker result, potentially more successful in the short-term) rather than understand and fix the root causes of delay in customer payments (takes longer, there is uncertainty on the degree of impact even if it is more sustainable in the longer term).

Of course, there are tactics that organizations can adopt with the 'push' OPEX as a program model to help lessen the likelihood of picking projects that managers won't care about. These tactics include creating a project hopper process and ensuring projects are systematically evaluated against meaningful evaluation criteria and increasing the consequences of not working on/supporting improvement projects by raising the visibility of the money 'left on the table' to top management as projects are delayed. My own experience, however, as an OpEx program deployment lead for a major telecommunications supplier, is that these tactics ultimately have limited success as they are trying to move OpEx up a manager's agenda when all the other pressures they face are naturally forcing it down the same agenda.

Hoshin Planning as a Strategy to Create Pull

The good news is that there is a proven approach that you can use to turn this situation on its head – one which naturally leads to the situation where senior executives are the principal drivers of OPEX activity and where improvement efforts are more focused on the real objectives of the organization.

This proven approach is known as Hoshin Planning (sometimes referred to as Hoshin Kanri or Policy Deployment). Hoshin Planning basically provides a systematic way to align the objectives and actions of the organization at all levels with the key breakthroughs the organization is trying to make. The words "Hoshin

Fig. 24.3 Hoshin planning translation

Kanri" were first used in 1965 by the Bridgestone Tire Company in Japan to describe their long-term planning system, which they based on best practices observed in Japanese Deming prize winners. The words "Hoshin" "Kanri" literally mean "shining metal" "management" – essentially describing the concept of a "vision compass" i.e. a mechanism to keep us all focused on our "true north" (Fig. 24.3).

In simple terms, Hoshin can be considered the marriage of "Management by Objectives" with the Deming "PDCA" (Plan, Do, Check Act) cycle. The core idea behind Hoshin is that goal deployment is a two-way process, where goals and targets, and the implications of achieving those goals and targets, are discussed at every level in the cascade through a process called "catch-ball". It is this "catch-ball" dialogue that ensures that the action plans resulting from the cascade of goals are tangible, realistic and as a whole the execution plan remains feasible.

Whilst the adoption of Hoshin planning was limited to a few well known exemplars (Toyota, HP, Bank of America, Danaher) in the 90s, the last decade has seen a significant acceleration in the number of companies adopting the approach – particularly in corporate America. In fact the last 3 years have seen over 50 new organizations adopting the approach including early steps from a number of major Pharma companies including Pfizer, Novartis and Bayer. One hypothesis for this recent increase in adoption is the combination of:

- The assessment that many Fortune 500 companies have reached a point in their Lean maturity that they are ready to embrace the next steps of Enterprise Lean of which Hoshin Planning is considered a key part.
- The need for large companies to deploy their capital following the financial crisis and the subsequent 'slash and burn' actions that they took to conserve capital. Many companies are looking for ways to intelligently deploy the over $2 Trillion that they have subsequently hoarded on their balance sheets to drive growth and efficiency.

- The increasing recognition and awareness of the effect that Hoshin has had on company profitability. Danaher Corporation, for example, one of the most profitable companies in the world, is a well known user of Hoshin Planning and awareness is growing through the wider dissemination of Lean thinking.

How Hoshin Creates Pull

In terms of creating leadership pull, the attraction of the Hoshin Planning approach is that it has the potential, if done well, to create ownership for improvement at every level of the cascade.

To understand how Hoshin Planning achieves this outcome we need to understand how the process that underpins Hoshin impacts, and even influences, leadership behavior. Whilst there are a number of variations of the concept, the basic process of Hoshin Planning is shown in the diagram below. Beyond the first stage which focuses on strategy development (a task that most leaders and organizations are reasonably proficient at), the key focus of the Hoshin process is on strategy deployment and execution (a task that there is clear evidence the majority of organizations struggle with) (Fig. 24.4).

Four key words can be used to sum up the Hoshin process – focus, clarity, alignment and follow-up. Regardless of how the strategy was developed (the Hoshin process offers little prescription in terms of how this should be done), the second step in the Hoshin process – the definition of breakthrough objectives is all about choosing a few things to do well and making sure for each of those things, that the 'job to be done' is unambiguously defined such that it can be universally understood. By forcing the leaders to define a few key breakthrough objectives (not more than 3 is the usual prescription), Hoshin effectively ensures top management's priorities are clarified and creates focus by ensuring that leaders focus on the "vital few" rather than the "trivial many". Without this basic step – effectively setting a "true north" for the leadership team to connect their efforts to – it's not surprising that operational managers struggle to link improvement actions to their personal priorities and why their priorities change with changes in day to day external pressures.

The next stages of the Hoshin process, in which annual objectives are developed and deployed, is where the process makes the connection between leadership priorities and improvement actions. These next two stages are essentially about creating alignment – i.e. ensuring the efforts of teams at all levels are directed towards the achievement of the breakthrough objectives. The principal tool that is used to "document" the deployment of goals in the Hoshin Planning process is known as the Hoshin X-matrix – one of a number of forms (sometimes referred to as A3's based on the size of the paper that would typically be used to create them) that collectively support the Hoshin process. The Hoshin X-matrix, shown conceptually in Fig. 24.5 below, essentially captures the causal linkage between the parent goals

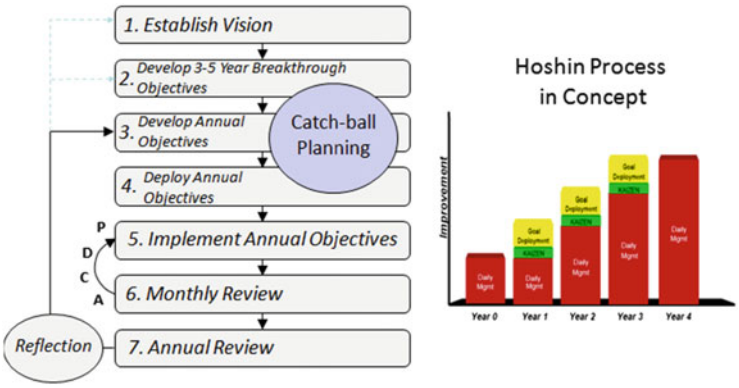


Fig. 24.4 The Hoshin process

at one level and the child sub-goals at the level below (which if executed successfully should lead to the achievement of the parent goals).

The power of the "X-matrix" format lies in two key concepts. The first is "visual simplicity" i.e. its ability to present a significant amount of information concisely and in a way which is easy (once you know how to read them) to absorb. The X-matrix format essentially enables a team to capture unambiguously on a single sheet of physical (or virtual) paper their collective plan to achieve the annual/breakthrough goals. Each completed X-matrix captures:

- The specific improvement priorities that they believe they need to focus on to deliver the annual and ultimately breakthrough outcomes;
- The logic of how these improvement priorities drive those outcomes;
- How the achievement of these improvement priorities will be tracked; and
- Who specifically will be responsible for executing each improvement priority.

The second is the idea that subsequent levels of cascade can be achieved through simply "rotating" of the X-matrix (through 90°). "Rotating" the X-matrix (as shown in Fig. 24.6 below) essentially 'reveals' a new "blank" level on each rotation, enabling the person to whom one or more objectives have been deployed to then cascade those objectives to either sub-objectives (that need further cascade) or to actionable priorities i.e. the objective can be directly translated into one or more improvement projects.

The 'rotate to cascade' model drives ownership in two ways:

1. Firstly, individual leaders, at every level, can clearly see (by following the link through each matrix back up the goal tree) a 'red thread' that connects their personal goals to the annual and breakthrough objectives (which if the organization has followed the hoshin process well will represent the basis on which senior management are rewarded and recognized).
2. It explicitly requires leaders to whom objectives have been cascaded to develop (again with their respective teams) a sub-matrix which further deploys the

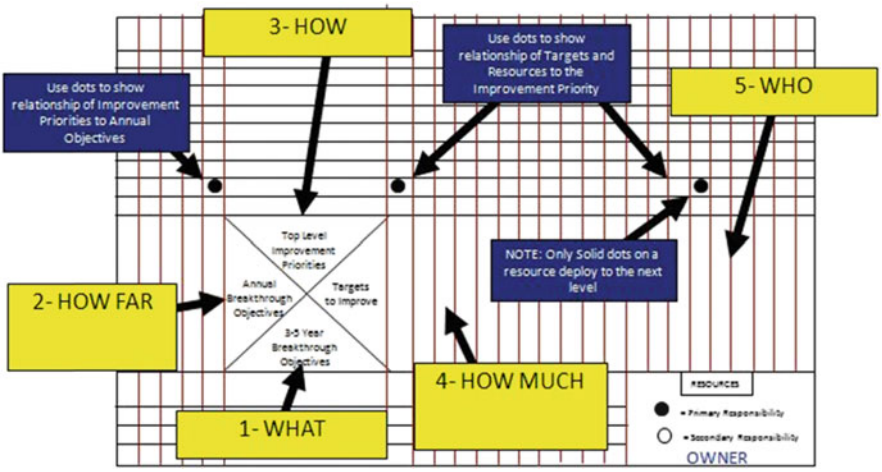


Fig. 24.5 The Hoshin X-matrix

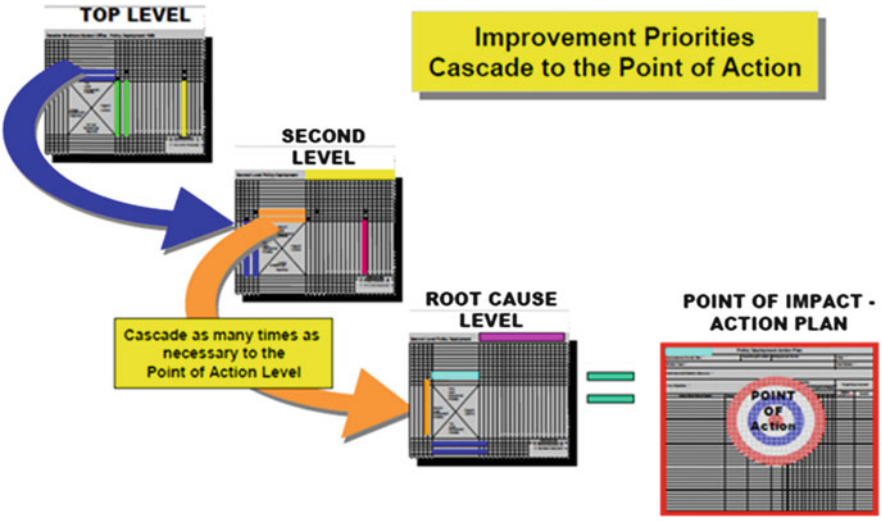


Fig. 24.6 Deploying objectives through rotation with the X-matrix

objectives that have been deployed to them. The "catch-ball" dialogue (which extends to include the team members assigned in addition to the objective owner to develop the action plans to meet each objective) forces a conversation which ensures that the actions which are identified to achieve the goal are well thought through and the targets that are set are meaningful.

Another concept that is frequently deployed by organizations implementing Hoshin is to have the team that is developing the action plan for each objective

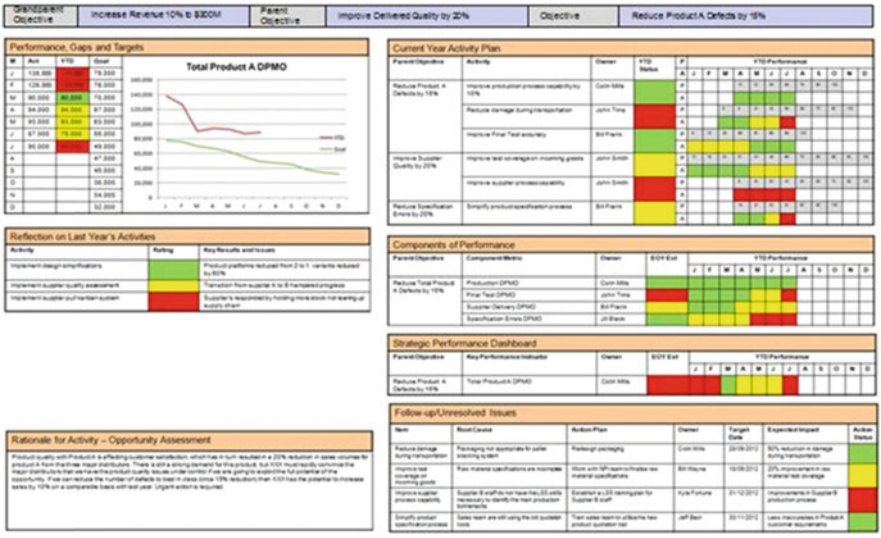


Fig. 24.7 Example Hoshin strategy A3

develop a detailed plan for that objective as part of the "catch-ball" cascade process. Known as a Strategy A3, this planning format both forces a level of disciplined thought about what the gap is that needs to be closed and what are the best strategies of closing it and provides a simple concise communication to the wider organization that explains exactly what has been assumed in the development of the plan (and related targets). A example of the Hoshin Strategy A3 format is shown below in Fig. 24.7.

Collectively these first 4 stages of the Hoshin process address the key things that we identified earlier as being critical to ensure ownership for improvement. Firstly, they ensure senior leaders can clearly understand the logic that connects improvement actions to the outcomes they want. Secondly, by creating a consensus at the organizational level on exactly what the organization is trying to achieve – they make it easier for leaders (whose reward and recognition is inevitably linked to the achievement of the breakthrough objectives) to make the link that says if I do these actions then not only will the outcome be achieved but it will be personally valuable to me. Finally, through the catch-ball dialogue – and the incentive that provides to ensure that the actions identified are pragmatic and effective, leaders can have a higher degree of confidence that the things that are included in the plan are the things that will get them to their desired outcome faster/more effectively than the other options that might be available.

The result is a dramatic increase in the motivation of leaders to drive execution of the tasks (specifically the improvement actions) that underpin the Hoshin plan. Whilst the first four stages of the Hoshin process create leadership motivation it's the later stages that sustain it. The reality, as we all know, is that no matter how well defined or robust a plan is it will never survive the implementation intact. Changes

in the external environment combined with incorrect assumptions and/or under/over performance will mean that the plan needs continual refinement if it is to stay credible and if leaders are to stay invested in it.

How Hoshin Sustains Pull

The fourth word that describes the Hoshin process is "follow-through". Step 6 of the Hoshin process is the implementation of a periodic review process, following the Deming PDCA (Plan, Do Check, Act) cycle typically monthly and frequently referred to as a Monthly Operating Review (MOR). This review utilizes two other Hoshin A3 forms – the first which provides a simple visual management tracking of achievement of the metric targets over time is known as a Bowling Chart. The second A3 form is known as a Hoshin Counter Measure. The Counter Measure effectively encourages a "5 Whys" style analysis of why a particular objective is off plan (i.e. the associated metrics are not tracking to the expected targets that represent the achievement of the outcome) (Fig. 24.8).

The power of the MOR is that it creates a Monthly "heartbeat" for the Hoshin process that ensures that leadership focus is directed towards the single question – "what do I need to do to enable us to hit the plan?" This laser focus on execution ensures effort is invested exploring options to get back on track before it becomes too late to act. Done well, the MOR will also become the discussion in which (having prepared for the review) the management team recognize that one or more underlying assumptions on which the plan is based haven't played out in reality and that a change to the targets is necessary to keep the plan achievable. Obviously, this needs to be a disciplined process (the goal must be to exhaust all options before changing the targets) but the result, when the process is done well, is that leaders remain motivated to implement the plan as they can see that it is not only making progress towards the goals they will be rewarded for (providing reinforcement) but it still represents the best bet they have of achieving those goals and getting the resulting reward and recognition.

Summary

Operational Excellence rarely receives the level of top management support that deployment leaders want. There are multiple reasons for this but at the heart is a disconnect between the outcomes that senior management want and the improvement projects that are typically initiated through programmatic 'push' based deployment approaches.

Hoshin planning offers the opportunity to turn this on its head and create a pull for operational excellence capabilities – as leaders seek support to execute on their plans. As we have seen the Hoshin approach, and in particular the alignment, clarity

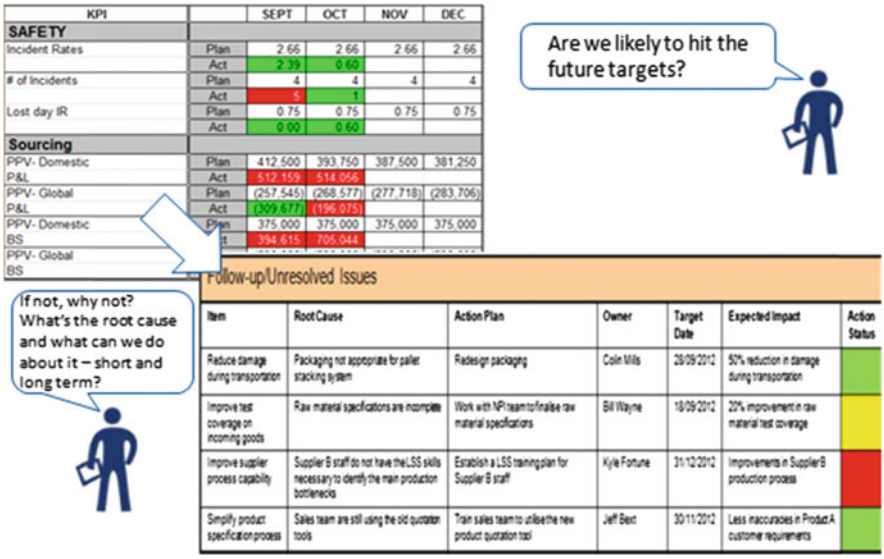


Fig. 24.8 Focusing on countermeasures in the monthly operating review (MOR)

and realism created by the catch-ball process helps address the key factors that erode the motivation of leaders to value and drive Operational Excellence activity.

Recent MBA research, completed in 2009, provide some compelling evidence that integrating Hoshin planning with operational excellence can have dramatic effects on the results generated by the program (Gupta 2009).

Figure 24.9 below summarizes the Performance Improvement Maturity Model – a model first introduced in 2005 by the author which has been widely used to benchmark the maturity of operational excellence activity in Global 5000 organizations (Docherty 2005).

The later stages of maturity (Alignment and Integration) assume that Hoshin Planning is used to align and integrate the operational excellence activity within the organization to create pull. This model was used in 2010 as the basis of a MBA research project in which the return on investment and productivity of improvement practitioners in over 40 organizations was correlated with an assessment of the maturity of that organization's approach to operational excellence. The summary results – shown in Fig. 24.10 below illustrate the significant impact on both ROI and improvement practitioner productivity (the number of concurrent projects they are able to support/execute) that linking Hoshin with operational excellence can realize.

Further information, including practical guidance on how to implement the Hoshin process and the tools needed to sustain it can be obtained from the www.i-nexus.com.

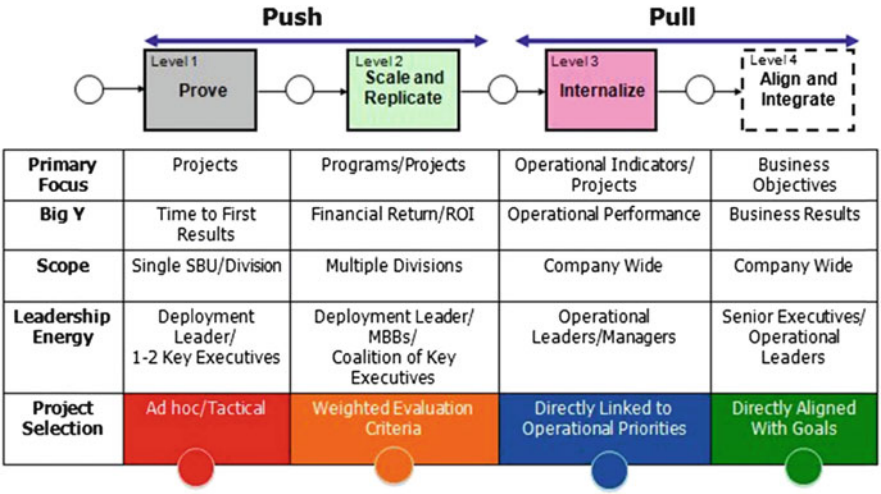


Fig. 24.9 The performance improvement maturity model

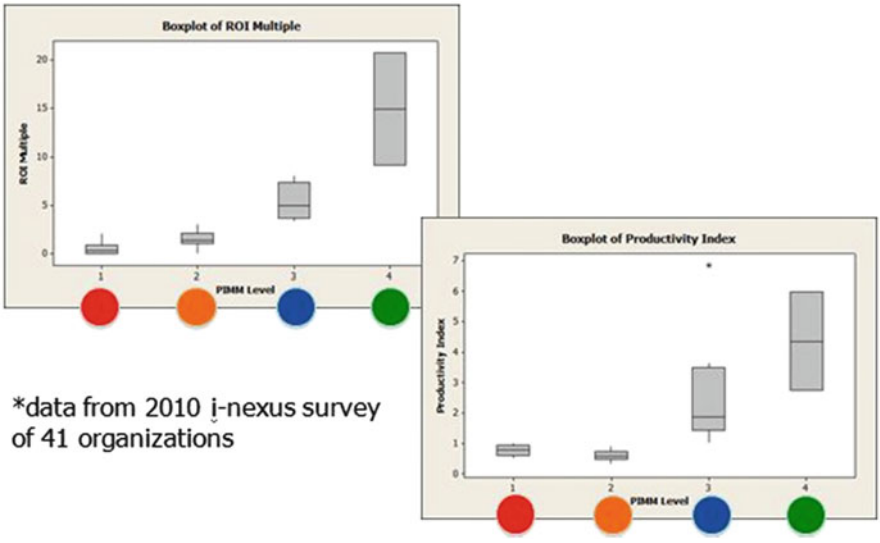


Fig. 24.10 Impact of using Hoshin to align and integrate OpEx activity

References

Bandura A (1977) Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev 84(2):191–215

Docherty P (2005) Uncommon practices, exceptional results, Docherty P (2006) i-nexus White Paper

Docherty A (2006) Why lean Six Sigma programs fail, Docherty A (2006) MBA dissertation, Warwick Business School
Gupta T (2009) Impact of maturity on performance improvement programs, Gupta T (2010) MBA dissertation, Warwick Business School
iSixSigma (2011) Lean Six Sigma costs and savings, iSixSigma 2011. iSixSigma Website

Chapter 25
Leadership Characteristics for a Sustainable OPEX-Implementation

Uta Walkhoff

Introduction

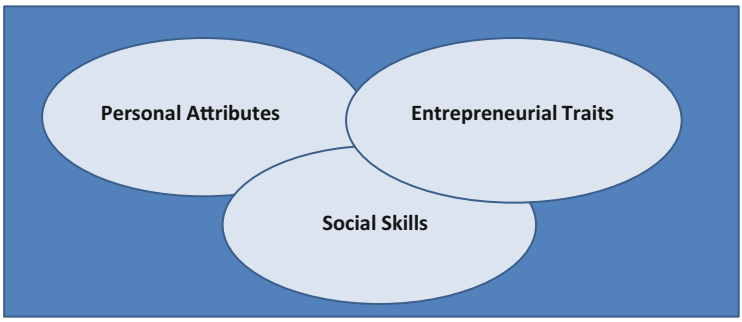
Through long-term collaboration with leaders of OPEX initiatives, and by monitoring their initiatives' development over the years, characteristics of successful leaders – of leaders who have implemented OPEX initiatives themselves, and of those who took them over at some point – have been determined. Some leaders successfully lead an OPEX initiative right from the start for many years, and maintain a positive OPEX culture that outlives the initial verve. Others have to put a lot of energy and effort into both execution as well as further development of their OPEX programmes. This raises the question of how, under comparable conditions, leaders differ from each other. Why does leading OPEX initiatives come naturally to some, whereas others have to work hard for it? The answer to this lies in the leaders themselves. It is not the concepts and methods, not the lack of resources or the pressure from everyday business. It is the personality of leaders that has a fundamental impact on the success of an OPEX initiative, affecting quality, speed, and outcomes of OPEX programmes.

What does successful leaders characterize, and how do they differ from less successful ones?

Knowledge can be imparted, solid framework conditions can be created, but the continuous success and the consistent advancement of an OPEX programme is closely linked to the person leading the programme. Observing successful leaders of OPEX programmes, a number of characteristics and behaviours stand out. Successful leaders have a credible and reliable image of the meaning and purpose of as well as the reasons for OPEX in their mind. They do not act at anyone's instruction; they themselves have found or derived compelling reasons for implementing OPEX. They are extremely business-oriented, irrespective of how large or small their area of responsibility is, and

U. Walkhoff (✉)
uwprocessconsulting, 69469 Weinheim, Germany
e-mail: uta.walkhoff@uwprocessconsulting.de

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_25, © Springer-Verlag Berlin Heidelberg 2013



Personal Attributes	Entrepreneurial Traits	Social Skills
Willingness to change	Result and target orientation	Empathy
Willingness to learn	Self-commitment	Team orientation
Creativity	Professional competence	Capability to network
Confidence	Consistency	Enthusiasm
Patience	Authencity	Readiness to deal with conflicts
Curiosity	Ability to improvise	
Courage		

Fig. 25.1 Characteristics needed to successfully implement and lead sustainable OPEX initiatives

they also have a number of personal character traits that make them very humane and credible. They personify their own values.

The following will highlight characteristics of leaders, and put them in the context of the successful and sustainable implementation of OPEX programmes.

Main Leadership Qualities Required for Successful and Sustainable OPEX Programmes

Years of observing leaders of OPEX and their skills have revealed three levels of special skills (Fig. 25.1):

Personal Attributes

Willingness to Change

OPEX always means change, leaving behind what is familiar and venturing into new territory. Leaders who are open to change, approach changes actively. Those

who like to play it safe and prefer to continue business as usual might find it difficult to handle an OPEX programme.

Willingness to Learn

Embracing new ideas implies learning and expanding one's knowledge. Those leaders who steer their OPEX programmes with curiosity and a willingness to change, are usually also prepared to learn. Themselves not shying away from this challenge, they demand that same willingness of their employees.

Creativity

Creativity means the ability to adopt a different angle, using unusual methods, and thinking outside the box. Creativity is often dealt restrictedly in OPEX programmes, via methods such as brainstorming or TRIZ. Successful leaders, however, integrate creative action in their daily leadership routine. They are capable of re-using already established models in a new context, adopting them to their needs, and encourage employees to think laterally.

Example

Why reinvent the wheel all the time? Creativity sometimes can be as simple as copy & paste. If another functional unit has developed a procedure that allows for optimisation, why not have a closer look at that procedure to see what of it can be adopted?

Confidence

Every OPEX success takes time. It is the leaders' role to provide the framework and to lay the foundations for successful OPEX programmes. Often, it is not immediately clear whether these actions will be rewarded with success. The next leadership levels, the teams and employees are going to deal with new challenges at different speeds. Pressure and control are completely inappropriate in such situations; rather, support and open communication between employees and leaders are required. If a leader has confidence in the competence of his teams and employees, they will feel that and deliver results.

Example

A lack of confidence usually manifests in increased control. Leaders who do not trust their employees and teams tend to resort to tried and tested

(continued)

instruments, such as weekly or monthly reports. This causes a focus on delivering requested reports, and often shifts attention away from OPEX contents.

Patience

OPEX programmes usually quickly deliver first results, the often cited so-called low-hanging fruits. Over the course and phases of the programme optimisations become more complicated and more complex and results will take time. Successful leaders not only have confidence, but also show patience, because they realise that things will slow down as soon as the low-hanging fruits have been picked.

Example

A lack of patience shows if leaders expect that a continuously increasing number of optimisation measures goes hand in hand with an equal increase in cost savings. Patience means to persevere through any dry spells in the OPEX programmes, in order to be able to reap the rewards afterwards.

Curiosity

Like scientists, constantly looking for new findings, successful and committed leaders are constantly curious and interested in the unknown. They do not cling on to known topics, but think laterally and never stop to take in new impulses from outside their actual area of responsibility. These impulses can also come from other industry sectors, sports or even culture.

Example

In order to show what outstanding results can be achieved with OPEX, an analytical examination of the functioning of an orchestra can be useful. World-famous orchestras are characterised by excellent musicians and the prowess of their conductors. Conductors and musicians constantly work on optimising their individual skills, and are only top-class as a whole when there are no individual mistakes. The direct connection with roles and results in a company is evident, and it pays to look at musicians' methods.

Courage

Besides curiosity, successful leader also display courage, time and again. As mentioned before, OPEX means constantly leaving beaten tracks, and venturing

into new territories. Leaders who are prepared to do so will quite often be lonesome in this. Unwaveringly conveying and seeing through one's own ideas, new directions and paths, not only to employees but also to the management, can be a true trial of courage.

Example

Potential scenarios that might come up in the course of an OPEX programme are: addressing mistakes outside one's own area of responsibility, announcing challenging business outlooks or correcting wrong decisions from the past. Working actively with these scenarios requires courage as well.

Entrepreneurial Qualities

Target and Results Orientation

Why going through all this trouble – is it worth it? A successful leader never loses sight of the merits of OPEX. OPEX means becoming better than others, pursuing this state, recognising, maintaining, and constantly developing it. However, the goals leaders are pitted against usually are: more profit, higher yield, less costs. Leaders who manage to sustainably and successfully pursue OPEX are capable of constantly breaking down and aligning business objectives, the goals of their own area of responsibility, and those of their OPEX programme at the same time. It is an art that needs to be mastered.

Self-Commitment

Successful leaders of OPEX do not need instructions. For all intents and purposes they are compelled and motivated by the goal and the purpose that needs to be served, and they orient themselves by that. In doing so, they provide guidance for their employees as well, be it deliberately or subconsciously.

Example

Irrespective of the business objective, a leader pursues the personal objective of making a certain area of responsibility the best it can be – be it a product, a pre-product, a marketing strategy, etc. If you listen carefully to leaders with strong self-commitment, this becomes evident in the form of expressions such as "my/our product" or "our strategy".

Professional Competence

Working in OPEX programmes requires profound understanding of, and expertise in, the respective business. Solid foundations are necessary to generate improved processes. Optimisations require a number of technical and factual decisions. Leaders who are far removed from the content structure of their area of responsibility will struggle at this point. Successful leaders always are professionals in the craft they are responsible for.

Consistency

Though courage, curiosity, and patience must be particularly highlighted among the personal attributes of successful leaders, consistency has its importance, too. From a business point of view, new paths must be approached with discipline, amidst all the creative, courageous, and patient leading. Otherwise, there will be disorientation and dispersion.

Open-Mindedness

A well-balanced management of OPEX programmes and one's own factual and technical responsibility can develop like a demanding game of chess: it is not only the next step that is important, but it is also the multitude of other possible options that need to be considered. Leaders who only manage their day-to-day business and lose sight of what could happen in the long-run might ultimately fail. With regards to the leadership responsibility for OPEX, this means dealing openly with scenarios and target-oriented controlling of effects and influences.

Authenticity

Leaders implementing OPEX in a way only conveying what is expected from them are going to fail. Employees will know if it is the leader's own will and conviction to establish OPEX as a fundamental part of management, or if he or she is just following orders. The implementation of OPEX entails new challenges for every employee, and therefore the employees' commitment will depend substantially on the credibility of the leaders.

Ability to Improvise

OPEX means constant change. However, environments do not always follow at the same speed, and suddenly prerequisites for a next step may be missing. The motto then is: being able to improvise using the options that are available.

Social Skills

Empathy

Individual personalities greatly differ, and so does acceptance of OPEX topics. Leaders with a good sense and feeling for difficult situations, who can therefore easily empathise with their employees, can grasp and deal with difficult situations to help. Moreover, they can deal with these situations easily and the employees and/or teams involved will return onto a positive and constructive path.

Team Orientation

Good progress can only be made by a team. Many leaders have excellent ideas when it comes to optimising their area of responsibility (especially those with distinct entrepreneurial qualities). At a first glance, it seems the most efficient way to simply order the implementation of these ideas. However, practice has shown that OPEX projects require a team in order to develop a solid foundation for the change and new ways that come with OPEX. That means that the biggest sceptics set the pace. The best way to overcome scepticism is through team-oriented action. Besides, it is much nicer to celebrate success in a team than alone.

Capability to Network

As mentioned multiple times before, OPEX means constantly approaching new subjects, trying out new ways and tackling things differently. Leaders who seek to achieve that solely based on their position's power will sooner or later reach their limits within the organisation. Leaders who have got the necessary vision to realise and estimate where change will lead, and what effects it might have, have proven time and again the benefit of frequent and early liaisons with colleagues and other functions. Their enthusiasm is contagious and inspires those they are in contact with, and being embedded in a thriving network also allows them to identify new trends in time.

Example

Networking is crucial for OPEX leaders, and especially so when it comes to optimising interfaces across topics or processes. Colleagues with which regular, good contacts have been maintained, will be much more likely to follow and share a collective way of optimization. That is, a good network will pay off in an efficient implementation of optimization measures.

Enthusiasm

Organisations tend to doubt and question things. Depending on the cultural environment, novelties are sometimes met with scepticism. Only leaders who can enthuse and inspire others, who convincingly advertise and communicate a cause, will be able to rouse sceptics from their immobility and motivate them to join in.

Example

As time goes by, the enthusiasm for an OPEX programme may need to be revived: due to the daily business it might be helpful to conduct review-workshops, and to remind teams and employees of benefits and needs of the OPEX programme. Successful OPEX leaders do so frequently, reminding their employees again and again of needs and perspectives.

Readiness to Deal with Conflicts

Change not only has supporters. There are many potential sources of conflict in OPEX programmes: someone's views may be disregarded; concerns may not be given an adequate forum. Leaders who recognise potential for conflicts, and actively and openly tackle it are usually more successful. They prevent projects from coming to nothing and avoid the waste of valuable time.

Coaction of Leadership Characteristics

All of the above described characteristics and traits appear in individually differing combinations and degrees. In order to be able to provide appropriate training, it is advised to assess each of the discussed characteristics using the checklist in Fig. 25.2. A leader might be strongly target-orientated, for example, but he or she might lack in the willingness to change. Individual leadership trainings can support, foster and advance individual capabilities (Fig. 25.3).

The Core Leadership Qualities for Sustainable OPEX Implementation

Of all the leadership qualities described above, four are core leadership qualities that deserve special attention: the willingness to change, target and results orientation, authenticity and self-commitment.

Personal Attributes	Value	Entrepreneurial Traits	Value	Social Skills	Value
Willingness to change		Result and target orientation		Empathy	
Willingness to learn		Self-commitment		Team orientation	
Creativity		Professional competence		Capability to network	
Confidence		Consistency		Enthusiasm	
Patience		Authencity		Readiness to deal with conflicts	
Curiosity		Ability to improvise			
Courage					
				Total:	

Values:
0: inexistent, 1 : low, 3: medium, 5: high

Fig. 25.2 Checklist to assess the leading OPEX performance indicator

Fig. 25.3 ***Occurrence and coaction of leadership characteristics (example)***: high valued authenticity and target orientation, less willingness to change, moderate self-commitment

Willingness to Change

Leaders who are not or only somewhat open to change will not succeed in keeping OPEX up and running on a continuing basis.

Target and Results Orientation

OPEX is concerned with optimisations, and constantly aligning this optimisation with superordinate corporate objectives. This is challenging, because superordinate objectives are guided by markets, customers, political conditions, etc. Constantly updated controlling of operative OPEX procedures according to those outside influences is especially challenging.

Authenticity

Only very few leaders are immune to worries and doubts, and understandably so – it is on them to constantly give the OPEX programme a consistent direction. As mentioned above, insecurities never go unnoticed by employees. It is an art form to lead an OPEX programme authentically and credibly in the long run.

Self-Commitment

No matter what happens around them, leaders who successfully lead long-term OPEX programmes always follow an inner voice, an inner commitment to corporate objectives, which gives them an unwavering presence even in very difficult situations.

Synergy of Leadership Qualities

Following an inner commitment, never failing to show decisiveness and credibility, taking into account all incalculable risks while not losing sight of the positive effects of changes – these are the characteristics of leaders who have got the persistence required for the sustainable and successful implementation of OPEX programmes.

Impact of Personal Motivators

Leaders are human. As such, they can be driven and motivated by incentives, and slowed down by inhibitors. Personal motivators can be material or immaterial. In addition to leadership characteristics, personal motivators are essential and can have a significant impact on the success of OPEX programmes. If personal motivators are not met, overall performance might fade. In addition to the leadership characteristics it is important to have a look at them. Here are some examples of possible effects of personal motivators:

Example 1: (Competitive) Ambition

People who approach their leadership role in a sportsman-like manner enter a race against competitors with their tasks. They are especially motivated when they win or are in the lead. In the context of OPEX, this can mean that for leaders with competitive ambition it is important to be declared as the winner. Public recognition and distinction are particularly strong motivators. If these personal motivators are ignored, an immediate, negative impact on their motivation for the OPEX project is likely.

Example 2: Harmony

Leaders who are very harmony-orientated can struggle with the OPEX programmes. They usually lack a basic personal attribute that has already been described: readiness to deal with conflict. New ways and changes not only have supporters, but also opponents. Approaching these conflicts and trying to withstand them is an enormous challenge for harmony-orientated people. People who seek harmony – even leaders – wish for a team where they feel in good hands, and strive for an unstressed working environment.

Example 3: Change

Not everyone is inherently willing to change. However, there are people who actually have got change as a personal motivator in their DNA. They need change in their own, personal biography as well as in their environment. If you deprive them of the possibility to change themselves or things, they will wither. As already mentioned, these people have got one of the main personal attributes for successful management of OPEX initiatives; however it is also possible that they shy away from conflict, which then works in the opposite direction.

Conclusion

Over the last few years, demands on leaders have continuously increased. Business and responsibilities are becoming more and more complex. If a manager is tasked with leading an OPEX initiative, this is usually considered as just another challenge. It is assumed that true leaders can handle this task if only the structural framework conditions are in place. But merely providing methods and resources is not enough. A sustainably successful OPEX initiative depends for a good part on the chosen leaders' personalities.

In their initial phases, OPEX initiatives are often almost self-perpetuating, and do not pose too much of a challenge to the leaders: the optimisation potentials are easily identified and comprehensible for everyone. Lean, Six Sigma or Lean Six Sigma provide comprehensive and field-tested concepts and methods. In this phase, the leadership task mainly encompasses creating the framework, such as allocating required resources, necessary time slots for employees, or training. These duties are not very different from leaders' usual tasks. Gradually, the demands become more complex. Suddenly it is no longer enough to provide methods and to manage time and resources. After the initial phase, which can substantially vary in length, leaders are confronted with situations that are clearly more demanding. Conflicts crop up,

convictions are questioned, optimisations are blocked by employees who are reluctant to change, and motivation dwindles among leaders. OPEX can be very demanding of leaders, and it is advisable to prepare leaders of all levels for this endeavour, and to actively support them.

Leadership and management trainings can have a positive influence on these aspects and boost them. An analysis of characteristics can reveal needs for development at an early stage, providing the basis for individual leadership development programmes. Supporting leaders in their characteristics helps to save valuable time and resources, and can contribute to making OPEX initiatives more successful and sustainable.

Chapter 26
Leading Operational Excellence in a Global Company

Mark McColgan

Background. Takeda Pharmaceutical Company Limited acquired the Zurich-headquartered Nycomed A/S in 2011. Takeda has its strong presence in the Japanese and U.S. markets, while Nycomed has a significant business infrastructure in Europe and high-growth emerging markets that will enhance Takeda's regulatory development expertise and commercialization capability. Nycomed manufactures branded medicines for hospitals, specialists and general practitioners, as well as over-the-counter (OTC) medicines. It has a diverse product portfolio of strong global brands adapted to local needs. Nycomed, as part of the Takeda Group operates more than 18 manufacturing facilities in 11 countries (Source: Nycomed/Takeda 2013).

Definition of Operational Excellence at Nycomed/Takeda

Total Productive Maintenance (TPM), Total Quality Management (TQM), and Just-In-Time (JIT) are all part of an overall OPEX methodology. They all share the same objective: Improving a business in different dimensions whilst involving all employees at all levels (and not just decision-makers) in order to be more successful in the long run. The involvement of all employees is a crucial success factor. A mere stringing together of TPM, TQM, and JIT methods and tools, however, does not make a company succeed in OPEX. The sole use of buzzwords, like often experienced in practice, only confuses people without adding value to any initiative.

M. McColgan (✉)
Operational Excellence & Technical Services, Takeda Pharmaceuticals International, Glattpark-Opfikon, Switzerland
e-mail: Mark.Mc-Colgan@takeda.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_26, © Springer-Verlag Berlin Heidelberg 2013

OPEX is heavily based on the principle of continuous improvement. The very foundation of continuous improvement is respect for and empowerment of every single employee. OPEX concentrates on the creation of value by eliminating waste, mastering complexity and reducing variation in manufacturing and office environments. To achieve this, OPEX has to center around people so as to ensure that processes are continuously improved. In daily work, this is always a fine line between doing the right things and balancing efficiency. This balancing act can only be executed under the guidance of true leadership – on corporate and individual level.

Implementation of OPEX at Nycomed/Takeda

Nycomed started with the aspiration to build up long-term OPEX skills in late 2008. The kick-off came with a "push" from top management via a case study to identify the potential of LeanSigma application to pharmaceutical manufacturing. A key success factor was to open employees' eyes to the need for change without upcoming changes being perceived as a threat. Right from the beginning, the objective was to launch a long-term umbrella initiative without branding it as a TPM, 5S or Visual Management project. It should be a holistic program, with a high level of involvement of different hierarchical levels. The general known LeanSigma methods should be continuously built in at every step of the overall initiative.

Nycomed chose a "Three waves to Operational Excellence" approach. At each deployment, a strong focus was set on the empowerment and training of the employees. After the "push" by the top management, the responsible team focused more and more on creating a "pull" initiative. By "pulling" topics and ideas from employees and business data, the workforce was made part of the development towards OPEX. Gained insights were then assessed and prioritized by the management, and teams empowered to make appropriate changes. In doing so, involved employees recognized that they were part of a larger team collaborating on a journey to OPEX. It was this trust in middle management and shop floor employees that made possible the change towards a real and sustained OPEX culture.

Nycomed started with the conscious implementation of LeanSigma by choosing representative sites (one solids/one liquids) and an OPEX core team of two persons. Wave 1 of 3 started with a value stream analysis, involving 10–15 Greenbelts, who were guided with full consultant support. Wave 2 was conducted in 2009, with a second value stream analysis involving another 10–15 Greenbelts as well as two OPEX experts. These experts were trained for a leading role on site level. For this wave, the value stream project was supported only by 50 % consultant attendance during the whole project time. In 2009, a central coaching team of experienced Master Blackbelts was recruited at corporate level. In 2010, wave 3 in the form of the third value stream project was conducted with another 10–15 Greenbelts as well as two further OPEX experts, both Blackbelts. Meanwhile, a further coaching of Blackbelts and a central coaching team of Master Blackbelts had become part of wave 3. In 2011, these Blackbelts worked together to establish a project portfolio of OPEX initiatives that drives Nycomed's plants towards functional performance

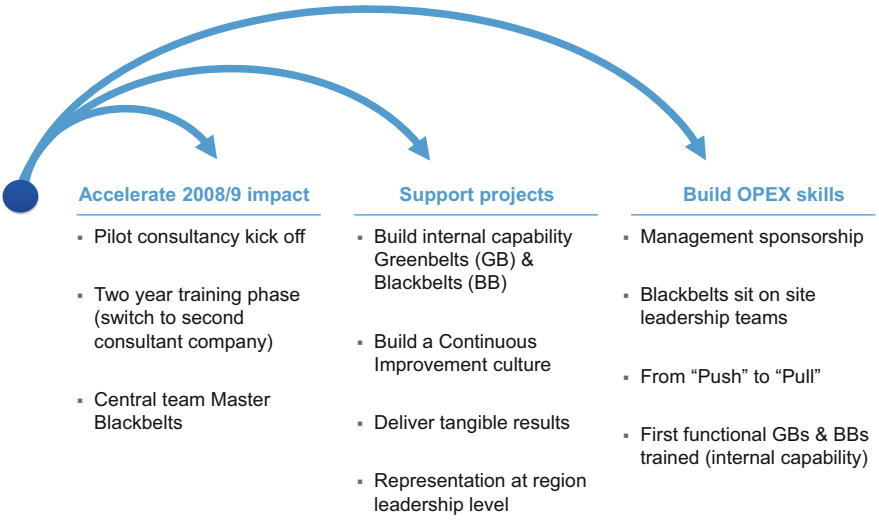


Fig. 26.1 Nycomed's OPEX roadmap (Source: Nycomed/Takeda)

and efficiency. Each defined activity was supported by a Master Blackbelt to reach the defined objectives and to ensure a sustainable implementation (Fig. 26.1).

Leadership and OPEX

> As we look ahead into the next century, leaders will be those who empower others
> Bill Gates

As described by Ancona (2013) from the Massachusetts Institute of Technology (MIT) Leadership Center, leadership moves away from a "command and control" model to a more "cultivate and coordinate" model. Leadership on company level depends for a good part on the strategy that has to be coordinated company-wide. In the case of OPEX, it is not only crucial how the OPEX initiative is organizationally embedded, but also how its leadership expresses on an individual level. These main "pillars", i.e. leadership on corporate and individual level, are described in following section.

Leadership on Corporate Level

At Nycomed, the OPEX program has always been part of strategic planning. It was designed as a long-term and non-market-driven program that gives high priority to employees on every hierarchical level. As the OPEX program is a company-wide initiative, the definition of the strategic plans needs to be easily understandable and

accessible. A long-term policy gives employees a vision of the to-be status, and directions towards it. A vision is important because it provides the motivation for people to leave behind current views and ways in order to allow for change. Perhaps most importantly, visioning makes it more salient to employees that their work is meaningful and important in contributing to overall objectives.

All employees, from shop floor to top management, need ambitious goals to achieve and to deliver tangible results. In the case of Nycomed, senior management has set such goals for each hierarchical level from the very beginning of the OPEX initiative. To measure improvements and to show the benefits of the new strategic direction, Nycomed has been using a holistic Key Performer Indicator (KPI) approach. It is key that it is transparent to employees how their work leads to improvements, and a set of meaningful measures, such as provided by a KPI approach, facilitates this. The adapted slogan "you can't manage what you can't see" refers to an implementation of a KPI system in which the top managements observes operational KPIs on the shop floor level; these shop floor level KPIs are then rolled upwards into management and business level KPIs.

Another key aspect in converting the methodological into an objective policy in form of an action plan is management commitment. This commitment is demonstrated by management presence on the shop floor. Employees have to see that the management is fully convinced of both the OPEX initiative as well as their abilities. Credibility throughout the company is very important for the sustainable implementation of OPEX.

Employee involvement, a further key aspect for a successful OPEX implementation, involves making workers feel appreciated and valued: True employee involvement is only possible when employees feel encouraged to be part of an OPEX initiative. One way to achieve this is to delegate responsibility to employees. Making people part of the program increases their motivation. However, it is also important to give employees the time necessary to work on the OPEX initiative. Top management has to provide a setting in which this is possible (Fig. 26.2).

Besides the strategic direction and the empowerment of employees, the organizational structure on company and site level is another factor of success for the sustainable implementation of an OPEX initiative. OPEX and continuous improvement require appropriate communication and information. All employees need to be informed and involved right from the start of the OPEX program. The top management needs to provide and support opportunities and platforms that allow for an exchange of opinions and ideas. This increases the understanding and acceptance of the OPEX program. To promote the exchange of knowledge, the best ideas should be made accessible to the whole company. As OPEX builds on people's ideas – utilizing facts and data for decision-making – it supports employees in developing better ways to do things. The objective is to make performance awareness part of the daily routine and to continuously improve the daily work. Therefore, employees should receive structured and professional training and support in order to reach specified qualifications.

In a global and networking-orientated company as Nycomed, the leadership of an OPEX initiative is not a solitary task – the ability to connect and build trusting relationships is a key competency. The central OPEX team, consisting of Master

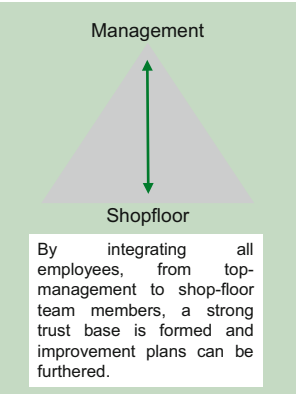


Fig. 26.2 Basic elements of an OPEX initiative (Adapted from Kondo 1998)

Blackbelts with at least 7 years of international work experience, does not stand alone but is part of regional and functional management teams. These teams are also responsible for coaching, training and mentoring other employees. Blackbelts at site are members of the management teams as well as coordinators of Greenbelts and Yellowbelts around active projects. This enables the development of key relationships within and across the sites of the network. The five Master Blackbelts in the core team and the one to three Blackbelts on every site use a collaborative platform and share their knowledge.

Leaders have to be able to sell the importance of an intensive change whilst showing that they understand the context in which teams are operating. This is only possible when leaders understand the details of the process they are part of. At Nycomed, the OPEX organization interacts with line management in a matrix. OPEX experts on site level are qualified as Blackbelts and work closely together with the functional line management and process owners. The central OPEX team, consisting of Master Blackbelts, coordinates the regional management teams. OPEX experts act as local coordinator of Greenbelts and Yellowbelts around the project execution. On-site level Greenbelts act as OPEX facilitators, and Yellowbelts as team members (see Fig. 26.3).

Leadership on Individual Level

While leaders try to create trust, optimism and harmony, they often earn anger, cynicism and conflict. Today, leaders need to possess more than general skills like assertiveness and strong communication skills. OPEX leaders need to be true change agents with empathy for the concerns and interests of other parties. This involves much more than the use of a set of basic tools or structures intended to keep change efforts under control (Kotter 2011). A certain level of emotional intelligence is required. This involves skills such as self-awareness (knowing

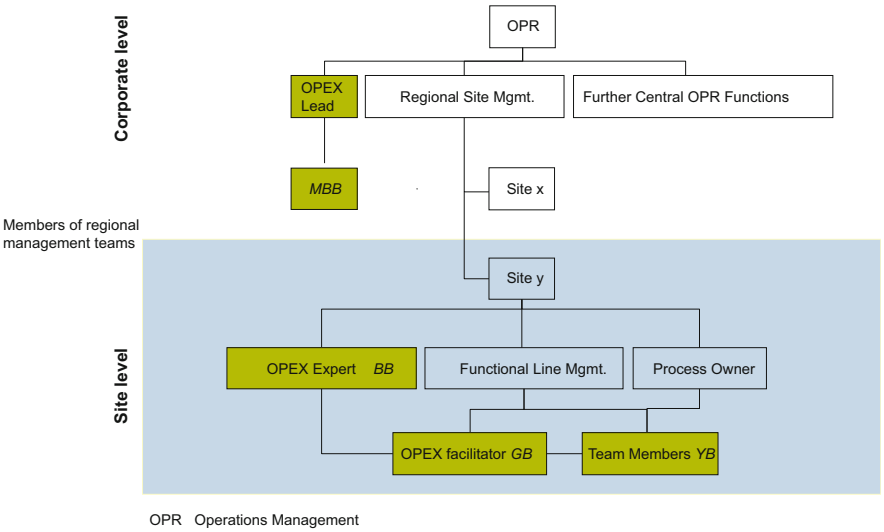


Fig. 26.3 Nycomed's organizational design (Source: Nycomed/Takeda)

one's strengths, weaknesses, and drives), self-regulation (controlling or redirecting disruptive impulses), motivation (relishing achievement for its own sake), empathy (understanding other people's emotional makeup), and social skills (building rapport with others) (Goleman 1998).

In times of increasing teamwork and the growing need to retain talents, also at Nycomed an eighth form of waste has been added to the classical seven types (see Chap. 18 "Matching Problems with Tools"): the underutilization of talent, clearly indicating the importance of the human factor (Liker 2004). Enabling employees (through structured and professional training), and making them part of an OPEX initiative (through employee responsibility) are key tasks of OPEX leaders.

Besides the more social orientated skills, technical skills are a further key priority to lead OPEX successfully. To get the commitment from employees, technical skills and process understanding are prerequisites. LeanSigma skills combined with the willingness to, and appreciation of, change are key ingredients to successfully lead an organization towards OPEX. Well-trained OPEX Blackbelts and Master Blackbelts, who are part of the team and the internal solution, can fulfill this prerequisite.

Only through close collaboration, OPEX leaders are able to choose their team according to their skills and help people to find their right place in the organization. Doing the right things without forcing them is a key rule. It is pulling and not pushing that leads an organization towards OPEX. Reflecting this way of working with the strategic planning of an OPEX program, objectives can be adjusted on an individual level and cultural aspects as well as geographical differences of a global company can be considered.

But at the end OPEX is also about results. OPEX leaders need to deliver results and make things happen (Ulrich 1968). To achieve this, leaders need to find a way

to get the right information from the organization to set the right (in the sense of explainable) priorities and objectives. This is needed for sustainable decisions and appropriate operational action plans. The "pull principle" at Nycomed was the right way to determine employees' needs while at the same time involving them. For resolute action plans, leaders need to take the responsibility and communicate their decisions in a "we" rather than "I" way. This ensures that the organization feels responsible and accountable because leaders talk and act according to employees' thinking (Drucker 2004). The OPEX core team at Nycomed has been able to translate strategy into action, and by doing so they have made changes happen. This has been possible by having a clear understanding of which key decisions have to be made by management, and what can and has to be delegated. This has made real team work possible.

Conclusion

> Leadership is lifting a person's vision to high sights, the raising of a person's performance to a higher standard, the building of a personality beyond its normal limitations.
> Peter Drucker

In times of necessary organizational change, leadership is a key success factor. Leadership is about knowing how to cope with changes while setting direction, aligning people and motivating others. It is about empowering the sites' employees to optimize existing production and functional processes (Kotter 2001; Ancona 2013).

OPEX at Nycomed was designed as a long-term and non-market-driven high priority program by the management, its leadership comprises understanding of how to create the conditions that motivate employees. To realize this vision, new ways of working have to be designed in a team. Visioning is a map of what could be, and sense-making creates a map of what is. Identifying which skills are required, drawing talents to the organization and ensuring that employees give their best are key abilities of a leading OPEX organization (Ulrich 1968).

Key principles for an OPEX leader are trust and sense creation, strong communication and the empowerment of employees in a network. But what distinguishes great from good leaders is emotional intelligence, a group of five skills that enable leaders to maximize their own and as well as their followers' performance. These skills are: self-awareness, self-regulation, motivation, empathy, and social skills (Goleman 1998). And very importantly, leadership involves constant development and a drive to improve capabilities (Ancona 2013). Leaders are learners and develop over time. They learn from success but also from failure, and from other managers and employees. Leadership is also a process that helps others to grow and develop. From an OPEX point of view, no process improvement ever ends. People need to be trained to start thinking in a continuous improvement mindset. This is enabled by OPEX leaders. The Nycomed OPEX core team on corporate level serves

as a competence centre for all pharmaceutical business areas in the Nycomed network. This helps to increase capability and core competences in all areas. The continuous optimization program for the Nycomed production network towards an OPEX organization is only possible with true leadership – on corporate and individual level!

References

Ancona D (2013) MIT leadership center: research. http://mitleadership.mit.edu/r-dlm.php. Accessed 15 Jan 2013

Drucker PF (2004) What makes an effective executive. Harv Bus Rev 82(6):58–63

Goleman D (1998) What makes a leader? Harv Bus Rev 76(6):93–102

Kondo Y (1998) Hoshin Kanri – a participative way of quality management in Japan. TQM Mag 10(6):425–431

Kotter J (1990) What leaders really do. Harv Bus Rev 68(3):103–111, reprinted in Harvard Business Review, December 2001:86–96

Kotter J (2011) Change management vs. change leadership – what's the difference? http://www.forbes.com/sites/johnkotter/2011/07/12/change-management-vs-change-leadership-whats-the-difference/. Accessed 14 Jan 2013

Liker J (2004) The Toyota way: fourteen management principles from the world's greatest manufacturer. Mcgraw-Hill Professional, New York

Nycomed/Takeda (2013). http://www.nycomed.com/products. Accessed 14 Jan 2013

Ulrich H (1968) Die Unternehmung als produktives soziales System: Grundlagen der allgemeinen Unternehmungslehre. Haupt, Bern

Chapter 27
Leading an Operational Excellence Program at a Geographic Area Level

Jürgen Werani

At the beginning of any Operational Excellence (OPEX) program it is of utmost importance to articulate (1) its purpose, i.e. the fundamental reason to launch such a program, and (2) its mission, i.e. the desired end state. It is also important to communicate how the purpose and mission of the program fit into the company's strategy and vision for its business development.

The following case study describes the Operational Excellence program of a global enterprise, from its infant days until it was eventually adjusted to meet upcoming requirements related to changes in the external environment. The case study also addresses challenges during this transformation. Although the selected case is taken from a globally acting enterprise, there are many elements that are relevant for any company, irrespective of type and size.

The fundamental reason to launch the OPEX program in this case was the relentless focus on Process and Product Quality.

Embedding an OPEX Program Structure in an Existing Organization

Generally there are several options to design a manufacturing organization in a globally operating enterprise. It could be by geography, e.g., Europe, Asia, Americas, by technology, e.g., Biologics, APIs, Solids, etc., by business units, e.g., patent protected products, off-patent products, consumer health care, or by markets, e.g., mature vs. developing markets.

For launching the global Operational Excellence program at this company, the OPEX program organization was embedded in the existing and well-established manufacturing organization, following a geographical set-up with five geographic

J. Werani (✉)
Schuh & Co. Complexity Management AG, St.Gallen, Switzerland
e-mail: juergen.werani@schuh-group.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_27,

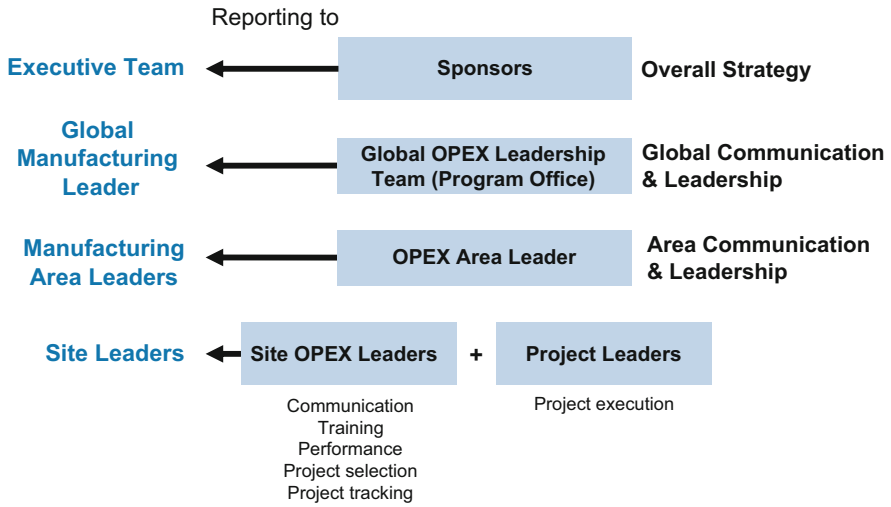


Fig. 27.1 The OPEX organization during the program

areas, as this was considered to better support a fast start of the program and to avoid any disruption due to upfront organizational changes. The size of the OPEX program team was deliberately kept small with six executive members, to guarantee fast decision-making, agility and flexibility (Fig. 27.1).

The OPEX program leadership team reported to a global steering committee, which acted as a sponsor and mentor, and consisted of several leaders of the global manufacturing organization. Each OPEX leader reported to the respective geographic area leader of manufacturing and was a permanent member of that leadership team, together with the HR leader and the regional site leaders. This way it was ensured that the OPEX leader was part of the strategic decision-making process. For each manufacturing site in the geographic area an OPEX champion was nominated. The champion was part of the site leadership team, reporting to the site leader. He deliberately did not report to the OPEX area leader to make the site leader responsible for the execution of the program. The site leader and the OPEX champion had OPEX objectives, and their performance was measured against these.

The OPEX area leader was given clear accountability for the success of the Operational Excellence program and was responsible for the architecture of the program, as well as for establishing and supporting a culture of continuous improvement (assets, quality, process flow and leadership). He provided leadership and direction for the program within his area of responsibility.

The OPEX area leader focused the organization on aligning activities and resources with value creation, though none of the resources (assets or people) actually reported directly to the OPEX area leader. He had to work cooperatively with the site OPEX champion and other functional leaders to promote the program, and had to be relentless about continuous improvement. The role of the function was to provide the resources required to achieve the Operational Excellence objectives as defined by the company's vision and mission elements.

The OPEX area leader led by influencing a matrix organization, and thus had to be equally effective as he would have had to be in a functionally operating organization with direct reporting lines. The challenge of such a leadership role is to avoid what are common problems of matrix organizations, that is lack of clear roles and responsibilities, accountability and effective decision-making.

The OPEX area leader was responsible for performance with respect to assets, quality, and product flow and provided leadership for the respective area. His objectives were:

- Provide and develop Six Sigma training material and courses
- Continuously develop other methods and tools to support OPEX
- Drive and own the Six Sigma/Lean behaviour and actions within the global organization
- Ensure that the OPEX program adheres to site and global governance guidelines
- Monitor performance of the program
- Provide leadership for the program and act as a role model
- Ensure development of future state value stream maps
- Act as custodian for networking and communication
- Be a mentor, coach and change agent

The OPEX Champion was responsible for establishing an environment (processes, KPIs, objectives, reporting and systems) that would raise the awareness for OPEX, and to change attitudes towards new thinking, new working and new leading. In particular, the OPEX champion was responsible for providing training in OPEX methods and tools (Six Sigma and Lean as well as Leadership skills) to foster OPEX behavior in the day-to-day business. His main responsibility was to:

- Maintain a close cooperation with the site leader and the OPEX area leader
- Put all means of training measures into practice
- Support, train and coach employees and project leaders in defining improvement projects and putting sustainable improvement measures into action
- Ensure that all administrative and technical processes are safe, add value and deliver the required quality products

The mission of the OPEX champion was completed when the ability "learning to see" (Rother et al. 1999), e.g., how to address adverse challenges and how to continuously eliminate waste, was deeply embedded in everybody's mind and applied in day-to-day business.

Influencing Skills and Behaviors

Influencing encompasses two capabilities which are essential to lead the OPEX program: persuading and negotiating. Persuading involves being able to convince others and implement appropriate actions, while negotiating involves the capability to discuss and reach mutually satisfactory alignments. The OPEX area leaders were

aware that they could not simply tell the site leaders what to do and how to do it, in order to drive the program through the transition phase. They had to change their attitudes, beliefs, ways of thinking and working, i.e. their behaviors, without using the power of authority. They had to act as advisors, coaches and consultants. Strong interpersonal and communication skills largely impacted the OPEX area leaders' ability to interact with site leaders, to appeal to them, and to gain their attention and commitment.

Influencing had four dimensions in the game of change:

- Working outside the office when travelling
- Working across cultures, with no or little common understanding
- Accepting change where buy-in was key to success
- Overcoming hierarchical organizational structures and barriers within the global manufacturing organization to foster thinking outside of the box and creating room for new ideas to be further explored

The question came up where the global team should be located: at headquarters or in their respective geographic areas. On the one hand, keeping the office at headquarters is advantageous as it allows the team to be close to where strategies are developed and decisions are made, while it has the disadvantage of the OPEX team being far away from the sites. Having the office located in the respective geographic area, on the other hand, has the obvious advantage of being close to the sites where the program is implemented.

The team believed that there was no way to lead such a program remotely, and decided to have the OPEX program leaders located in their respective geography. Particularly at the beginning of this program, it was felt that personal interaction and face-to-face meetings would pay off, although travel costs back to headquarters had to be balanced.

Although the OPEX program leaders in each area made good overall progress, it turned out that some sites progressed faster than others. Differences were analyzed and found to be linked to culture. Therefore, an assessment was designed that all sites had to go through, addressing eight parameters: inertia, culture, corporate commitment and support, management commitment, structure, people, process, integration. The results of the assessment showed that only a few sites scored high for all factors, while the majority was good or excellent at one or the other, providing useful benchmarks. Finally, it was the site leader's responsibility to benchmark the good practice and copy it.

Results of this cultural assessment and why some sites were performing better than others have been reported in Friedli et al. (2010).

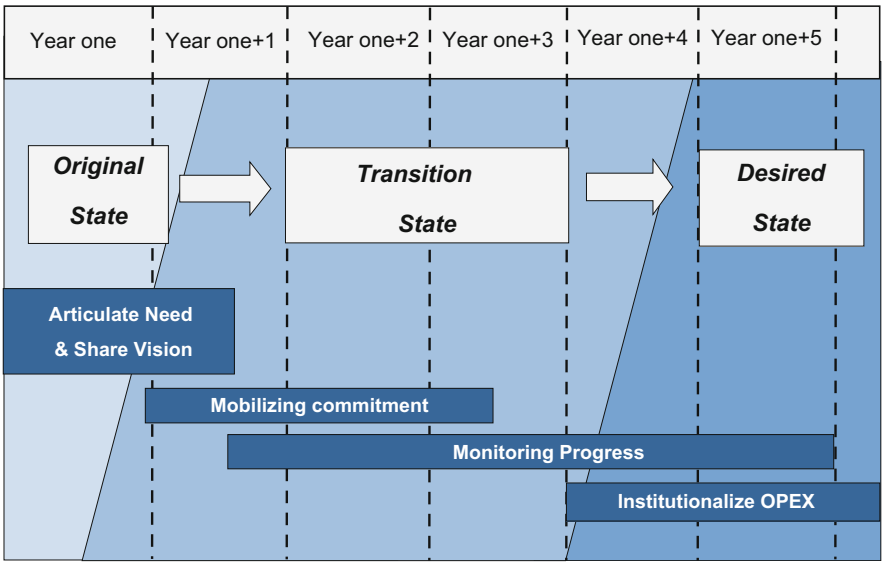


Fig. 27.2 Projected phases of OPEX

The Program Execution

The program was initially designed to achieve the desired end state within 6 years, with the global OPEX team taking the lead for the change. The first year's focus of attention was to articulate the need and to share the purpose and to define the mission of the program. In the transition state, the focus was all about mobilizing the commitment and monitoring the progress (Fig. 27.2).

Originally, the OPEX program was focused on Quality (Right First Time). At the beginning of the program, this was the right approach: addressing any quality-related deviation using the Six Sigma methodology as the standard tool for root cause analysis. Training in Six Sigma methodology (Yellow Belt, Green Belt, Black Belt) and applying Six Sigma tools went hand in hand with successfully completing projects as part of the learning experience. Standardization of training modules was found to be important, as only the strict use of standardized training materials provided one common "Six Sigma language". The standardization of the training programm was one of the first tasks of the global OPEX leadership team.

Of course, this OPEX program was a major change management journey, and during the transition state the OPEX leaders applied five key principles:

- Competencies and skills: knowledge and capabilities that enabled the colleagues to be effective leaders.

  The initial focus was to ensure that colleagues were trained in the OPEX program methodology and would apply it correctly and consistently. Making progress with successfully completed projects was important to share best

practices and successes, as well as to share lessons learned and failures. It demonstrated that the passion for root cause analysis is the core of OPEX. During this part, the role of the OPEX leaders focused on mentoring teams using OPEX tools and encouraging them to improve their OPEX skills.

- Performance: summarized the way the company produced quality products, safely, on time, and at optimized cost.

  Performance was measurable; the sites understood what was important to business and developed meaningful measurements. The processes were in control and the organization continuously improved product-based process capability. Employees were aligned with the business – the good company performance pushed the business further forward. To achieve this, everybody was trained in root cause analysis to ensure sustainable process improvements and avoid quick fixes. To just meet compliance requirements was not enough, it was adding value that was the driving passion for each of the company's actions.
- Systems: comprised the way in which the organization functioned as a whole as all individuals are interrelated with each other, at both business and personal levels.

  All outputs were considered as someone else's inputs and thus had to be Right First Time in order to allow colleagues to get their outputs Right First Time, too. Everybody in the organization had an understanding of how the various elements were linked to the bigger picture. Systems have different categories, e.g., people, equipment, measurement, process, materials and environment, and all of them were considered when analyzing issues.
- Organization: roles, skills and objectives were aligned in a way that facilitated the successful implementation of an OPEX approach to everything the employees did.

  The OPEX leaders ensured that each site had a clear OPEX strategy that supported the company's mission and vision. The OPEX leadership team was responsible for putting the OPEX strategy into action and for monitoring progress. Sharing of good practices was encouraged within and between sites. There was a shift in focus from non-value-added activities such as inspection and historical reporting, to proactive and predictive activities. The organization was adaptable, willing and able to embrace new science-based technologies and methodologies. The sponsors were committed to allocating resources and time to support a proactive approach to process improvement and problem solving.
- Shared mindset: a common set of values and beliefs that link people within an organization to a common mental framework and influences their thinking, actions and emotional bonding to the organization.

  Everybody took personal responsibility for their work, everybody was accountable for their performance, constantly seeking ways to improve. The new thinking was expanded to actively seek process improvements rather than improvements being dictated by perceived constraints of internal or regulatory nature. Instead of relying on opinions and past experiences, decisions were based on data. The commitment to OPEX was visibly demonstrated at all levels of the

organization. A common language was used and a common understanding of OPEX demonstrated. Internal and external customer needs and expectations were considered in the day-to-day business.

The desired end state was defined by five mission elements:

- Performance: using metrics, KPIs, and process capability indices; open mindset and willingness to share results, facts and figures
- Process understanding: understanding the variation and dynamics of processes through root cause analysis by means of Six Sigma and PAT
- Culture: understanding and following defined new values, leader behaviors, new ways of working, new ways of thinking and new ways of leading and communicating
- Paradigm shift: understanding the rationale of moving from empiric knowledge to manufacturing science about products and processes as well as using risk assessments
- Organization: introducing a co-development process as well as the integration of API in drug product manufacturing

Project Tracking: i-nexus

With increasing numbers of successfully completed projects and active Green and Black Belt projects, monitoring the progress of the concurrent projects became a challenge for both leaders and project managers. It was then when the global OPEX team had to look into a suitable tool for project tracking. The OPEX leadership team had chosen i-nexus, because it ensured the consistent application of Six Sigma methodology, was readily accessible, provided a clear reporting structure, facilitated project review and coaching, and last but not least could be used to leverage knowledge and best practices globally.

The i-nexus tool served the project leaders, process owners, project sponsors, OPEX champions and area OPEX leaders in the same way. Project leaders got a tool to create projects based on the Six Sigma methodology templates, to share their project plans and to produce deliverables and project documentation reports. The project owners got the opportunity to electronically review and authorize projects plus automated notifications of deviations in the schedules as well as risk exceptions. The project sponsors got a tool for real-time visibility of deployment status and resource utilization. The OPEX champions and OPEX area leaders were able to define best practices once the repository was filled with a good number of projects, and they were in the position to manage resources for the OPEX program.

As a matter of fact, there was also the idea to use the i-nexus project repository as a data base for knowledge sharing – it could have provided an internal search platform like Google. However, no matter what efforts the area leaders made, this idea of using i-nexus as a searching platform hardly took off, because of the reluctance to accept the ideas of others. Hence, the leaders searched for other

ways to share the growing knowledge base. Another attempt was made later in the process with the introduction of Communities of Practice (CoP).

Process Analytical Technology (PAT)

Process Analytical Technology, defined by the FDA September 2004 as "A process for designing, analyzing, and controlling manufacturing through timely measurements (i.e. during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality", seemed to fit the purpose of the OPEX program (Guidance for Industry). The OPEX leadership team saw PAT as an opportunity to further enhance their program – its concept based on facts and figures was in line with the Six Sigma methodology. It provides process and product data through off-line, at-line and/or in-line (real time) measurements.

In this context, "analytical" was viewed broadly to include chemical, physical, and microbiological data, as well as risk analyses conducted in an integrated manner; however, it focused on the process and not on the product. Process Analytical Technology was considered as a tool, and not as a goal in its own right. Hence, it was complementary to the OPEX program. However, the global OPEX program team was not the owner of the PAT initiative, which was owned by a Technology and Innovation team. The challenge and task for the global OPEX team was to sell PAT to the site leaders and liaise with the Technology and Innovation team for alignment.

The link between PAT and the OPEX program was defined by the following objectives of the PAT initiative:

- Monitor multiple parameters to enhance process knowledge
- Determine Critical to Quality (CTQ) process parameters
- Determine CTQ attributes of input materials
- Use root cause analysis to remove sources of unwanted variation in CTQ parameters and attributes
- Use direct feedback control to reduce variability in CTQ parameters and attributes where possible
- Stop monitoring non critical parameters

In the context of OPEX, PAT served as a source of information in terms of facts and figures for any root cause analysis or product and process improvement projects.

An additional challenge was to convince the site leaders to place PAT investments in their annual budget, as there was no compelling short-term argument regarding an immediate return on investment. Thus, the OPEX leader had to use influencing skills, supported by the global and area manufacturing leadership team. The demand for new ways of thinking, new ways of working and new ways of

leading was stretched. Short-term thinking had to be rebutted with bold and hard arguments, in order to open the mindset for PAT as sustainable long-term benefit.

So far, the project pipeline had been filled with projects from the Six Sigma trainings and sporadic quality deviations. However, this approach led to isolated improvements and neglected the focus on the optimization of a value stream or product family. As a consequence, limited benefits in the effectiveness and productivity of operations were observed.

Product-Based Process Capability

Following the Six Sigma approach, the global OPEX team introduced the methodology of product-based process capability. Product-based capability metric is a comprehensive measure of the effectiveness of a process that lays the foundation for efficiency improvement. Historically, process capability was used by some companies in the context of Annual Product reviews. In 2003, the FDA science-based GMP guidance for the twenty-first century identified process capability as a means of demonstrating process understanding. A process capability demonstration project was initiated to build on the previous experience with the use of Six Sigma tools. To broaden the scope of the product-based process capability the complete process chain from API intermediate through API and drug product to primary packaging was included. Two pilot products were chosen for this process capability demonstration project, specifically to determine the different challenges for high and low volume established products. As a result of these two pilot studies, a guidance document was issued, which served as a standard method for the deployment of product-based capability studies and was further expanded to equipment-based process capability.

Co-Development

Once the product-based capability approach was established, it was realized that such an approach was not really Right First Time: instead of adding value, resources were wasted on mistakes that could have been fixed earlier in the process, when products emerged from development into commercial production.

The problem, though, was that in the early development the fact and data base was very thin, simply because only a few batches had yet been produced in full scale. Nevertheless, many of the activities associated with product-based capability, such as defining critical to quality (CTQ) attributes for product and process with corresponding risk assessments to verify these assumptions, can be defined in early stages of scaling up. When these issues came up, the strategy of Quality by Design (QbD) was born. This was the perfect fit to the OPEX program; to get the task completed was not a technical challenge, but rather an issue of managing across

functions and different areas of responsibility – a challenge for a matrix organization. The result, though, was brilliant and a so-called co-development process was established during the transition state of the OPEX program.

Agility (Lean Manufacturing)

Almost at the end of the transition state, after having established product- and equipment-based capability studies, the OPEX program further progressed into the direction of Lean manufacturing to focus on value-added activities, creating continuous flow.

Value Stream Analysis is an approach to data capture and analysis, and to the implementation of effective change within cross-functional or cross-company processes required to achieve a truly Lean enterprise. The OPEX area leaders put together a training program following insights from the global Six Sigma training. Similar to the product-based product capability work-stream, a pilot program was launched. Unlike in Six Sigma training, the Lean training started with the global manufacturing leadership team and was then cascaded down in the organization, getting broader and more specific. To demonstrate the benefit of the Lean methods and tools, the OPEX area leaders developed a simulation game serving as a backbone for the training.

More details on the training concept can be found in Werani et al. (2010).

Communities of Practice (CoP)

The organization failed to take advantage of the knowledge repository provided in the i-nexus data base to build communities of practice for the purpose of knowledge management, and was therefore looking for another solution: Communities of practice (CoP).

Communities of practice are groups of people who share a concern or a passion for something they do, and engage in a process of collective learning in a shared domain of a human endeavor. Their objective is to learn how to improve their practice by regularly interacting with each other.

CoPs' scientific background lies in explicit and tacit knowledge. Explicit knowledge is easier to replicate than tacit knowledge; it also is easier to document and to share, but accounts for only 20 % of the knowledge pool. Tacit knowledge, in contrast, is harder to articulate and to transfer, but leads to a competitive advantage and enhances competencies. It makes up 80 % of the knowledge pool (Nonaka 1991).

Based on common business interests – such as PAT, value stream analysis or product-based process capability – the OPEX leaders thus formed CoPs. They saw a big advantage in establishing CoPs with regards to orchestrating knowledge

management, moving knowledge from Push to Pull and eliminating the feeling of isolation. However, they were aware of the challenges and limitations associated with this commitment to being open to others' ideas and having to travel for joint meetings. After the launch of the CoPs, it seemed that accepting ideas from others was not an issue anymore; yet, they were stopped because of the huge travel cost associated with the regular meetings which had to be organized to keep the momentum. The concern of knowledge management still was not resolved.

Communication

Once the OPEX program/organization was established, a major task arose at the passage from the first state into the transition state: communicating and sharing knowledge and best practice among employees of one site and between sites in the network. The responsibility for this task was shared by the OPEX champions and the OPEX area leaders.

Area OPEX meetings were held on a biannual basis, with participation of all site leaders, OPEX site champions, sponsors and stakeholders and the OPEX leadership team. The purpose of these events was to raise the awareness and motivation of the OPEX community and to get a buy-in from the laggards. Most important, however, was to foster a mutual understanding, to build relationships and to share knowledge. The meetings featured invited guest speakers on various themes, presentations of best practices or special projects by selected OPEX champions, and in particular OPEX progress in the context of the business development. These events were extremely interactive with lots of opportunities to practice teambuilding.

For the same purpose, the same type of event was organized in between global OPEX meetings. Less costly but highly effective local events were organized and led by site leaders, e.g., OPEX market places demonstrating achievements and best practices. Often, these events were organized in connection with budget review meetings or regular site visits from executives.

In addition to events, other means of communication were widely used to share best practice or results of pilot and special projects, such as global and site newsletters, OPEX-specific intranet platforms, brochures and posters (Fig. 27.3).

Outlook

At the end of the transition state and beginning of the desired state, methods and tools had been broadly established (Fig. 27.4). The methods and tools were the enablers to support the OPEX Strategy:

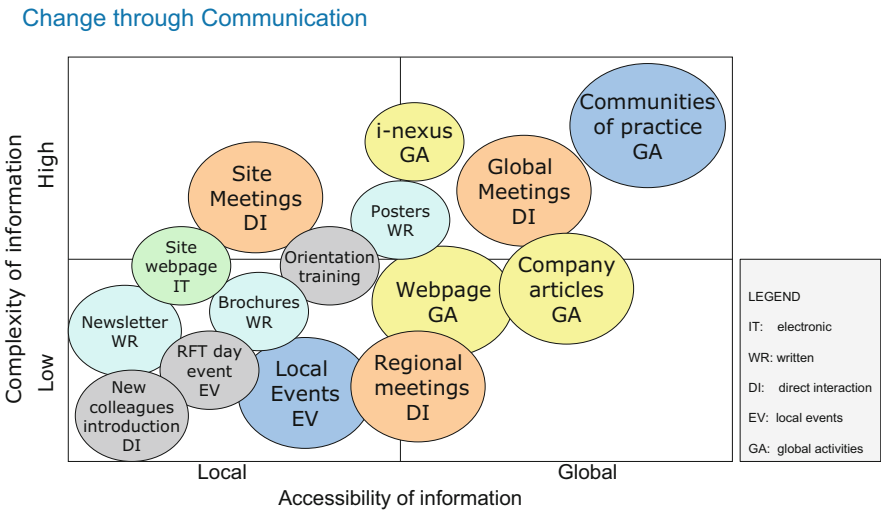


Fig. 27.3 Means of communication

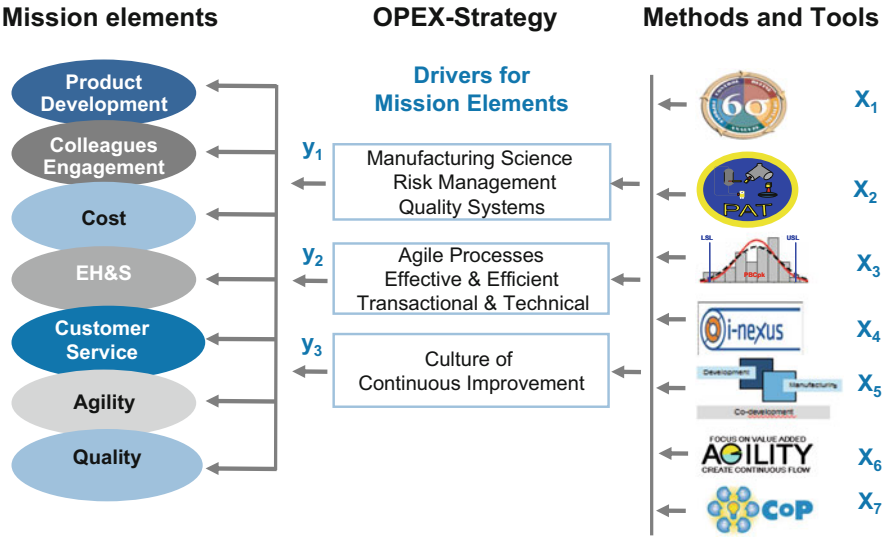


Fig. 27.4 Positioning OPEX

- Manufacturing Science, Risk Management and Quality Systems
- Agile Processes, effective and efficient for all transactional and technical processes under a holistic perspective
- Culture of Continuous Improvement

The drivers of the OPEX strategy impacted the program's seven mission elements and the progress of the OPEX program was measured against those drivers which represented the KPIs. The performance against the KPIs were on the agenda of every site leader, the OPEX champion, the OPEX area leader and all executives over several years. This way, the momentum of the program was kept and integrated into the day-to-day business. Leading with KPIs, however, was not enough. All means of communication practice served to continually remind of the program's purpose and the changes the company aspired to achieve.

After 6 years, once the methods and tools of Lean had been trained, the program further developed from the original focus on Quality (Right First Time) without leaving this intention into the direction of Lean.

This progress towards Lean was influenced by changes in the pharmaceutical industry: slowdown of industry pace, decline in new product approvals, no attractive return on R&D investment, and growing off-patent sales. These changes created new business realities, triggered by severe pressure on revenues and margins, increasing volatility of demand, growing product portfolio complexity, growing technological complexity, more stringent and complex regulatory requirements and the need for improved utilization, efficiency and flexibility. In addressing the business challenges, the pharmaceutical companies developed various strategies to optimize research productivity, to find new opportunities for established products, to address growth in emerging markets, to invest into complementary business, and to focus on innovation and a culture of continuous improvement.

Many companies addressed the business challenges and changed their global manufacturing organization to be better aligned with the business and promising a faster decision-making. As such, OPEX became part of cross-business transformation teams. This way, the OPEX organization was complementary to other teams, for example Lean and Agile or Technology and Innovation. The transformation teams were newly managed across global manufacturing, and their prioritization was based on urgent business needs with a very close alignment to the business.

Summary

The OPEX program was executed in three main waves:

The first wave addressed product and process robustness of established products associated with

- Black Belt, Green Belt and Yellow Belt training
- A retrospective approach, giving first-hand confidence in quality and reliability
- A proactive approach, predicting future quality through product process capability studies
- Securing process robustness as prerequisite for Lean implementation

The second wave addressed the application of Lean principles through

- Applying principles for optimization
- Using Lean methods of optimization to put strategy into action
- Maintaining verified, stable and robust manufacturing processes

The third wave seamlessly extended the process robustness of established products to products emerging from development by means of

- Design for Six Sigma (design it right)
- Product and process capability studies

To continuously maintain the momentum for such an OPEX program, and to become an OPEX-driven organization, it is important to

- Recognize that culture change requires determination and a great deal of patience
- Keep in mind that the process of making OPEX a permanent part of the business is long and unglamorous
- Acknowledge that there are no shortcuts
- Continue to monitor process quality and robustness at every level of the organization

Problem solving and Lean are integrated and embedded in the daily work and not a distinct topic on someone's personal agenda. Therefore, leaders with direct day-to-day responsibility for manufacturing areas must become coaches and teachers in supporting the operation. However, they have to adapt to their new roles, which means supporting colleagues in learning by doing, applying problem solving tools and fostering the process of continuous improvement. If these leaders make OPEX part of the daily work, OPEX gets reinforced and used every day and the OPEX leaders will have fulfilled their mission. The OPEX organization is still in place, although it has now been adopted to face new challenges and changed business needs.

References

Friedli Th, Gronauer Th, Werani J (2010) In search of key influencing factors. In: Pathway to operational excellence in the pharmaceutical industry, overcoming the internal inertia, Ed.-Cantor-Verlag

Guidance for Industry. PAT – A framework for innovative pharmaceutical development, manufacturing, and quality assurance. FDA, Sept 2004, p 4

Nonaka I (1991) The knowledge creating company. Harv Bus Rev 69(Nov–Dec):96–104

Rother M, Shook J, Womack J, Jones D (1999) Learning to see: value stream mapping to add value and eliminate MUDA, Lean Enterprise Institute, US

Werani J, Bellando-Randone G, Goetzfried M (2010) Making operational excellence work – training and coaching supporting behavioral change. In: Pathway to operational excellence in the pharmaceutical industry, overcoming the internal inertia, Ed.-Cantor-Verlag

Chapter 28
Continuous Improvement: A Path Towards Excellence

Kim Sandell, Jesper Eriksson, Karin Eriksson, Maria Stigell Warnström, and Kirsti Gjellan

The Pfizer Strängnäs Site. The Pfizer facility in Strängnäs, Sweden, has been producing large molecule biotech products since the mid 1980s. Today, the plant is a flexible multi-product facility with state-of-the-art platform technology.

The site has a unique position within the corporation, being one of only a few that manufacture active pharmaceutical ingredients with biotechnological processes.

So far, the site only works with internal corporate supply and has four different customers to supply with active pharmaceutical ingredients (API). The APIs produced are transformed to usable drugs by the customers. The drugs are distributed worldwide with the largest sales in the EU, Canada, Japan and USA.

Site Leader Reflections and Introduction to the Strängnäs Transformational Journey Through the Continuous Improvement Pathway

For decades, the Strängnäs culture has had a strong foundation by having a strong collective and loyal approach – people strongly care about each other and the products they produce. In addition, the Strängnäs culture is characterized by its exceptional problem-solving spirit; people easily get together to correct and prevent problems. Together, these two factors formed a crucial basis when the transformation started. We built on already strong and positive elements when it came to kick-off the continuous improvement focus. **Our first conclusion thus is** "Do not throw the baby out with the bath-water"; build on the strengths that are already existent within the organization.

K. Sandell (✉) • J. Eriksson • K. Eriksson • M.S. Warnström • K. Gjellan
Pfizer, Strängnäs, Sweden
e-mail: kim.sandell@pfizer.com; jesper.eriksson@pfizer.com; karin.eriksson@pfizer.com; maria.stigell-warnstrom@pfizer.com; kirsti.gjellan@pfizer.com

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_28,

Getting from 1 implemented improvement per year and employee to 24 in only 5 years is telling regarding the rise in energy that a CI culture generates, driven by the fact that an implemented improvement makes every-day work life easier for individuals and teams, within the framework of safety and quality principles. The mandate and trust given to every employee with the CI targets was an important extension, fostering the already present engagement in improving and correcting our operations. The challenge was to get people to document their CIs, which leads us to our **second conclusion, "keep it simple"**.

However, we could not have started this transformational journey in which everyone is involved in improving and building new capabilities without a true sense of urgency (Why and What). Kotter (2008) describes in his book *A sense of Urgency* how "A real sense of urgency is a highly positive and highly focused force." (Kotter 2008, p. 8). He also emphasizes that a successful burning platform strategy "aims at the heart as well as the mind of people" and it is "focused externally on the important issues" (Kotter 2008, p. 44). So when the site's burning platform was built in close relationship with the customer interface, it was both headed towards increased competitiveness (decrease costs by 50 % in 5 years) as well as the opportunity to gain market share by increased productivity and by that serving more patients.

The burning platform was also so challenging in that it demanded new ways of working – in order to take steps towards the goal, we needed to collaborate cross-functionally in the product flow. Kotter (2008) describes in his book eight different elements of creating change where creating a sense of urgency is number one; after this comes the guiding team, visions and strategies, communication, empowerment, short term wins, never letting go and making change stick. All of these elements are equally important to make the transformation happen. **Thus, our third conclusion is to focus on the trust, courage and energy towards a direction/burning platform that joins people, functions and supporting groups and makes them collaborate, because that is the only way to reach the targets.**

Our last and most important conclusion concerns the power of people and the leadership required. As leaders on this transformational journey we had to provide trust, guidance and inspiration to make change happen. We had to focus on the Why and What (shaping the future) in every communication and by that involve all colleagues in creating the How.

By focusing on Why and What, we stopped asking for results as we realized that asking for results only gives you what you ask for, but does not uncover the true potential every colleague has. We also learned that trust is everything, and that control is a true waste of human capability. The results achieved so far are beyond expectation, generating more control over daily operations than ever, because we view every problem as an opportunity to improve and to remove waste from the value chain. In our culture, we today appreciate not having metrics on green lights all the time; a stretched target means that metrics will be yellow and red, too.

Our challenge now is to keep the high energy and to continue doing things we used to consider impossible in the past. Kotter (2008) describes the risk of *Complacency and false urgency*. To keep a meaningful sense of urgency demands of us to

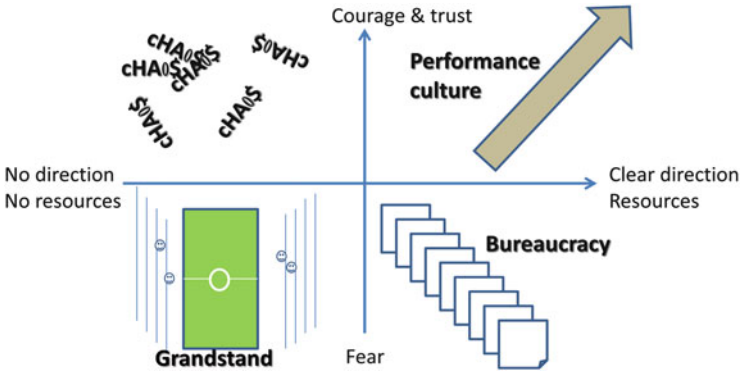


Fig. 28.1 Model explaining the importance of *courage* & *trust* and *clear direction/resources*. If there is no direction/no resources, the organization either ends up with a grandstand culture where people are waiting for things to happen (fear), or if the courage/trust is high, chaos is the result. If there is a clear direction/resources, a performance culture can be obtained if there is a high degree of courage and trust; however, if the organization is driven by fear, bureaucracy will be the result

continue to create our future and to move the targets forward in a stretching and aspirational way – everyday. Site leader and Site Leadership Team have to make sure that, through any storm of challenges, we do not lose sight of where we are heading and build a solid base for the future, in an inspiring way that engages the whole crew. My role is also to make sure that we create opportunities to develop people in the spirit of the sense of urgency and that we make great business on this journey.

Method Development: Building a Site Method

Learning from Mistakes and Building on Things That Work: Continuous Improvements as a Driver for Engagement

In what way can a focus on continuous improvements (CI) affect the transformation of a culture?

The Strängnäs site has adopted a model presented by Åslund (2001), which is based on the assumption that two components are required to reach a performance culture. The first component, courage & trust, is about letting go of the control and pushing mandate from managers out in the organization. The second component, direction/resources, is about giving direction to unleash the engagement obtained in the courage & trust dimension (Fig. 28.1).

The courage & trust axis is the most important, but also the most difficult one, since it means reaching the heart of people, i.e. it is not enough to fling out tools into the organization and to then demand the use of them. Instead, the demand has to come

from the employees working in the processes. For the management, this means that the focus has to move from control to guidance, from focusing on "how" to create systems for using the energy of employees to improve the business. A continuous improvement culture is an important contributor to the courage & trust component, because it is one way to transfer the responsibility from managers to all employees, encouraging and enabling the people who know processes best to initialize their improvement.

The direction/resources component is important to channel and coordinate improvements in order to make people strive for the same objective: understanding why they are doing what they are doing, and visualizing the future in a compelling way.

To facilitate the transformation towards a performance culture, different toolboxes could be used in maximizing the quality and pacing improvements. Examples of toolboxes are: innovation and creativity tools, Six Sigma (problem solving and reduction of variation), Lean (work smarter), Human Error Reduction, 7 Habits (Covey 2004) (a way of moving towards a synergistic approach, both at individual and organizational level) etc. However, at an organizational level the focus should not be on the tools (the "how"), but on the "why", "what", and "who".

Our Journey

The first real OPEX initiative was started in the beginning of 2000, when the site organization was changed to self-steering teams. This meant that the teams were responsible for almost everything without having a holistic overview. The result was failure! There were several reasons: too much responsibility was put on the teams, there was no burning platform (i.e. there was no driver for the change), changes were not tested and implemented too fast, new silos were formed etc.

Six Sigma: The next OPEX initiative was the Pfizer-rollout of the Six Sigma methodology (cf. Chap. 8). The site had its first black belt in 2005, and one site goal was that all employees should at least have the Method 1 training. In the beginning, the number of projects was measured, which led to a multitude of completed projects concerned with all sorts of problems, hiding the true power of the Six Sigma. It turned out that the problem was that all improvements were done under a Six Sigma umbrella instead of using Six Sigma for problem-solving and reduction of variation. However, the initiative continued and peaked in 2008 with 100 % of employees having been trained as Yellow Belts, 10 % being greenbelt-trained and 1 % of all employees being Black Belts. A combination of different factors caused the Six Sigma initiative to go on hold: (i) a lack in seeing the purpose of using the tools, (ii) a stop in measuring the usage as well as (iii) a total focus on the startup of a new facility and the process-fitting of two new processes. Six Sigma had been perceived as something used in the "spare time", and now there was no more spare time.

Small Improvements: During the startup of a new facility in 2009, a lot of problems were identified. This was the perfect setup for focusing on small

continuous improvements. The power of small continuous improvements is that it is very easy to relate to them, i.e. "if you have a problem, fix it". The result was that people started to take more responsibility. The approach was to focus on small improvements without any complicated systems, rewards, or definitions. After a couple of years, continuous improvement had become integrated in everyday work. A CI network was established at the site, with representatives from each department. Due to the improvement mindset, the Strängnäs site took less than 5 years to go from one implemented improvement per employee per year to over 24 implemented improvements per employee per year.

Lean: As Lean was rolled out in 2010, we started to apply these tools and set up various projects. Currently, 12 employees are being educated in Lean tools. Employees have started to realize the meaning of waste, which gave the site confidence that is possible to do "impossible things".

The Future Trip: In 2010, a major breakthrough occurred when 10 % of the colleagues were selected and assigned part-time roles as change agents with four focus areas. Suddenly, the number of people working regularly on Operational Excellence had increased fivefold! The cross-functional teams had members from all departments and levels, and they worked on how to improve the Strängnäs site to realize our vision of becoming a world-leading biotech supplier. The Future Trip is still running, and to date about 25 % of the colleagues are involved in building the future of the site.

Hoshin Kanri Business Plan: In 2012, the Hoshin Kanri concept was introduced for the business planning process (inspired by Dennis 2010). This meant that the direction became clearer and the connection between everyday work and improvements was visualized. Also in 2012, the site based its business plan on the voice of customers, which in our case became a burning platform, making it easier to get a buy-in for why we had to do things differently.

Go-with-the-flow: One result from the "Future Trip" is a proposed new way of working together in a product flow-oriented way, meaning that we work production-focused in cross-functional teams. The benefits of this are reduction of non-value added work, and incorporating quality in production (Modig and Ålström 2012).

Continuous Improvements: What Is Working for Our Site and What Turned Out Not to?

The New System: Power to the People!

The continuous improvement system used at the Strängnäs site is based on the theory that small improvements are an effective way to start improving the business (Östberg et al. 2010). The pros of small improvements are that they are easy to implement, i.e. since they are small there is no need for complex systems and

approval loops. Often, the improvements are done by a colleague or a team that directly benefits from the improvement. Since it is easy to implement and detect small improvements, the results are fast and direct, which increases the engagement leading to even more implemented improvements. Further, the number of improvements itself means an increasing chance, to discover really good improvements. Finally, using the concept of small improvements makes it harder for competitors to steal them, since changes are gradual and rarely communicated outside the site.

No economical rewards are associated with continuous improvements. Employees have it as personal goals, and occasionally we do something together as a site to recognize all the good work and efforts (cake is usually involved). Additionally, a company day is held twice a year. Such company days are focused on the improvement journey. For one of the past company days, families were invited with activities for both adults and children. For the Strängnäs site, one of the main success factors for implementing the continuous improvement culture has been the focus on simplicity. Each group has a CI responsible person that is a member of the internal CI network. The role of the CI responsible person is to encourage the CI thinking, and keeping track of the number of improvements. A definition of an improvement has been developed and spread: "If you perceive it as an improvement, it is an improvement". Continuous improvement, in its essence, is a mindset; the results will follow over time. When it comes to systems, one should bear in mind that the system itself does not change anything; doing something requires – to do something. "It is easier and much safer to sit around and have intellectual conversations, to gather large databases, to invest in technical infrastructure – and never actually implement anything" (Webber 2007, p. 2).

How It Works: Putting the Pieces Together

A tool without a context is only a tool. It is crucial how and when to use tools. Done the right way, tools will be an important factor in improving the business. However, chances are that new tools become a passing fad; after a while, people may stop using them and slip back into old habits. The risks for this to happen is even higher when there is a lot of pressure on people and the organization, which is a paradox, since especially in such times the proper usage of the tools could have a large positive impact.

To prevent slippage, several approaches could be used, either one-by-one or by combining several, e.g., (i) formal leaders are demanding the use, (ii) the tools are embraced by informal leaders, (iii) measuring the usage of the tools, and (iv) getting an organizational understanding for the reason why the tools are used. In Strängnäs, we are working with all four approaches, but the most powerful one is to get people to understand why we have to use the tools, in what way they can help us achieving our short-term and long-term goals, and that they help us in becoming a little bit better every day. Having a clear long-term breakthrough objective based on a

burning platform (in our case a 50 % cost reduction), helped the Strängnäs site to create the sense of urgency that is needed to get an organizational buy-in regarding the usage of the principles and tools.

The choice of tools should be dictated by the type of problems that arise. There is no point in having goals about the number of times tools are to be used (except for small continuous improvements where the numbers of implemented improvements have shown to make a difference in the transformation). Instead, we are trying to convert needs from the process and the customers to activities, where the toolbox is a help in choosing the most efficient solutions. That is, the customer and flow needs are transformed to tactical and strategic improvements/actions. In this context, the small continuous improvement culture is a large contributor to improving the process on a tactical level. Focusing on small continuous improvements helps to timely identify and correct flow needs, by the people that know the process the best.

The focus on small continuous improvements has lead to a cultural change where every employee is encouraged to look for and correct problems. This change in culture has created a trust in the organization that allows us to dare run pilots to explore and test things without having a perfect theoretical solution in place beforehand. After the pilot, we use CI to further improve.

Can We Prove That a Continuous Improvement Culture Increases Engagement?

Over the last 3 years, it has felt like the engagement at site has increased. The question is, do we have the data to support this?

We have not performed similar surveys each year, but for 2009 and 2010 we have used the Gallup® survey and it should be possible to compare results between the years. We decided to compare data from the three largest departments: manufacturing (including process support), engineering and quality.

What Do We Want to Achieve?

We had three main objectives:

1. Increase engagement by empowering employees to take charge of improving their daily work situation by focus on improvement implementation
2. Change the culture to become more trusting and that by focusing on how we work results beyond expectation will materialize as a consequence
3. Deliver on our tough financial targets and ensure long-term survival/competitiveness

Results

A statistical analysis was performed to answer four questions:

Question 1; do engagement scores between the departments differ?
Question 2; could it be shown that it was implemented actions that have improved the engagement scores?
Question 3; is the site's engagement score higher compared to other parts of Pfizer Inc?
Question 4; is it possible to link a higher engagement score to a higher number of implemented improvements?

The data was obtained from four different sources:

Gallup® surveys (Buckingham 2005) from 2009 to 2010, the Pfizer Voice colleague engagement survey from 2012, our improvement database that has been capturing improvements since 2010 and the financial model used to derive budgets and long-term scenarios.

Details of the analysis can be found in Sandell (2012).

Question 1; do engagement scores between the departments differ?

One-way Analysis of Variance (ANOVA) was used to compare the engagement score from the three groups Engineering (T), Quality (Q) and Manufacturing + Technical services (M + TS). The analysis showed that for 2009 there was a difference between Quality and Engineering (T) and for 2010 there was a difference between the means for Manufacturing + Technical services (M + TS) and Quality (Q).

Question 2; could it be shown that it was implemented actions that have improved the engagement scores?

While the T and Q departments improved their engagement scores from 2009 to 2010, the manufacturing department's engagement score decreased. This result may be related to changes in management in manufacturing department – associated negative effects may have dominated the positive effect of implemented actions.

Question 3; is the site's engagement score higher compared to other parts of Pfizer Inc?

As the Gallup survey was also conducted on a company-wide level it is also possible to compare site performance across the network. The data was collated at a site level, the biotech sites in Europe, the overall manufacturing organization and Pfizer overall. The Strängnäs site had a better average engagement score than the operating unit it belongs to and the global Pfizer manufacturing organization. This difference was shown to be statistically significant by performing a paired *t*-test for the scores of the 12 questions, which gave a significant higher mean for the site.

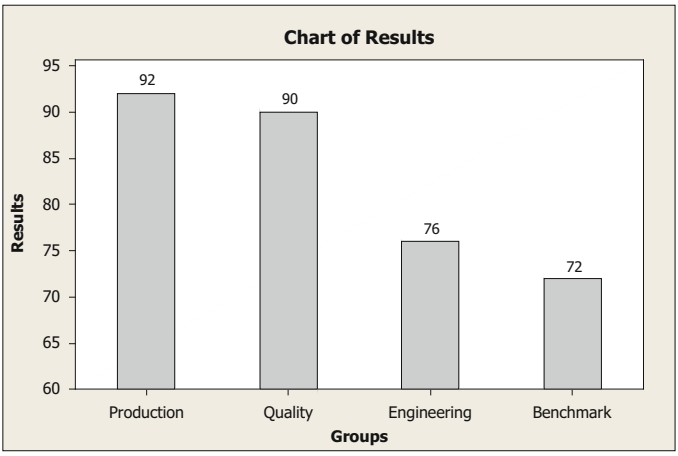


Fig. 28.2 Bar chart showing responses on the question "I feel encouraged to come up with new and better ways of doing things"

In conclusion, the site's Q12® score is significantly higher than that of other parts of Pfizer.

Question 4; is it possible to link a higher engagement score to a higher number of implemented improvements?

To link the Q12® engagement survey to the philosophy of continuous improvement and to determine if engagement drives a higher number of implemented improvements, a regression was performed where the number of Improvements/person was plotted against the Q12®-score for each department. Since there was only Gallup data available on department level the data consisted of only three data points. A regression analysis was performed which could not answer the question.

In the Pfizer Voice colleague engagement survey, one question specifically addresses the continuous improvement culture, i.e. "I feel encouraged to come up with new and better ways of doing things."

The results show that the score for the different groups at the site are above the benchmark of 72 % (see Fig. 28.2). Both production and the quality groups have a score of over 90 %.

Conclusion

The Culture of Continuous Improvement is reflected in the Strängnäs Pfizer Voice 2012 results generating very good results for Climate and Engagement!

- Eighty-eight Percent of our colleagues feel favorably encouraged to come up with new and better ways of doing things (10 % feel neutral); this is 16 % above benchmark figures

- Ninety-five percent of our colleagues in Strängnäs say that "the people I work with cooperate to get the job done" (13 % beyond benchmark)
- Strängnäs colleagues "can see a clear link between my work and the Pfizer's objectives" (3 % beyond benchmark).

Acknowledgements The Site Strängnäs colleagues for being courageous, engaged and committed to the CI work at site and their passion for serving the products, patients and the business.

Simon Orchard, VP Biotech Operations Europe, for showing trust, guidance and inspiration throughout the transformational journey.

Pat Field, Network Performance Lead, for his continuous support throughout the Continuous Improvement Journey.

References

Åslund M (2001) Den tysta motorn. Egmont Richters förlag, Malmö
Buckingham M (2005) First, break all the rules. Pocket Books, London
Covey SR (2004) 7 habits of highly effective people. Free Press, New York
Dennis P (2010) "The remedy" (2010) lean productivity network. John Wiley & Sons, Hoboken, New Jersey
Kotter J (2008) A sense of urgency. Harvard Business School, Boston
Modig N, Ålström P (2012) Detta är lean. Stockholm School of Economics Institute for Research, Stockholm
Östberg L, Schroeder DM, Robinson AG (2010) Små idéer – stora resultat. Swedish Standards Institute Förlag AB, Stockholm
Sandell K (2012) Is there a connection between workforce engagement and continuous improvement?. Henley Business School, Reading
Webber AM (2007) Why can't we get anything done?. www.fastcompany.com

Part IV
Gaining the Future

Following present discussions about saving costs through outsourcing, neglecting improvement potentials by optimizing existing plants, one wonders if the pharmaceutical industry is about to lose its roots in advanced countries. We remain optimistic: Having assessed many plants' manufacturing capabilities, we believe that the benefits of keeping production in high-developed regions outweigh by far what can be gained by transferring manufacturing abroad for the sake of costs.

We make this case in more detail in the first chapter. The final chapter of the book introduces an approach to optimizing production from a true network perspective. After having focused on site optimization for the past years, we argue this is the next step the industry has to take. The leaders of global OPEX programs are in the driver-seat to lead this development as they already manage from a multi-site perspective.

Chapter 29
The Future of Pharmaceutical Manufacturing

Prabir Basu, Thomas Friedli, and Daniel Bellm

Pharmaceutical Manufacturing Is Complex: Moving Towards a True Science-Driven Management

The pharmaceutical industry is definitely a high-tech industry, for its role in discovery of new medicines for the treatment of unmet medical needs. Pharmaceutical manufacturing is complex and sophisticated due to various reasons, but in its current state probably cannot be categorized as really high-tech, too. In fact, pharmaceutical manufacturing was considered as relatively low-tech[1] even by the pharmaceutical companies themselves as recently as in 2002. When ex-FDA commissioner Mark McClellan sought a benchmark for future pharmaceutical manufacturing performance, he looked outside the industry, and challenged Pharma, "You need to improve…Other high-tech industries have achieved enormous productivity gains in manufacturing in the last 25 years. We should expect nothing less from the Pharmaceutical industry."[2]

The main reason for the relatively low-tech systems for pharmaceutical manufacturing was very clearly stated in FDA's Critical Path document published in March 2004[3] – "Applied Sciences Required for Medical Product Development has not kept pace with tremendous advances in basic sciences". This is also the

[1] CAMP Member Companies (2002) Quality by design: a challenge to the pharma industry, March.

[2] Abboud L, Hensley S (2003) New prescription for drug makers: update the plants. Wall Street J, 3 Sept 2003.

[3] FDA white paper on critical path, Mar 2004.

P. Basu (✉)
Pharma Manufacturing and cGMP Consultant, 1911 E Wood Lane Mt Prospect, IL 60056, USA
e-mail: pbasu001@gmail.com

T. Friedli • D. Bellm
Institute of Technology Management, University of St.Gallen, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; daniel.bellm@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_29, © Springer-Verlag Berlin Heidelberg 2013

main reason, why pharmaceutical manufacturing has failed to become a real competitive advantage for US and European pharmaceutical companies. Currently, it is relatively easy to duplicate or reproduce pharmaceutical manufacturing processes and build a plant to manufacture them opening the door for (at least on paper) smooth outsourcing activities. On the other hand, it is not very easy to discover new molecular entities because it is really high-tech and requires very sophisticated technologies and highly trained people. U.S. and European companies have invested heavily in developing very sophisticated and advanced technologies to discover new therapies and as a result, they are very successful until today.

The best way to characterize pharmaceutical manufacturing is that it is very expensive and it is very complex. Simon[4] defined complexity by saying that a complex system has a large number of parts, whose relationships are not "simple". Pharmaceutical manufacturing is exactly that. It has many elements and many parts, and there are many relationships among those elements. These relationships are not simple relationships and currently, they are not even very predictable relationships. A certain property of an excipient can impact the manufacturing of a dosage form in the fourth step of a five step manufacturing process. The presence of an impurity in the first step of an Active Pharmaceutical Ingredient (API) process can impact the processing of a dosage form many steps down. The only way to pre-determine these effects today is to actually carry out multiple experiments and scale-up studies to understand the impact of the variability of that particular property on processing of that step. The relationships between the multiple factors are complex and need to be understood. The physical property of the excipient and the impurity in the API mentioned earlier may in fact even interact with each other. Sometimes when viewing one unit operation or one particular step of a process, it might appear simple. But, the complexity arises due to the many factors and sub-factors of the manufacturing operation and their interactions.

Some of the main reasons why pharmaceutical manufacturing is very complex and expensive are:

API Manufacturing

1. API manufacturing often involves multiples steps of extremely complex chemical reactions. In a large number of situations for a new molecular entity, some of these reactions are being discovered and scaled up for the first time.
2. Due to very tight limits on impurities, multiple steps of tedious separation steps follow the reaction step. This is not equivalent to designing a reactor in a petrochemical plant or a chemical plant. No one has scaled up this process before. This is probably the first time it is being done. There is no data, equation or any references to fall back upon. There are no text books how to do this, nor is

[4] Simon HA (1962) The architecture of complexity. Proc Am Philos Soc 106(6):467–482

it taught in any school or university. The chemists and engineers have to do this based on their cumulative knowledge and experience.

3. The starting material may not be available in commercial quantities. In the author's experience, sometimes the first few grams were made as a result of a special request by a company like Sigma-Aldrich just for trying out this particular reaction. If this API needs to be made in larger quantities, then sourcing of the raw material itself becomes a challenge. Sometimes, there will be just a single source in the world that is able to supply this material in larger quantities.
4. The raw material could also be very expensive and may be one of the key reasons for the API, and finally the drug being so expensive.
5. Often, highly hazardous materials, high pressures, very low temperatures or very high temperatures are used in the API processing steps. The author has experience of running reactions with ozone in a reactor cooled by liquid nitrogen. Now, these types of capabilities are not commonly available and are very expensive, very difficult to set up, control and operate.
6. Due to multiple separation steps, the yields can be very low and the waste generated/active ingredient ratio is very high.
7. Pharmaceutical API's are sometimes even purified by chromatographic separation as the last and final step to ensure the right specification. The complexity and expense of these operations can be easily understood.
8. Since perennially, API process development and hence API supply for making safety studies and clinical supplies are on the critical path to any new drug to the market, scientists involved in API process development usually are under tremendous time pressure. Often quantity has to take precedence over quality of the process.[5, 6]
9. Since time available for development studies and scale up studies and resources available for development work are never sufficiently available, development and understanding of the process steps, and in particular the solid form remains in most cases incomplete. This results in an unpredictable solid state which often creates issues during further processing during manufacture of the dosage form.

Dosage Form

For solid dosage form manufacture, largely the processes are developed by trial and error and the process developed in most cases depends on the experiences of the scientist responsible for the development and the combined knowledge of that company. There are a handful of common unit operations such as blending, granulation, drying, etc. and a handful of common excipients that are commonly used to develop the dosage form process. However, the main complexity arises due to the following reasons:

[5] Basu PK (1998) Pharmaceutical process development is different. Chem Eng Prog 94:75–82

[6] Basu PK, Mack RA, Vinson JM (1995) Consider a different approach to pharmaceutical process development. Chem Eng Prog 95:82–90

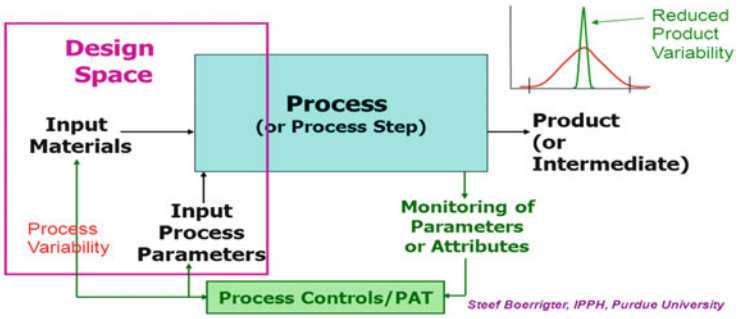


Fig. 29.1 Designing a flexible process

1. Variability of Raw Materials, including the API

   In recent efforts to implement Quality by Design (QbD) or to design quality into the products rather than ensuring quality by inspecting the final products, scientists in pharma companies are looking at ways to reduce product variability by designing flexible processes (Fig. 29.1). Implementing QbD requires fully understanding a process which includes understanding the interactions between the variables and the impact of raw material variability on the quality of the intermediates and the final product. Then only, one is able to appropriately control the process to reduce product variability. This is an expensive and time-consuming proposition and only a few companies in the world have the knowledge and resources to implement it.
2. Lack of predictable First Principles Models to Design Pharmaceutical Unit Operations

   A model is a representation of underlying physical/chemical phenomena.[7] It is also a representation of the essential aspects of a system which represents the underlying knowledge of that system. Understanding the process is a prerequisite to developing and using models. However, if models are available and can be used, it drastically reduces the number of experiments and improves predictability of the manufacturing process. Having good models for manufacturing processes also facilitates trouble shooting and problem solving. Models can be used to simulate operating conditions by varying the variables and studying the impact of the change on the final product quality. Reliable first principle models of most unit operations in pharma are not yet available for wide use. Recently, there is a flurry of research activities in this area. However, much needs to be still done. Other industries such as the petrochemical and chemical industries have been conducting research in developing reliable models for process and plant design for years. Pharma has a lot to catch up on.

[7] Chatterjee S (2011) Role of models in the Quality by Design (QbD) paradigm: a regulatory perspective. AAPS annual meeting, Aug 2011

3. Lack of Automation and On-Line In-Process Controls

   Quality of process control directly affects the performance and reliability of a process. Thus, appropriate process control determines the quality of the products produced by a process and can affect how efficiently a process is being operated. A properly designed control system is able to "absorb" a variety of disturbances and keep the process in a good operating region (Design Space). However, to design a good process control system, the process must be very well understood, and one must have a model of the process. A process model must be developed and based on the model, suitable control strategy and system hardware can be selected. Implementation of sophisticated process control systems and process automation is still very rare in pharma. Conventional pharmaceutical manufacturing is generally accomplished using batch processing with laboratory testing conducted on collected samples to evaluate quality.[8] Therefore, a large part of the control of manufacturing is achieved through manual processes and manual interventions. This obviously, results in unwanted events, variability and undesirable quality.

4. cGmp

   The major difference between pharmaceutical manufacturing and other types of manufacturing is that pharma has to follow cGMP's. cGMP or Current Good Manufacturing Practice is a set of regulations, codes, and guidelines for the manufacture of drug substances and drug products, medical devices, in vivo and in vitro diagnostic products, and foods. These set of principles and procedures, when followed by manufacturers of pharmaceutical products, helps ensure that the products manufactured will have the required quality. Need for documentation of every activity is one of the reasons for high cost of manufacture of pharmaceuticals and the inability to change a process without proper regulatory review and approval makes it difficult to implement any continuous improvement program.

   For example, the FDA's "Guidance for Industry PAT" mentioned above clearly states that "Unfortunately, the pharmaceutical industry generally has been hesitant to introduce innovative systems into the manufacturing sector for a number of reasons. One reason often cited is regulatory uncertainty, which may result from the perception that our existing regulatory system is rigid and unfavorable to the introduction of innovative systems. For example, many manufacturing procedures are treated as being frozen and many process changes are managed through regulatory submissions."

5. Cleaning Requirements and Avoidance of Cross Contamination

   The other key reason for complexity and high cost of pharmaceutical manufacturing is the absolute requirement to avoid cross contamination between the products being manufactured with any other external impurities. Cross Contamination is one of the highest risks for patients using pharmaceutical products. Not only the presence of small amounts of a highly potent unwanted

[8] FDA (2004) Guidance for industry PAT – a framework for innovative pharmaceutical development, manufacturing, and quality assurance

compound in a drug can cause severe damage but also carryover of products into another pharmaceutical product can be of high risk to the patient. This is not only a safety risk but can cause complete stoppage of production at a site and huge financial loss. This makes it necessary to design, build and operate complex cleaning procedures, cleaning systems, buildings and equipment and protective clothing, gowning procedures, etc. The design of such plants become complex and capital requirement to build such plants can be high. Often equipment and facilities such as HVAC have to be dedicated for the manufacture of a particular drug though the utilization of that equipment cannot justify a dedicated facility as such. Though these are not very difficult systems to design and build these days, but they require huge investments.

6. Validation

   Validation is essential since that is the only way one can prove that if the drug was made using a certain process in a certain equipment configuration, the right quality product will be made. There are no predictive models to predict the scale-up success. The only thing that is known is that the drug produced under certain conditions in certain equipments, met the specifications. To ensure that the process is under control and is in a validated state, one must continue to collect and evaluate data, from the process design stage throughout production. This will establish the scientific evidence that a process is capable of consistently delivering quality products.

Why Hasn't High-Tech Been Applied to Pharmaceutical Manufacturing So Far?

When one describes an industry as "high-tech", by it one evaluates and describes in general the state of technological advances and modernization in that industry. It is a relative term and can be used to distinguish something that is technology-free or systems with relatively low technology requirements from something which is more modern and uses the recent advances in science, engineering and IT technologies. High tech is always the result of a complex scientific process of research and development that goes beyond the current boundaries of equipment and technologies.

For years, the emphasis in pharma has been to manufacture a product of the right specification as long as the plant and process comply with cGMP's. Excellence in manufacturing or building a truly sophisticated, fully automated high-tech manufacturing process, even perhaps a fully automated continuous process with real time release to manufacture a product has been the goal of only a few pharmaceutical manufacturers. In general, these have not been necessarily the primary goals of many manufacturers particularly those in the generic business where margins are lower and competition is high.

When one travels to countries like India and China, manufacturers are very proud to show their huge modern stainless steel plants and talk about their SOP's, training programs, and FDA inspections. They have a large source of cheap and

skilled labor and their cost of capital is also significantly lower. They can therefore more easily duplicate and build a clean and modern manufacturing facility and develop all the cGMP systems at a significantly lower cost. It is not so difficult to do that. No special technologies have to be designed or licensed. It is not like building an aerospace plant or a petroleum refinery where specific technologies have to be either developed or licensed. By high-tech in pharmaceutical manufacturing, one has the image of a plant made largely out of stainless steel, with very high degree of cleanliness and often operators working in protective gears and having complex gowning procedures. But, the basic manufacturing processes are little understood, they are manufactured with mostly manual operation and supervision and very little automation and instrumentation. It is like running a recipe over and over again and making sure that the recipe is being followed exactly as written. Some of the reasons why pharma manufacturing cannot be really classified as high-tech are as follows:

1. The ease at which new entrants can become potential manufacturers is rather striking. The technology is widely available to build a plant, and one does not need to license any technology. Companies around the world, with very little expertise in pharmaceutical manufacturing, are able to build plants and then hire consultants from the US or Europe to prepare SOP's and regulatory documents and provide training to their local employees and can start manufacturing API's and dosage forms for the US and European markets. It is the complexity of documentation and regulatory and quality systems, not the inherent technologies that prevent even larger numbers of manufacturers from starting up new pharmaceutical manufacturing plants and becoming potential suppliers to the Western manufacturers.
2. The ease at which generic manufacturers all around the world can literally reproduce the brand-name companies' drugs has to mean that the process of manufacturing cannot be really high-tech.
3. Even today in the twenty-first century, the science of developing pharmaceutical processes without extensive experimentation and without conducting a series of scale-ups and trials and errors is not available. There is a tremendous gap in the knowledge which should be precompetitive in nature.
4. Experimental design and design space are concepts which are only a few years old in the pharmaceutical industry while these techniques are being used for example in the auto industry since the 60s and sometimes even earlier. Even today, only a hand full of pharmaceutical companies is using these techniques and only for a few of their products.
5. Real-time release is practiced very rarely. Real-time release testing is a "tool", and a replacement for slower analytical techniques. For example, dissolution is replaced with a calibrated NIR instrument.[9] With advanced Process Analytical Tools (PAT) in place, one can control a process in real time which will provide a

[9] Ali Afnan (2011) Real-time release: it's time for action and not debate. PharmaQbD, 22 Feb 2011

data-driven assurance of quality. However, implementation of this requires high quality process understanding and use of sophisticated instrumentation such as NIR and FTTR, etc.

6. Unlike distillation columns, and complex reactor and separation equipment configurations in the petrochemical and chemical industry, there is very little use of model based equipment and process design. Large chemical and petrochemicals plants are usually continuous where raw materials are continuously fed to the process units and product streams are continuously withdrawn. Advanced process control and optimization techniques are used for controlling these continuous processes. The process control systems typically consist of integrated networks of computers, operator workstations, instrumentation, and other control hardware. With the current revolution in information technology and smart instruments, there is a revolution in terms of process control, diagnostics and data collection in these industries.
7. Model Predictive Control (MPC) is also being widely used for advanced process control and to perform difficult control problems. To enable MPC, a reasonably accurate dynamic model of the process must be available. The model and current measurements are typically used to predict the future process behavior. The plants are controlled based on both predictions and measurements.
8. Use of sophisticated modeling tools such as CFD is rare and sporadic.

Reasons for the Current Status of Pharmaceutical Manufacturing

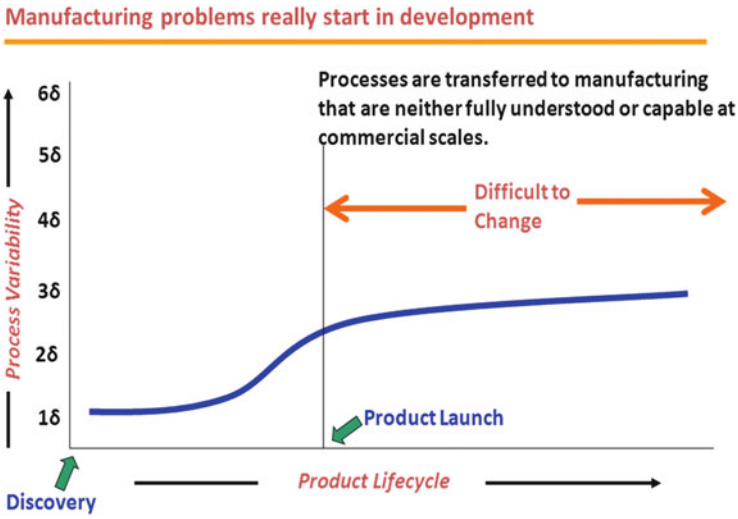
The reasons are many fold. Most of them are unique to this industry.

1. Uncertainty

   The uncertainty in the new drug approval process and regulatory constraints do not provide an environment for scientists to develop robust manufacturing processes in manufacturing. The development group at a brand name pharmaceutical company may be involved in developing 15–20 or even more compounds simultaneously without much assurance of which ones will be approved as marketable drugs. The resources of any company are not infinite. As such, the priority of the limited resources is to ensure that lack of clinical supplies do not hold up any clinical trials. There are many dedicated scientists in these companies who try their best with limited resources to develop the best possible processes until these processes become frozen and then they cannot be changed anymore.
2. Development is the Root Cause of Manufacturing Woes

   Problems faced in manufacturing are a result of incomplete or insufficient process development. These are residual problems that were not completely resolved before the process was transferred to manufacturing. Thus manufacturing becomes an experiment. This experiment can be also very

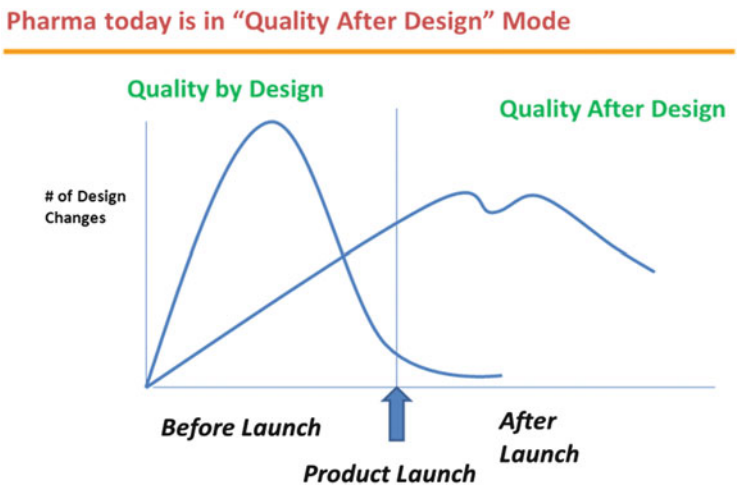
expensive. The problem is a direct result of the uncertainty mentioned above, and due to the lack of a well developed, publicly available knowledge base for scientists and engineers to use for process development and scale-up. Often, individual companies develop sophisticated knowledge for process development and scale-up. But, rarely this knowledge is shared.



Pharmaceutical product development today is more of an art than science.[10] Once the new drug is discovered, product development and manufacturing are left to traditional "tried and true" practices. This is one of the key factors why pharmaceutical manufacturing is not as advanced as the manufacturing technologies of other industries. Marked advances in chemistry, chemical engineering, computer modeling, instrumentation, analytical techniques, and product formulations that could be used to increase efficiency are only being recently applied in pharmaceutical product development and manufacturing. Even that is limited to a few companies in the world. Empirical methods used today are labor intensive and time consuming and cannot predict manufacturing performance.

Pharmaceutical products are most often developed not with manufacturability in mind, but with an aim to meet short-term clinical supply needs to meet the registration timelines. Often small biotech companies are operated by scientists with no knowledge of manufacturing and supply chain issues. R&D and manufacturing operations ideally must have close interactions – though the level of interaction varies from company to company, in general it is not as much as in other industries such as chemicals, petrochemical or engineering industries. This problem is getting more acute with increased outsourcing – manufacturing may be located 5,000 or 10,000 miles away from discovery or product development.

[10] FDA (2004) Challenges and opportunity on the critical path to new medical products, Mar 2004



3. Regulatory Constraint

   In most industries, manufacturing processes are continuously improved to improve productivity, quality, safety, etc. However, once a drug is approved, continuous improvement is limited by regulatory constraints. Different levels of regulatory approvals are required for different types and levels of process changes. Pharmaceutical companies have to weigh their resource requirements to the benefits achievable from making these changes before they can decide to employ their scarce resources. This is particularly a problem with older drugs where there are generics already in the market and the margins are very small. In the author's experience, many times improvement ideas are not pursued after a cost-benefit analysis. Industry and the regulatory agencies must come together to find a path forward whereby changes to old processes can be made so that innovation can continue even after registration and approval of a drug without sacrificing quality. There must be a way!

4. Management Apathy

   Historically, pharma companies, especially the brand names one, are driven by their potential to discover new remedies for unmet medical needs. The R&D pipeline and whatever it takes to get these new discoveries to the market as fast as possible drives their profitability. Some pharma companies do take pride in their manufacturing capabilities and invest in excellence in manufacturing. In fact, the saying in one of the pharma companies that the author had the good fortune to work for a short period was "We make what we sell". However, in general, manufacturing appears to be the step child in some pharma companies. David Smith, AztraZeneca's Executive Vice President of Operations, said[11] "Manufacturing for AstraZeneca is not a core activity. AstraZeneca is about innovation and brand-building . . . there are lots of people and organizations that

[11] Pagnamenta R (2007) AstraZeneca to outsource manufacturing. Times Online. 17 Sept 2007

can manufacture better than we can." Of course, he was referring to outsourcing to Indian and Chinese companies. When push comes to shove and there is pressure to reduce cost, many pharmaceutical companies resort to cost reduction via outsourcing rather than reducing cost by investing in their own plants and reducing wasteful operations. S. Schwan,[12] CEO of Roche said "Those who fail to bring sufficient innovation will be squeezed out of the market". Mr. Schwan was probably referring to discovery science as is always the case with pharma executives. But, lack of real innovation in manufacturing science and increased reliance on outsourcing, are also having serious consequences in pharmaceutical manufacturing.

5. Invention is Rewarded in Pharma, but not Innovation

"In its purest sense, "Invention" can be defined as the creation of a product or introduction of a process for the first time. "Innovation," on the other hand, occurs if someone *improves on* or *makes a significant contribution to* an existing product, process or service."[13] A product like a microprocesser was invented by someone. But, once it was invented, there has been continuous improvement in the technology which has made it faster, smaller and cheaper. In an article[14] titled, "Arguing by Analogy: What Pharma Can Learn from the Car Business," Roger Longman identified several key lessons that the pharmaceutical industry can learn from the automobile industry. Mr. Longman's article focuses mainly on research and development. However, this analysis can be extended further to find striking similarities between the current status of manufacturing in the pharmaceutical manufacturing with that of the automobile industry in the late 50s and early 60s and the key lessons that U.S. pharmaceutical manufacturing business can possibly learn from what has happened to the U.S. auto industry.

In the late 50s and early 60s, the automobile industry in the U.S. was highly profitable and Japan had just then started entering the automobile manufacturing business. In fact, in 1948, the total automobile exports from Japan to the U.S. totaled only around 300.[15] The automobile industry in the U.S. was focused on engine power, vehicle speed, artful design, luxury and size of cars, but not so much on reliability and defects. Quality was of lesser importance. U.S. automobiles were then generally competitive with European products and superior to Japanese products.[16] However, the Europeans and the Japanese had lower labor costs and had an advantage on price. Rather than trying to reduce cost through innovation by improving manufacturing and investing in

[12] Hensley S (2008) Roche CEO warns big pharma and biotech face rough waters. Health Blog, Wall St J

[13] Gasty T The difference between innovation and invention. http://www.pbs.org/idealab/2012/03/the-difference-between-invention-and-innovation086.html

[14] Longman R (2008) Arguing by analogy: what pharma can learn from the car business. The RPM report, 20 Nov 2008

[15] www.jama.org/home.htm

[16] Juran JM (1993) Made in U.S.A.: a renaissance in quality. Har Bus Rev, Jul–Aug

technology, the U.S. manufacturers responded to this price competition by shifting manufacturing to low labor-cost countries like Mexico. The main difference between the Japanese automakers and the U.S. automakers was that the Japanese measured quality and invested in innovative technologies to continuously improve quality of their automobiles while the U.S. automakers pursued cost savings by looking for cheaper sources of labor.

The main reasons for lack of innovation in pharma are:

(a) Lack of a "Commons" for technology for Pharma

According to Pisano and Shih,[17] industries require a "Commons" to sustain innovation. "Industrial Commons" is defined by them as the area of knowledge which is precompetitive and can become a foundation for innovation and competitiveness. This can include R&D know-how, advanced process development and engineering skills, and manufacturing competencies. Pisano and Shih have given a historical example as the birth of the pharmaceutical industry in Germany and Switzerland due to the knowledge base existing in those countries in late 1800s related to synthetic dye chemistry and since they were chemical companies which had strong research labs and deep technical expertise in synthetic dye production. Pisano and Shih states "Cutting-edge high-tech products often depend in some critical way on the commons of a mature industry".

Pharmaceutical technology is unique. But, it has not been able to adopt knowledge from other mature industry commons such as the chemical industry. The case in point is that there is no discipline equivalent to "Chemical Engineering" available to pharmaceutical scientists. It would not be very hard to imagine the state of the chemical industry today if not for a discipline such as chemical engineering. Our chemical processes would be very inefficient, costly and wasteful. Thus pharma industry has not benefited from the knowledge and expertise such a discipline can bring in modernizing manufacturing. This is one of the reasons why scale-up and developing robust manufacturing processes remain the most challenging problem in pharmaceutical manufacturing.

Not having a mature "Pharmaceutical Engineering" discipline has also led to an "Eye-lash Learning Curve" in pharmaceutical development and the techniques are rather empirical. Development of each new manufacturing process for each new molecule is largely a new journey. There is not enough model-based development with predictability of performance.

The other major technology gap for pharma is its limited knowledge and understanding of the behavior of organic solids. Organic compounds are produced by living things. Inorganic compounds are produced by non-living natural processes. As such, properties of organic solids are variable and hard to quantify and measure and thus predict performance of processes that use them. Inorganic solids also tend to be dense and granular. Organic solids on the

[17] Pisano G, Shih WC (2009) Restoring American competitiveness. Har Bus Rev, July–Aug

other hand, can be fluffy powders, fine needles, flakes, or plates. They can be either amorphous or crystalline and their forms can vary depending on the processing conditions. There are many other complications involving the processing of organic solids the and understanding of the science is far from complete. This "industry commons" also has not developed to the benefit of the pharma industry.

(b) Limited patent life and stiff price competition with generics

Brand-name pharmaceuticals have only a few years to recover the cost of developing these new drugs due to the impending competition with generic suppliers. Generic producers have no burden of the cost of product invention and thus are able to make the same drug at a much lower cost. Thus, brand name pharma companies do not have much incentive to invest in expensive manufacturing process improvements because they know that by the time they would complete the development and get the new process approved by the FDA, they will probably not have much time to recover the cost of such a development activity.

(c) Availability of cost reduction opportunities through outsourcing

Outsourcing is on the increase. Facing severe cost pressure, the industry rather than investing in quality, technology and innovation in manufacturing to reduce cost, is looking for cheaper labor sources in India and China. The emphasis has been to reduce cost by outsourcing rather than through innovation.

(d) Regulations inhibit innovation

The inability to freely conduct continuous improvement in pharma inhibits innovation. OSHA's Guidelines for Process Safety Management of Highly Hazardous Chemicals – Compliance Guidelines and Enforcement Procedures (29 CFR 1910.119) has many similar components as do cGMP guidelines such as management of change, incident investigation, training, need for procedures, audits, etc. However, OSHA's VPP Starr program created in 1982, recognizes and partners with businesses and worksites that show excellence in occupational safety and health. Sites are committed to effective employee protection *beyond* the requirements of OSHA standards. VPP participants develop and implement systems to effectively identify, evaluate, prevent, and control occupational hazards to prevent employee injuries and illnesses. In return, OSHA removes participants from programmed inspection lists and does not issue citations for standards violations that are promptly corrected. These sites are also allowed to manage their own change control program rather than having to go back to OSHA to receive approval for every change that is made in the equipment, system or plant.

Pharma companies, on the other hand are so afraid of getting stuck in the regulatory approval process, that they would rather operate an inefficient out-of-date process and never make any changes throughout the life of the process since its inception. Some of the drug shortage problems for older drugs can in fact be traced to this issue.

Pharma Manufacturing Important

Manufacturing is a very important component in getting safe drugs to patients. In fact, it is the last step in the chain of very complex events before a drug reaches the pharmacy shelves. When that critical link is broken, it opens the door for something like the heparin crisis. As it is, a typical pharmaceutical supply chain is very complex with ingredients coming from all over the world and the products being manufactured and distributed all over the world. Outsourcing in countries like India and China definitely reduces cost, but also substantially increases the risk of poor quality. These countries have a highly skilled labor force, but their regulatory culture is evolving. The manufacturing plants in these countries are also not inspected by the FDA as often as their counterparts in the Western hemisphere. David Kessler, former commissioner of the FDA told USA Today after the heparin crisis that the news of heparin crisis should not have come as a surprise to anyone. According to USA Today, Dr. Kessler said that China in 2008 was a lot like the USA in 1906. According to him,"That's why we developed an FDA."[18] Those of us, who have been involved with regulatory compliance for a number of years in the pharmaceutical manufacturing arena, know that the high quality standards and cultures cannot be achieved overnight by reading some books, manuals or FDA Guidance Documents or employing consultants. It is a culture that requires number of years of training, experience and practice and usually a site or a manufacturer evolves into a high quality one over time, sometimes even through making some unfortunate mistakes. There are world-class pharmaceutical plants in India and China. But, the fast majority of pharmaceutical plants that have cropped up in India and China are focused primarily on providing lower cost and are facing tough competition even internally in their own countries. It is difficult for them to maintain low cost while investing in compliance.

Improving Pharma Manufacturing

In the previous chapters of this book, there are a number of examples of how implementing an OPEX program, pharma manufacturing plants have been successful in improving their efficiencies, become more effective and reduce cost. This is a far better approach than to reduce cost by outsourcing. Data shows that cost of labor is only 20 % of the total cost of manufacturing. Thus even if labor was 50 % cheaper, it does not completely justify outsourcing. In fact, it does not even consider the hidden costs of outsourcing:

- Outsourcing creates several foreign entitles that now have to be inspected by the regulatory agencies to ensure that they are making intermediates or drugs that

[18] Wise E (2008) USA Today, 19 Mar 2008

are safe and efficacious. This puts tremendous burden on our regulatory agencies which already have very limited resources.
- Internal costs of outsourcing are often ignored when making outsourcing decisions. Companies who successfully outsource must add sufficient technical, regulatory, quality and supervisory resources to oversee these outside entities.
- Physical separation and distance of the manufacturing facilities from research and development sites severely impact the quality of processes that are transferred to manufacturing due to lack of interaction and lack of manufacturing input in process development.
- Historical examples from other industries, e.g. Textiles show that outsourcing is often the end for innovation in production processes as it is cheaper to involve more human labour in the production to overcome weaknesses than to improve processes and use technologies to support production.

The following are some recommendations how to improve pharma manufacturing for the future:

Reward Innovation

To build excellent facilities and systems requires investments. Companies who have invested heavily in manufacturing are not being rewarded appropriately. Why should pharmaceutical plants invest in people, systems and facilities to achieve excellence? To encourage investments in manufacturing excellence and for building a culture of continuous improvement, the industry needs to have certain incentives to do so. Conditions must be created where pharmaceutical manufacturing plants can implement changes rapidly as long as they satisfy certain predetermined regulatory requirements, operational control and excellence. If a pharmaceutical manufacturing site decides to make the substantial investment in people, equipment, systems and technology to become an "Excellent" site, then the regulatory agencies should provide these plants with incentives of reduced regulatory oversight once these manufacturing plants attain a certain "Excellent" status based on a predefined criteria. If the industry and the regulatory agencies are willing to work together, then this is definitely an achievable goal. If this can be achieved in the process safety area under OSHA, there is no reason why similar systems cannot be implemented in the cGMP area. Ultimately, this approach will encourage continuous improvement and implementation of OPEX in many plants.

Pharmaceutical manufacturing sites, which implement an OPEX program and attain a predetermined standard of excellence, should be allowed to make continuous improvements in their plants and processes without having to seek prior regulatory approvals. Instead, these plants will just keep the regulatory agencies informed of the changes being made on a regular basis. These plants will have the responsibility to prove to the regulatory agencies that they have internal controls and systems to assure safety and efficacy of drug products produced as a result of these changes.

Implement cGMT's and not only cGMP's

Drug and device manufacturers should be encouraged to develop their products in compliance with not only cGMP's but also cGMT's or Current Good Manufacturing Technologies. cGMT guidelines can be developed by the regulatory agencies using a process that they normally used for developing other guidelines. These guidelines will guide manufacturers how to develop and manufacture their products in a manner that is consistent with the best available science irrespective of where they are made. "Good Manufacturing Practice" does not necessarily ensure "Good Manufacturing Performance". The inspection of manufacturing facilities should include assessment of whether the site is practicing cGMTs in addition to cGMPs. As a consideration for whether a drug qualifies for a risk-based facility inspection, i.e. the abbreviated schedule, the regulatory agencies should consider the level of technology used in the manufacturing process, as well as the use of appropriate Quality by Design and Process Analytical Technologies. In addition, the technology used to manufacture drugs and devices should be included as a key component of the inspection record.

Reward Pharmaceutical Manufacturing Facilities for Implementing OPEX

Consumers (patients) should start demanding to know where and how their drugs are being manufactured. Consumers have a right to know the quality of the plant and the technology used to make the medicines they buy or take. If they had a choice of buying a drug manufactured in a plant that was successfully inspected by the FDA, compared to buying it from a plant that has never been inspected by the FDA, or from one with questionable audit reports, perhaps the consumer would be willing to even pay a higher price for that medicine with higher quality! Perhaps a system to provide numerical ratings of pharmaceutical manufacturing sites should be developed and implemented. In a recent article[19] published by Dr. Janet Woodcock, Director, CDER, FDA, it has been suggested that FDA publicly rate pharmaceutical products based on the quality processes and the equipment that was used to produce them. This proposal should cover manufacturing plants, too. The buyers of pharmaceutical products such as patients or hospitals have no way to determine whether or not a particular drug was produced using the latest equipment while fully complying with cGMP's.[20] On the other hand, pharmaceutical companies do not have any incentive to implement

[19] Woodcock J, Wosinska M (2013) Economic and technological drivers of generic sterile injectable drug shortages. Clin Pharmacol Ther 93(2)

[20] Moad J (2013) www.manufacturing-executive.com. 6 Feb 2013

programs like OPEX and perhaps score very highly on a rating program like this. Perhaps, this system can provide the right kind of incentive to invest in quality.

Develop, and Cultivate a "Pharmaceutical Commons"

The Semi-conductor Industry Example

In 1987 the U.S. semiconductor industry largely conformed to the ideal in neoclassical economics of free market competition.[21] But in the early 80s, American semiconductor manufacturers could no longer compete with vertically integrated foreign manufacturers supported by huge government subsidies in making chips that were both high in quality and low in price. Rather than continuing to develop proprietary product designs, U.S. chipmakers recognized that they could only defeat foreign Japanese competitors if they worked together to select manufacturing standards and improve their manufacturing processes. However, such cooperation was difficult to achieve in an industry previously characterized by secrecy, fierce rivalry, and antitrust sentiment. In 1987, a consortium called Sematech (SEmiconductor MAnufacturing TECHnology) was launched where 14 U.S.-based semiconductor manufacturers and the U.S. government came together to solve common manufacturing problems by leveraging resources and sharing risks. By 1996, it was realized that the U.S. semiconductor industry had regained strength and market share. At that time, the Sematech decided to end the matching federal funding.

Sematech managed to overcome obstacles and created a viable organization that enabled U.S. manufacturers to resume world leadership in the semiconductor market. Three different perspectives for analyzing the consortium's achievements are presented in the book by Browning and Shetler:

- Horizontal collaboration between chip manufacturers, vertical partnerships with their equipment suppliers, and collaboration with academic and national laboratories created a viable, cooperative consortium of organizations that had previously been competitors.
- The consortium built a close relation with the government by gaining assurance of antitrust exception, securing support from the Department of Defense, and heading off excessive government control of Sematech's operational activities.
- Sematech successfully carried out its technological strategy of producing increasingly miniaturized silicon chips and improving its equipment and manufacturing processes.

[21] Browning LD, Shelter JC (2000) Sematech: saving the US semiconductor industry. Texas A&M University Press, College Station.

Pharma Needs to Follow the Sematech Lead

If manufacturing and the resultant delivering of high quality medicines to patients in the U.S. are truly important to our pharma companies, then they perhaps should follow the Sematech lead and agree on precompetitive research areas where they can collaborate and conduct research for the good of all pharmaceutical companies, brand-name, generic, big and small. Gradually, Sematech has changed its R&D model to incorporate broader industry participation – including equipment and materials suppliers, packaging/assembly companies, and international companies. They have also engaged with and collaborated with universities, and other consortia in order to foster technology innovation and accelerate the commercialization of new materials and nanostructures for future transistors. Their model and huge success proves that collaboration drives innovation. Among the principal benefits of networking, are risk sharing, and speeding products to market and pooling of complementary skills. There is evidence that those firms which do not co-operate and which do not formally or informally exchange knowledge limit their knowledge base long term.[22] Pennings and Harianto[23] present the theory that Networking is deemed important for facilitating access to strands of technology that are alien to a firm.

There are several potential areas of collaboration in research in pharma which could transform pharma manufacturing forever. Many pharma companies around the world are working on these areas and spending significant resources to create their own protected knowledge base. It is time for them to come together and decide on a "commons" and collaborate to develop the knowledge much faster. Some examples of these areas are:

1. Continuous Manufacturing

   It's been too long that pharma has been dependent on tried and true practices of batch processes. Continuous production is compact and is amenable to continuous monitoring of product quality and not just at the end of the process or batch. Continuous processes will also reduce variability and will drastically reduce capital cost to build a plant. Continuous manufacture will improve productivity to such an extent that there will no longer be any advantage of building these plants in countries with cheap labor. Rather these plants can be built early in development so that they can make clinical supplies and then gradually start making the commercial supplies too.

   There are a lot of technological gaps that need to be closed which should be precompetitive to make continuous manufacturing a viable alternative for the entire industry, brand-name and generics, small and large to adopt universally.

[22] Pittaway L et al (2004) Networking and innovation: a systematic review of the evidence. Int J Manag Rev 5(3–4):137–168

[23] Pennings JM, Harianto F (2013) Technological networking and innovation implementation. Organ Sci 24:1, Jan–Feb

2. Pharmaceutical Excipients

   Pharmaceutical excipients have a profound influence on the performance of a drug product. Good understanding on excipient properties as well as the variability exhibited by excipients has been shown to be critical in the design and manufacture of pharmaceutical dosage forms. Unlike other industries such as the chemical, ceramic, aerospace, petrochemical, etc., where database for material properties are available for scientists and engineers, there is a lack of public repository of information in the pharmaceutical industry. Such lack of understanding on excipient properties as well as the variability associated with excipient material and measurement methods are big impediments to designing and operating high quality manufacturing processes and the root causes of many regulatory issues.
3. Automation and Process Analytics

   Automation not only increases productivity, but also plays an extremely important role in achieving consistent quality of products and safety of the manufacturing process. Today, with modern information technology, automation has extended its range to include data traceability, data management and providing on-line, on-demand information. However, automation relies on many subsidiary technologies, such as sensors, analyzers, software, modeling, etc. Achieving consistent quality has been an age-old problem in pharmaceutical manufacturing. But, this is achievable with common sense automation provided all the other subsidiary technologies were well developed. This is definitely a pre-competitive area of research where pharma companies can collaborate to develop specific technologies and platform-technologies which can be easily and uniformly applied across the industry.
4. Process Simulation and Modeling

   Simulation and modeling provides a deeper understanding of production processes. They also provide a better idea for the best locations for the online sensors and sampling and help tremendously with risk analysis. Work has been going on in this area in several pharma companies and in academia for the last 10 or 15 years. But, there is a need to bring all the resources in academia, industry, regulators and equipment manufacturers together to develop technologies that are pre-competitive and can in general raise the capabilities of simulation and modeling of the entire industry.

Pharmaceutical Manufacturing Should Compete Through Quality

Too often, quality is defined by how well one follows some procedures or how well one responds to deviations, incidents, or rejected product or batches, etc. A manufacturing organization must feel and be committed to quality because history of manufacturing in other industries such as the automobile industry has shown that quality is ultimately rewarded and is the true competitive advantage as well as the very basis for any manufacturing organization. James E. Olson, President of AT&T,

said, “A lot of people say quality costs too much. It does not. It will cost you less.”[24] According to Hayes and Wheelwright,[25] the emphasis in quality in a manufacturing organization is the recognition that it is not simply the task of the manufacturing function or the quality department. The whole organization must be committed to quality. The degree to which quality can be a competitive advantage depends on overall management commitment to quality. According to ICH Q10 Guidance document, “Leadership is essential to establish and maintain a company-wide commitment to quality and for the performance of the pharmaceutical quality system.” This is also the message of OPEX.

Towards High-tech Manufacturing

Data from the St.Gallen OPEX benchmarking shows that high-performing plant that can deal with increasing complexity (cf. Chap. 18) are mostly located in developed countries. They can rely on an over-average level of education and the physical proximity to their development knowledge base. The answer to the current challenges in the industry is not to outsource more and more operations to low-cost countries but to further build up a solid knowledge base about pharmaceutical production processes, to continuously apply true science on the improvement of production processes starting in development and to use technology and automation to reduce the global cost differences. With this approach pharmaceutical manufacturing would have a real future in the developed countries, helping to keep quality high and laying the basis for science driven pharmaceutical commons. There would still be a need for local production in other world markets but these plants in the network would be supported by the established plants leading to a plant network system with differentiated roles and responsibilities. How such a system can be managed is described in the last chapter of this book.

[24] Olsen JT (1985) The state of quality in the U.S. Today. Qual Prog 33

[25] Hayes RH, Wheelwright SC (1984) Restoring our competitive edge. Wiley

Chapter 30
Managing Global Pharmaceutical Manufacturing Networks

Thomas Friedli, Fabian Liebetrau, and Richard Luetzner

Introduction into Global Manufacturing Networks

The importance of manufacturing for the global economic situation is undisputed. The manufacturing of physical goods attributes 16 % of the overall global gross domestic product (GDP). With every US dollar of manufacturing output another 19 cents of service revenue is generated. The manufacturing share of global trade is estimated to be 70 % (Manyika et al. 2012). Various studies illustrate a global growth in overall international manufacturing activities (Harre 2012; Zhan 2012). In the last 20 years an increasing amount of corporations developed and still maintains a global footprint. In 2011 employment at foreign affiliates accounted for 63 million jobs while generating 27 trillion US-dollars in sales (an increase of 450 % since 1990) (Zhan 2012).

As the majority of global market volumes shifts from developed countries to developing countries international companies try to conquer their share of the emerging markets (Zhan 2012; Diethelm 2013; Malik 2013; Viñals 2012).

Pharmaceutical companies currently employ 650,000 direct employees in the United States and 663,500 employees in Europe. Nevertheless, employment in this industry is not exclusively focused on high-income countries. A lot of indirect jobs are provided in low- and middle-income countries like Russia (70,900 employees), Egypt (37,500 employees), Turkey (13,100 employees), and Colombia (16,350 employees). Additionally, a direct link between research and manufacturing capacity does not exist. Some countries have little research compared to their manufacturing capacity whilst other countries are focused on research with only little manufacturing capacity (IFPMA 2012). Our benchmarking study on Operational Excellence in the pharmaceutical industry indicates that pharmaceutical companies today maintain networks of globally dispersed manufacturing sites.

T. Friedli (✉) • F. Liebetrau • R. Luetzner
University of St.Gallen, Institute of Technology Management, Dufourstrasse 40a 9000, St.Gallen, Switzerland
e-mail: thomas.friedli@unisg.ch; fabian.liebetrau@unisg.ch; richard.luetzner@unisg.ch

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7_30, © Springer-Verlag Berlin Heidelberg 2013

Entering a market with at least a small share of the steps along the value chain is often a necessity due to import tariffs. Companies that have invested in foreign subsidiaries are likely to do it again. Additionally, companies that have not yet expanded with their manufacturing facilities to locations besides their home market are increasingly pushed to build up a global footprint as they are not able to compete with global competitors (Zhan 2012). After the financial crisis companies perceive the climate for foreign direct investments (FDI) as increasingly optimistic. The investment in foreign facilities leads to an increase in companies with globally dispersed manufacturing activities. So far, only few companies manage their globally dispersed manufacturing activities holistically, in the sense that the sites in a network are optimized from a network and not a site perspective. However, those companies that do manage their manufacturing networks holistically see a huge potential for building up a sustainable competitive advantage in the management of international manufacturing networks.

Frameworks for the Management of Global Manufacturing Networks

Multinational companies often do not use the full potential of their globally scattered manufacturing sites. Mostly, they use them to "[. . .] benefit only from tariff and trade concessions, cheap labor, capital subsidies, and reduced logistics costs. Therefore, they assign a limited range of work, responsibilities, and resources to those factories." Other companies, however, may use their sites to unlock all the potential by getting access to customers and suppliers, or accessing knowledge and skilled workforce. Those companies use their sites as a competitive advantage (Ferdows 1997).

Another common issue within manufacturing networks is a lack of transparency. In several projects we discovered that managers often don't know neither the potential a site has, nor the purpose and reason of their sites, nor the range of competences the respective sites have. Furthermore, sites are developing but it is often not possible to describe the current state of a site, not even to speak of prescribing the path this very site will take in the next years. Assigning for example well defined roles to the sites within the network can help to overcome these problems and unlock hidden potential.

Acknowledging that there are many levers for the management and (re-)design of a manufacturing network, the Chair of Production Management at the University of St.Gallen developed a management architecture that comprehensively describes the different dimensions of a holistic management approach towards optimizing such a manufacturing network. Comprising the three core dimensions of manufacturing network management from academic literature and based on assumptions of contingency theory, the management architecture displayed in Fig. 30.1 serves operations managers as a framework when managing their networks. The three core dimensions are: (1) Global Production Strategy –

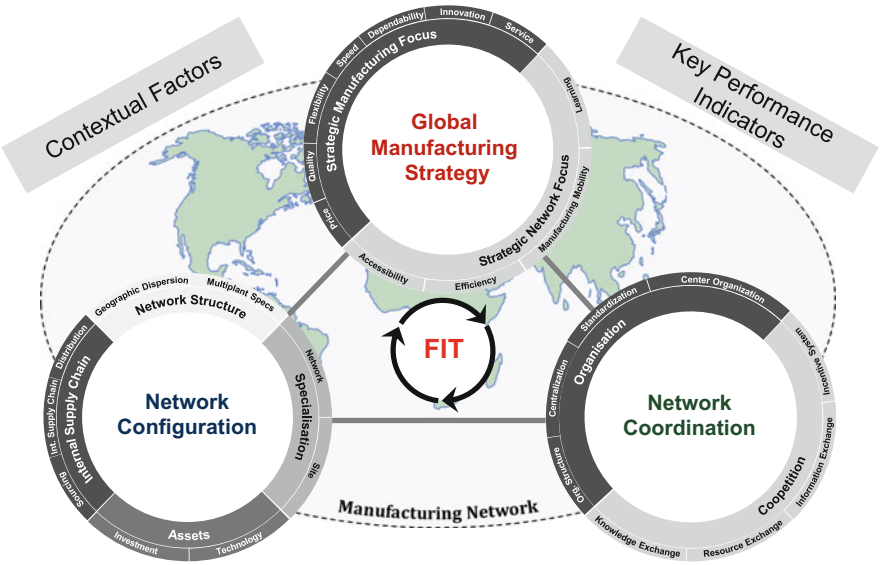


Fig. 30.1 Management architecture for a holistic network management (Friedli et al. 2013)

comprising both manufacturing and network focus – (2) Network Configuration – addressing the physical structure of the network – (3) Network Coordination – focusing on the interplay between the network's sites.

While Network Configuration has been widely addressed by several authors and in sufficient depth, Network Coordination has mostly been ignored so far. Nevertheless, this is an important lever for network management (and has a direct relation to Operational Excellence) that is used to shape the relationship between the sites, especially through shaping the degree of coopetition within the network. Coopetition – a concept of Brandenburger and Nalebuff (1996) means that network units simultaneously compete and cooperate in selected areas with each other. There are several levers to foster coopetition amongst the sites systematically. In the following, we present some management frameworks for the network coordination. They support OPEX managers when shaping the interplay between the network sites and must – following contingency theory – be implemented not solitary but in a concerted way, aligning the different decision dimensions to each other. Only then, a sustainable network optimization can be realized.

Site Role Portfolio

Site roles have been identified and described by many authors in scientific literature, so far. Amongst those, the site role concept of Ferdows is the most recognized approach when assessing or defining roles to the manufacturing sites within a manufacturing network. Other authors that are paid attention to are Vereecke/Van

Dierdonck (2002), Vokurka/Davis, Feldmann/Olhager, and Maritan et al. Since Ferdows laid the foundation for further research in this field with his lead factory concept, which is the most popular approach, we will focus on his work and take it as a starting point for our framework.

Ferdows identified six site roles, each depending on a different set of competences and strategic reasons for the respective site. He differentiates three strategic reasons for a site: (1) access to low-cost manufacturing, (2) access to skills and knowledge, and (3) proximity to market. Depending on the set of competences a site has, the several times empirically validated (Mundt 2012) site roles are: source-factory, offshore-factory, the probably most popular role of the lead factory, the contributor factory, and the server factory (Ferdows 1997). Numerous researchers have tested and modified this site role model and, amongst other things, found that the competences are assigned step by step to the sites as competence bundles, starting with production-related, supply-chain-related, and finally development-related competencies. It is important to note that these site roles only represent a snapshot of a dynamic evolution of the sites, since site managers are supposed to evolve their sites and therefore pick up new competences over time (Ferdows 1997), (Feldmann and Olhager 2009a), and (Mundt 2012).

Vereecke et al. (2006) have presented different site roles portfolios, considering, for example, the intra-network flow of innovation and people and the communication between the network sites. Their roles are therefore: the isolated factory, the receiver factory, the hosting network player, and the active network player. This approach would be rather suitable for what the authors call "internal information and knowledge network".

A third approach we would like to briefly address is the typology of Vokurka and Davis (2004) who focus on the assigned product and process structure. Their site roles are: the standardizer, the customizer, and the automators.

Based on Ferdows' site role portfolio, we developed a management framework for the construction of a site role portfolio. Both, strategic reason for a site and the site competence are visualized in this framework and constitute the role of the site within the network. The hexagonal game board shape comprises Ferdows' three strategic site roles on its edges, which also enables a position in a between-area as a combination of two strategic site reasons. To visualize the competence of the sites, concentrically arranged layers with different shades of gray are used. Each layer represents a different level of competence. The specific set of competences and the corresponding amount of layers may be pre-defined for each network. Our generic site role portfolio is based on the assumption that competences are bundled in three sets: low competence, average competence and high competence (see Fig. 30.2). A qualitative competence evaluation of the network sites can be a suitable approach when defining the competence level. Other approaches may include a qualitative analysis of the sites with help of a matrix analysis.

Further information for educated management decisions can be visualized with the framework (see Fig. 30.3). The site is represented by a token on the board, defined through its strategic reason and its type. The size of the token indicates the production capacity installed at the site whereas the inner ring indicates the utilized capacity. Therefore, overcapacities or upcoming overloads can be easily detected.

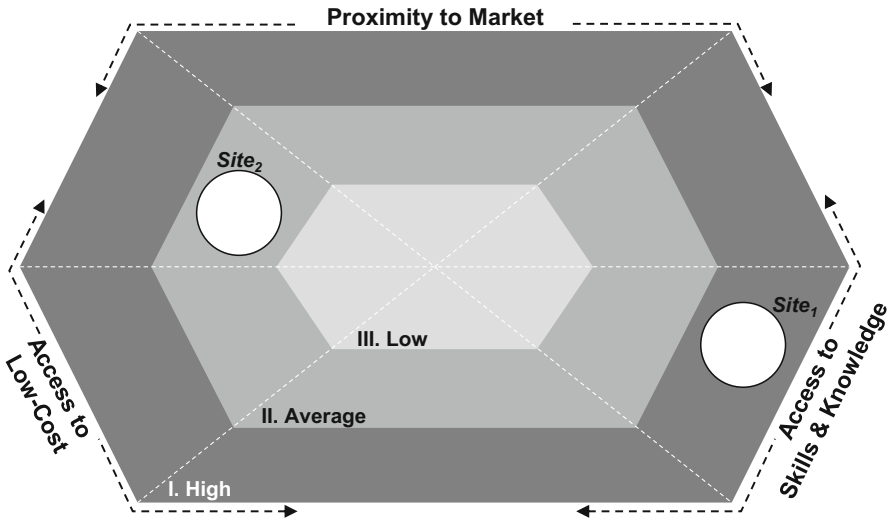


Fig. 30.2 Generic site role portfolio (Friedli et al. 2013)

Another information displayed in the framework could be the processes actually performed by each site. Each performed process or activity is outlined by a segment of a specific shade or pattern within the inner ring of the token. Since pharmaceutical sites typically perform the whole range of manufacturing activities, one might also use this option to indicate the variety of produced products or provide other site specific information. In some cases we indicate the processes performed by the site for the whole network with a star (Mundt 2012).

The following case study of a European manufacturing network illustrates the use of our site role framework. The case study represents the outcome of an 18 months long project with the Profile Ltd. This company is a polymer processing producer of plastic profiles. Production is focused on high volume products, hence, the company is process driven.

Example 1.1. The first step when mapping the site role portfolio of the Profile Network was the evaluation of the sites within the network with the site type matrix (Fig. 30.4). To describe the bandwidth of competences performed by the sites, eight processes were identified and hierarchically ordered (x-axis). There were two kinds of processes: four technology levels (as bundles of manufacturing processes for different types of products, e.g. basic products, commodity products, standard products, and prime products) and four operations processes, e.g. ramp-up and logistics. Technology level 3 and 4 are currently the same since level 4 is not yet defined. Therefore, all sites perform technology level 3 or higher. With the evolution of the sites, further competences are added successively and context-dependent. The y-axis displays the strategic importance of the sites, calculated as product of production volume multiplied with the singularity of their products manufactured and technology applied multiplied with their contribution to the network in terms of processes wherefrom other sites can benefit. The eight sites

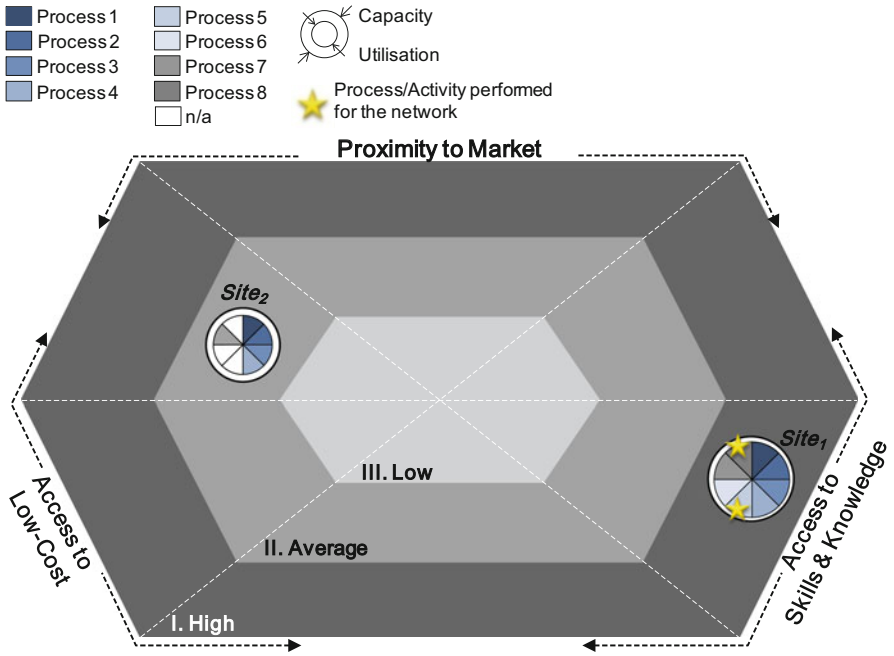


Fig. 30.3 Generic site role portfolio with extended information (Friedli et al. 2013)

are evaluated and categorized accordingly in the matrix – their site type can then easily be derived. The four site types (prime sites, leverage sites, critical sites, and basic sites) reflect the set of competences and the importance of the site within the network and are company-specific for the Profile Ltd.

Example 1.2. In combination with the strategic site reason, the position of the sites in the site role portfolio (Fig. 30.5) was determined. The concentrically arranged four layers of the board represent the four different site types – each consisting of a different level of strategic importance of the site (as the network's dependence on this very site) and the bandwidth of competences performed by the site, as described above.

The board also provides defined target zones for the lead factory, start-up sites, and standard sites, indicated by highlighted areas on the board. These target zones are company-specific and were evaluated in discussions with the network management.

In the case of the Profile Ltd. network, site 6 is a special site. It was once established to enter the North American market but with only limited manufacturing competencies. After several years it got stuck on its evolution from a start-up site to a standard site. A targeted market break-through did not happen to be successful, hence the sites is characterized by large over capacities (Mundt 2012).

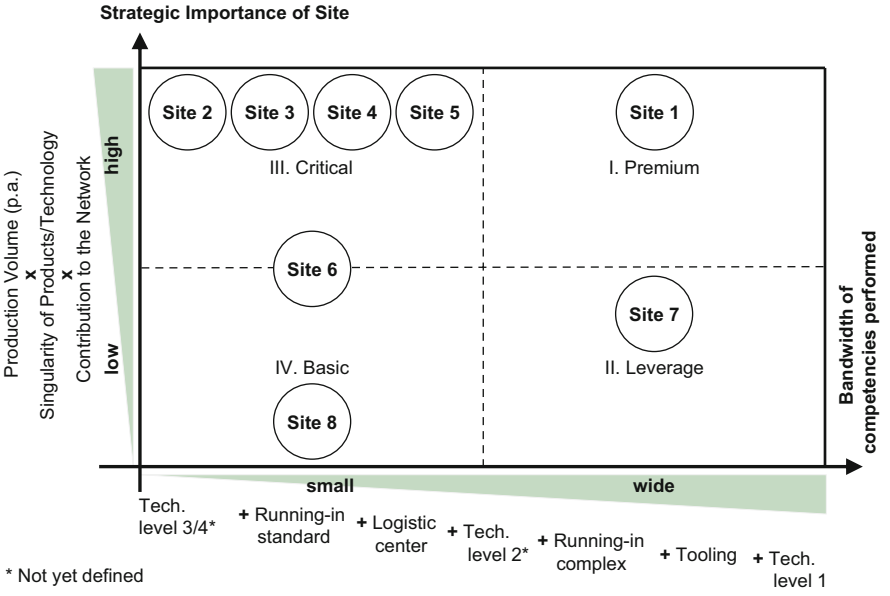


Fig. 30.4 Site type matrix for the profile network (Mundt 2012)

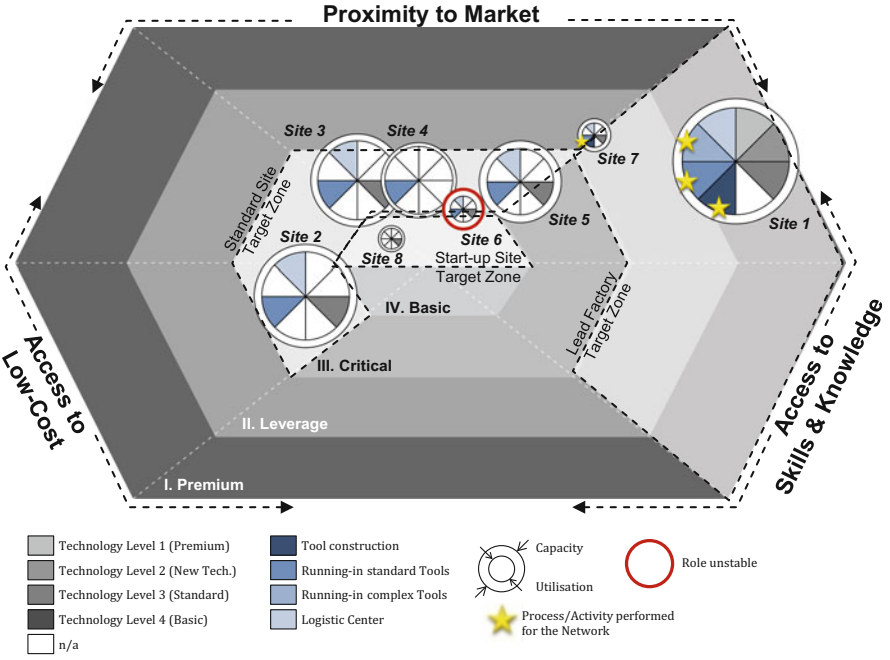


Fig. 30.5 Site role portfolio of the profile network (Friedli et al. 2013)

An important question, especially in the context of pharmaceutical companies, aims at the scope of the network. It is obvious that assigning strategic site roles amongst the own production sites is a necessity when starting to organize the manufacturing network. Nevertheless, besides company internal production sites, there might be sites producing for the network that are not under direct management of the company, e.g. contract manufacturing organizations (CMOs). Although these manufacturers are not part of the network discussed here, their respective sites should also be considered when mapping the site role portfolio for the manufacturing network. One of our project partners for example only operated four company internal production sites but directly accessed approximately 60 external first tier production sites with respective strategic reasons and specific sets of competences.

Centralization and Standardization Framework

After defining the site role portfolio for the network, each network site was connected to its very role. This leaves us with the question about the interaction of the sites within the network – that is, the interaction between the sites and the headquarters. In the first case, sites can behave either competitive (e.g. competing with each other for scarce resources for example) or cooperative (e.g. cooperate with each other when sharing resources for example). In general, four institutional levers to foster the organizational interplay of the network's units can be distinguished. These are: (1) centralization and standardization, (2) resource allocation and sharing, (3) the incentive system, and (4) sharing of information and knowledge (Mundt 2012).

The decisions made to influence centralization and standardization in the network determine the degree of autonomy within the network (Maritan et al. 2004) and (Feldmann and Olhager 2009b). When centralizing decision authority in the organization, this restricts the sites' autonomy and decisions tend to be made for the benefit of the organization as a whole, which rather suppresses different needs in respective parts of the organization. On the other hand, decentralization of authority leads to redundancies and inefficiencies but takes individual needs more into account than centralized organizational forms. Additionally, organizations with decentralized authority and high decision autonomy at site level are often quicker to adjust to local customer or market needs.

Standardization, as a second decision area, is also assumed to influence the degree of autonomy of the network's units: "Intuitively, standardization of processes gives headquarters the opportunity to retain parental control, even if their execution is decentralized" (Mundt 2012).

The benefit of clearly defined degrees of autonomy (decomposed in standardization and centralization) within the network are linked to what we said before: Firstly, several network capabilities can only be realized when the network's parts are adequately defined (e.g. production mobility can only be

achieved when certain processes and/or products are standardized). Secondly, efficient management of the network is directly linked to transparency of the network's units and therefore making the status quo of the network transparent and discussable is a beneficial task. Thirdly, centrally defining the network's configuration reduces contradicting and – on network level – suboptimal particular interests of the individual sites (decentralized interests with local rationality). The beneath described framework for mapping and discussing the degree of centralization and standardization, and therefore shaping the autonomy of the manufacturing network's units, helps operation managers when aiming at the above mentioned targets. Furthermore, inconsistencies in the current state of the network are made visible and the mapped status quo can serve as a starting point when designing the future condition of the network. Mundt (2012) explicitly stated to this:

> The centralization and standardization framework provides managers with an aggregated perspective on the allocation of authority and the degree of autonomy in their network. This is necessary since the responsibility areas cannot be considered independent; changing one might affect the position of another. Thus, instead of limiting the scope to single processes, systems, or decisions, the holistic view of the framework enables to understand the linkages between the responsibility areas/categories.

To define the degree of autonomy within the network, we consider three responsibility areas as crucial decision areas that have to be positioned in the framework: systems, decisions, and processes. Centralization depends on the allocation of these responsibility areas within the network.

Hence, the y-axis reaches from "central unit" to "each site individually" which indicate the organizational unit that carries the responsibility for each respective area. Depending on the organizational structure of the network, other levels can be added like a region or a subset of sites. Standardization on the other hand, is displayed on the x-axis, representing different levels with respect to the responsibility area. Firstly, for systems, under which we subsume the activities derived from Porter's Value Chain, we consider the degree of formalization and implementation across the network. The levels reach from individual and heterogeneous tools to standardized and homogeneous tools in the network. Secondly, decisions address the organization (strategy, structure, roles and manufacturing-related IT decisions), products (Make-or-Buy, responsibilities, transfer prices), and processes, technology, and capacity (selection, allocation, and capacity development). The levels represent a rising degree of standardization, from no or only local standardization over documented rules and guidelines to audited processes and routines and finally standardized tools and methods. Thirdly, processes include strategic processes (e.g. strategic sourcing and logistics, long-term sales and operations planning) as well as operative processes (supply-chain planning, short-term production planning and scheduling, and pure manufacturing and operations processes). The level of standardization is, similar to the responsibility area of the decisions, evaluated on the x-axis from documentation of processes over auditioning and controlling to implementation in IT systems, which limits process variations. Hence, decisions and processes share the same x-axis whereas systems are linked to the second x-axis in Fig. 30.6.

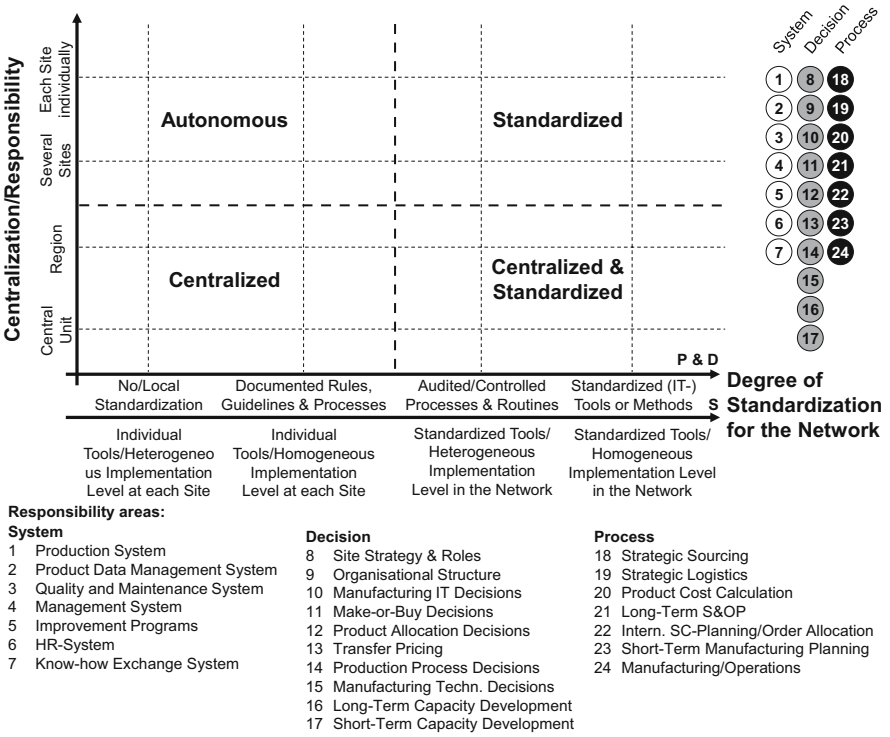


Fig. 30.6 Generic framework "centralization and standardization" (Friedli et al. 2013)

In addition to the three responsibility areas and their corresponding axis, the framework promotes four generic network positions as combinations of the two dimensions centralization and standardization like a typical portfolio matrix would do. These four network positions are:

- Centralized Network: Main responsibilities at central levels but only with limited standardization. Typically younger or emerging networks or networks shifting from decentralization to centralization – with responsibilities already shifted towards central units but standardization still lagging behind – occupy this position.
- Centralized and Standardized Network: Often stems from the Centralized Network where standardization was consequently implemented. Processes and decisions are regulated through formal guidelines and control structures whereas systems are homogeneously rolled out across the individual sites. Typically established and centralized networks with hierarchical structures occupy this position.
- Autonomous Network: Antithesis to the Centralized and Standardized Network: responsibilities are assigned to the sites and only little standardization guides

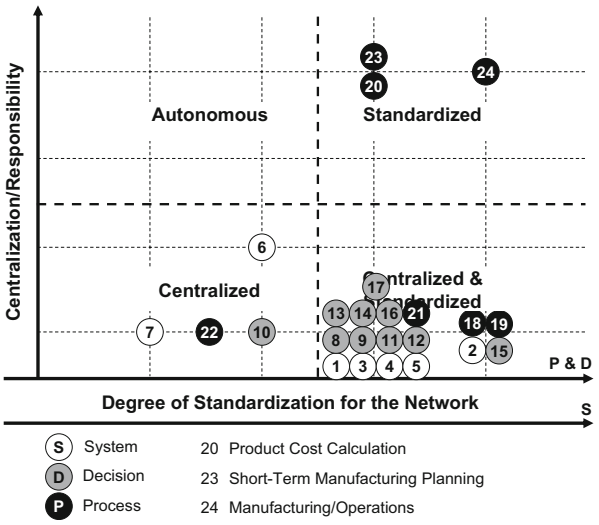


Fig. 30.7 Centralization and standardization framework in the profile network (Mundt 2012)

their actions. High degree of decentralization. Suitable for world factories or local-for-local production sites.

- Standardized Network: Standardization as mean of parental control over decentralized organization units. Execution of processes and making of decisions are carried out by sites with respect to rigid central guidelines and standards. Process discipline of the sites is a mayor challenge.

Example 2. We applied the framework to the production network of the Profile Ltd. in joint workshops and discussions with the network management. Figure 30.7 represents the results of our work and draws the picture of a strongly centralized and standardized network. System-related activities are dedicated to either the central business division or the superordinate corporate unit. Roll-outs are typically carried out top-down, from the central unit across the network. Naturally, strategic decisions are made solely on central levels.

The manufacturing sites of the network play the role of extended work benches. Hence, their responsibilities are strictly limited to scheduling and production tasks only (processes 20, 23, 24). Nevertheless, the sites conduct these processes in accordance with the centrally defined and controlled guidelines. This rigorous standardization and tight control of processes and technologies enable the manufacturing resources (i.e. extrusion lines and blue-collar workers) to be highly mobile. Within only 2 weeks, the resources can be transferred from one site to another and put in operation at the new site. This is only possible due to a highly standardized product that is barely adapted to local needs. Additionally, process discipline within the network is enabled by the strong hierarchical culture and mind-set of the employees.

The context of pharmaceutical companies is heavily shaped by externally enforced regulations and guidelines setting rigid standards for the whole value creation process, from regulation for research over guidelines for clinical trials to certification of manufacturing processes and beyond. Hence, pharmaceutical companies typically occupy a network position with a relatively high degree of standardization. Nevertheless, we encourage managers to actively challenge previous assumptions and make the status quo of the network transparent. Questioning established configurations of the network which are not touched by regulations and re-defining the degree of autonomy within the network may unlock latent potentials or lead to more efficient or expedient responsibility structures.

Information and Knowledge Sharing Framework

Sharing of information and knowledge within a manufacturing network often happens to be a challenge in everyday business. In several industry projects, operation managers reported difficulties concerning, for example, the flow of information about successful practices within the network. Sharing information and knowledge is also important for good management. Transparency about production volumes for example enables load leveling in the network. Increased data quality in general enables managers in making well informed decisions. Nevertheless, it is crucial to note that it might be strategically worthwhile to avoid complete transparency within the network. Some information or knowledge can be sensitive for the company and therefore only be accessible to a limited and very strictly controlled target group whereas other are deliberately excluded from this information. One example could be information that is not shared with employees in countries with low safety standards concerning intellectual property.

Chew et al. consider information sharing in manufacturing networks as the main coordination mechanism. Accordingly, they find the management of information flows as important as the management of the flows of physical goods between sites (Chew et al. 1990). To support operation managers in designing the network flows of information and knowledge, Mundt developed the management framework presented in Chap. 20, Fig. 20.2. We have described this framework there.

To map the status quo of the information and knowledge sharing within their manufacturing network, operation managers would evaluate the current exchange structure and the degree of transparency for the respective information and knowledge categories. Evaluating the exchange structure, information and knowledge might flow either from plant to plant (decentralized exchange), from plant to network with central coordination (centralized coordination), in a mixture of both (centralized and decentralized), or from the center to the plant (centralized provision) with the center as single source for creation and promotion of information and knowledge. The centralized and decentralized position can be willfully intended or reflect a current transition process from an either centralized to decentralized exchange structure or vice versa. The degree of transparency indicates the sites' access to information and knowledge available in the network.

When designing the to-be constitution of the network, the future exchange structure is determined according to the intended degree of autonomy within the network. The degree of transparency then is defined with regard to the intended degree of parental control over sites and therefore the amount of central power to manipulate the sites' activities. The gap between status quo and the designed to-be network draw necessary development paths for the network.

Example 3. When discussing the information and knowledge sharing in the manufacturing network of the Seals Ltd., a typical example of the isolation position was the result. Financial performance data (5) and product innovations (10) are collected or provided in a centrally coordinated manner. In other categories there is only little exchange of information or knowledge which is rooted in the historical development of the network with a strong focus on independent and autonomous market area plants. Hence, product changes and improvements (11) as well as innovations in technology and processes (12) are mainly anchored decentralized. This leads to severe barriers and makes global and centrally controlled product quality and process standards almost impossible. However, the management faced problems when moving both categories into a transparency position (Fig. 30.8).

According to Yu-Chung et al. pharmaceutical companies work in knowledge intensive environments. Therefore, knowledge management should be a high priority on their agenda. Managing their knowledge effectively, such companies can "accumulate core knowledge, build corporate intelligence and gain a competitive edge." The authors define knowledge management as "a managerial activity which develops, transfers, transmits, stores, and applies knowledge, as well as providing the members of the organization with real information to react and make the right decisions, in order to attain the organization's goals." The authors identified the strategy and organizational culture as most critical aspects for adopting a knowledge management system in pharmaceutical companies (Yu-Chung et al. 2005). With regard to these findings, operation managers in pharmaceutical companies should consider the two dimensions when applying the framework and pay attention to potential influential factors, e.g. impact of cultural factors on willingness to share information and knowledge within the network. As mentioned above, avoiding knowledge or information drain might be a critical task to accomplish when working in knowledge intense environments. Especially under the impression of increasing product piracy network managers must prescribe the overall direction of how to handle information and knowledge in cooperation with the relevant decision makers.

Resource Allocation Framework

Each network site depends on the resources it has access to. At the same time, some resources might be scarce in the network and thus subject to competition or cooperation between the sites for those resources. Some sites possess or have

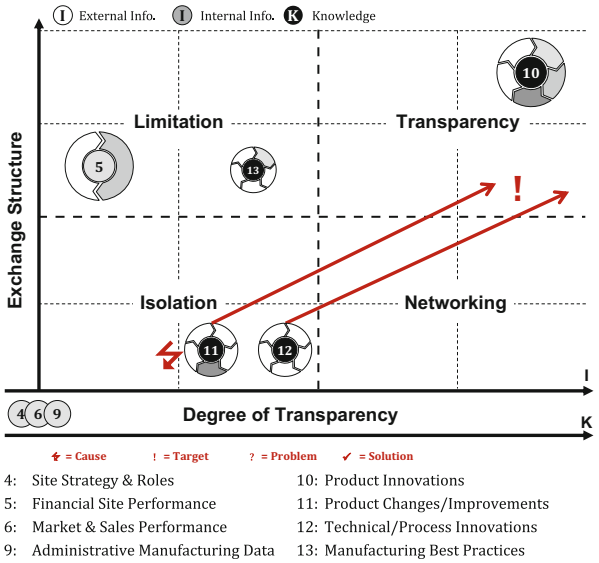


Fig. 30.8 Framework "information and knowledge sharing" in the seals network (Mundt 2012)

power over resources, whereas other sites are dependent on those resources and therefore stay in a certain relation to the possessing sites. This constellation extensively affects the relationship between the network sites and can – on the one hand – lead to conflicts between them. On the other hand, a surplus of resources means high capital commitment which negatively affects performance indicators like ROI and overall efficiency. Nevertheless, it might be of strategic importance to ensure a certain degree of overcapacity for seasonal or unexpected demand peaks. Whatever the individual pathway is, making the resource situation within the network transparent and discussible is an important task for network coordination.

The intensity of resource sharing (x-axis) and the resources scarcity in the network (y-axis) are represented in the resource allocation framework developed by Mundt. Both decision dimensions define the resource strategy of the manufacturing network and therefore deeply shape the sites' interactions. Different resource categories (1–6) of the network have to be evaluated and positioned in the framework, according to their scarcity in the network and their degree of sharing between the network's sites. Sharing can be physical (e.g. through moving machinery or people) or non-physical (e.g. through granting access to resources). The ratio of resource possessing and demanding sites is reflected by the size of the tokens which represent the resource categories (see Fig. 30.9).

For each network, a company-specific refinement or extension of the resource categories might be necessary. The framework provides four generic network positions:

- Dedication: Resources are available in sufficient amount and allocated at almost each requiring site. Especially networks with mainly autonomous and market-responsive sites follow this strategy, so would world factories, which serve

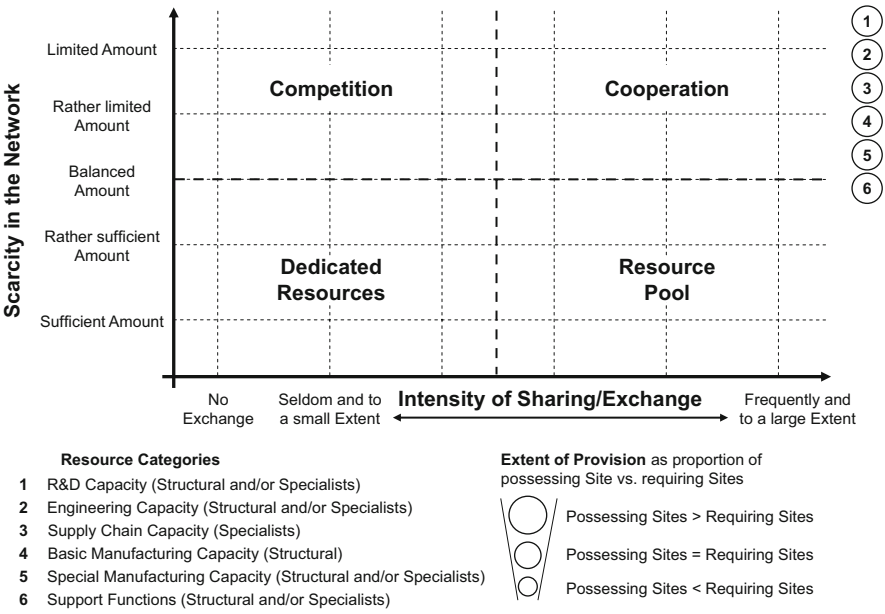


Fig. 30.9 Generic framework "resource allocation" (Friedli et al. 2013)

global markets with short and unstable planning horizons. Sharing is often not possible since resources are specifically tailored to the specific needs of the respective sites. This strategy comes along with high capital intensity but speaks in favor of a customer focus.

- Competition: Resource sharing is limited and resources are dedicated to the distinct sites. The overall amount of resources in the network is limited and not sufficient; hence, resources are scarce, either intended through limited availability or in favor of economic aspects. This scarcity leads to competition especially between sites with similar structures. Competition arises for the initial allocation of resources or for their usage. Such mechanisms can be used as levers for the network management.
- Cooperation: Similar to the competition strategy, cooperation only provides insufficient amount of resources to the network. However, resource sharing between the sites attenuates competition. Often, coordination of resource sharing is assigned to a central unit. Although this strategy can be implemented willingly, resources also might get trapped in this position when seasonal peaks or times of economic growth outrage availability.
- Resource Pool: Bundled resources are available to all requiring network sites. This strategy is coined by high intensity of sharing (by moving resources or granting access to fixed assets). Due to sufficiently available resources, neither competition nor cooperation is necessary. This strategy calls for a systematic pricing system, to allocate usage-based costs of resource sharing amongst the network sites.

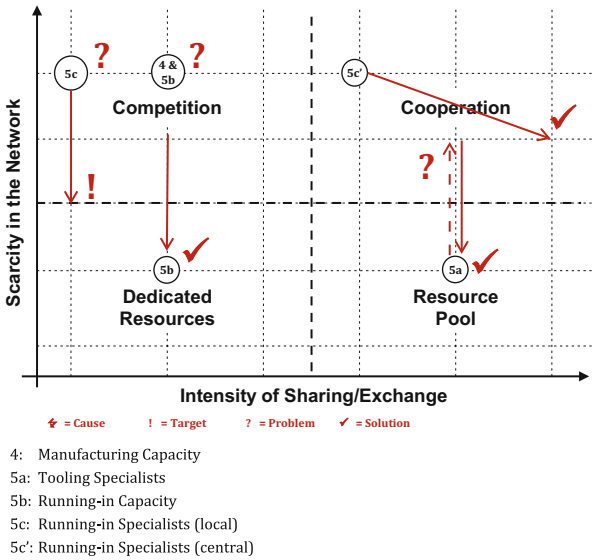


Fig. 30.10 Framework "resource allocation" in the profile network (Mundt 2012)

Example 4. When discussing the future tooling strategy for the manufacturing network of the Profile Ltd. the framework was used for the mapping and redesign. Tooling requires three types of resources: Engineers for tool construction (5a), capacities for tool testing and ramp-up at the local sites (5b) and experienced ramp-up specialists (5c and 5c′). The tool construction is a resource already pooled at a global unit providing this service to the network sites. The ramp-up processes are carried out at the local sites on the very extrusion lines which cover daily business. Hence, production (4) and ramp-up capacity (5b) stress the same resources. Ramp-up specialists are specially qualified and experienced local operators (5c) which sometimes are supported by a task force at the central unit (5c′). Now, several problems arise from this set-up. Due to increasing internal demand, tool construction capacities will run short, soon. Seasonal peaks in customer demand lead to over usage of local production capacities, which in turn negatively affect ramp-up capacity. This puts the ramp-up specialists under severe pressure. Management decided on the following changes: A new IT-support and process improvement will enable the central unit to increase efficiency. Strictly separating production and ramp-up capacities at the local sites through distinct extrusion lines for the ramp-up changes the position of this resource to dedication. Increasing the amount of ramp-up specialists at the central unit will balance the unstable demand for this resource and facilitate sharing (see Fig. 30.10).

Pharmaceutical companies are mainly process driven hence show some similarity with the Profile Ltd. Just like our example company, process competences are a key element in the manufacturing strategy. Accordingly, establishing a centralized unit which holds all process competences to support the network sites in the

cooperation position might be a suitable scenario for such companies. The concept with global launch sites is quite close to this approach.

Incentive System Framework

Using incentives to underpin targets is a common measure when motivating network sites for an intended behavior. The incentive system is a crucial lever when shaping the sites' interplay between cooperation and competition. Since operations management used to focus on individual sites rather than taking the network perspective, current incentive systems often only address goals on site-level and set incentives depending on individual performance rather than agreeing on common goals and linking them with achievements of a set of sites or the network as a whole. It is important to mention that several configuration and coordination mechanisms in the network can be supported or be negatively affected by the incentive system.

Targets on site level can foster competition whereas targets on network level with a common goal can have beneficial effects on cooperation between sites (Bartol and Srivastava 2002). Linking the rewards to individual site performance (e.g. bonus tied to site performance) can positively affect competition between sites. Allocating rewards to equal parts between sites would rather foster a culture of cooperation. Both target setting and reward allocation are represented in the incentive system framework depicted in Fig. 30.11 on the y-axis and the x-axis respectively. It differentiates the organizational level for which the targets are set ranging from the single site to a group of sites or the whole network. But also organizational levels above the network can be operationalized, e.g. a division to which the network belongs or the whole company can be organizational units that targets are set for. When mapping or designing the allocation of rewards, operation managers choose between site-oriented allocation, tying the reward to the site's individual performance, or commonly shared allocation, sharing the reward amongst all sites or a group of sites independent of their respective individual performance (see Fig. 30.11).

The relevant performance categories are mapped in the framework depending on the level on which targets are agreed on and the allocation of rewards (i.e. either based on individual performance or to equal parts). Performance categories can be subdivided into specific performance measurements, e.g. operational performance comprises lead time, inventory levels, or overall equipment efficiency and others. Each performance category must be linked to an adequately chosen reward type. While financial payments (i.e. bonus) appear to be well-known and widely applied, other types of reward can be beneficial. Luo for example suggests fostering knowledge sharing and best practice exchange with rewards such as "increased percentage of retained earnings, name recognition as an excellence center or global champion, higher autonomy dedicated by corporate headquarters, and greater resource support for future operations" (Luo 2005). Three different kinds of rewards are considered in the framework: (1) financial payments, (2) reputation

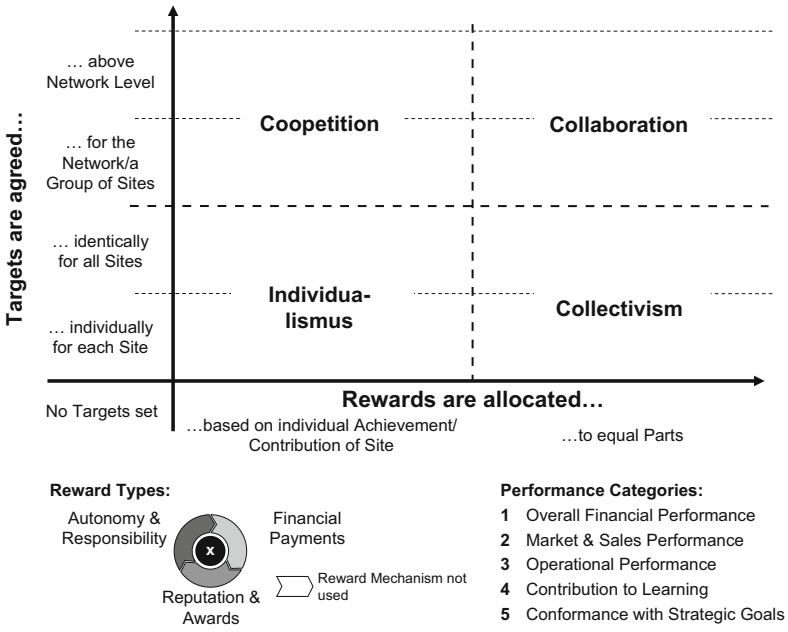


Fig. 30.11 Generic framework "incentive system" (Friedli et al. 2013)

and awards, and (3) autonomy and responsibility. The incentive system framework leads to four network positions:

- Individualism: Targets are agreed on site level and rewards are allocated depending on the sites' performance. Site-related targets are set for plants with different products and processes. Focus lies on outcome-related performance and targets give site managers clear directions for the sites evolvement.
- Collectivism: Targets are agreed on site level, too. However, rewards are allocated equally and without consideration of the sites' individual performance, it is the overall achievement of all sites that counts Often, central support functions are found in this position. The functions provide services to the network sites which they could not afford by themselves, hence is financed via a fee every site pays.
- Collaboration: Targets are agreed above site level, e.g. for a group of sites or even the whole network or above network level. Like in the collectivism position, rewards are allocated equally and independently of site performances. Group targets are expected to have positive effects on cooperation, innovation sharing and knowledge exchange. The risk of free-riding can be mitigated through high transparency and traceability of sites' contributions and through keeping the group of sites small.
- Coopetition: Targets are agreed on group level. To further mitigate the risk of free-riding, rewards are allocated – at least partially – depending on the

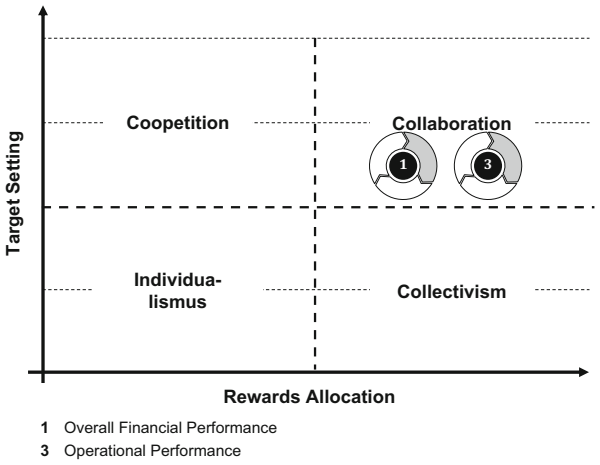


Fig. 30.12 Framework "incentive system" in the floor care network (Mundt 2012)

individual site performance as contribution to the group target. Cooperation is a key element when achieving the group target. Nevertheless, competition evolves from the sites' willingness to achieve a high individual reward.

Example 5. The manufacturing network of the Floor Care Ltd. illustrates the usage of the collaboration position to actively foster cooperation between the network sites. Some of the sites perform relatively weak whereas some are outperforming the weak sites by far. Therefore, operational (3) and financial performance targets (1) are set separately for these site groups as group targets, i.e. the same targets are valid for all sites (see Fig. 30.12). The rewards of the high-performing sites, however, are tied to the progress of the weaker sites. With this constellation outperformers are encouraged to actively support the weak sites while the weak sites are encouraged to accept this support.

As performance measurement and management is one of the most frequently discussed topics in operations management, a multitude of publications has been written with only the few of them being broadly recognized (cf. Marr and Schiuma 2003; Taticchi et al. 2010; Braz et al. 2011; Nudurupati et al. 2011; Bititci et al. 2012; Gopal and Thakkar 2012). However, it is commonly agreed upon that performance measurement and management systems should comprise diverse performance measures which are balanced between financial and non-financial aspects and qualitative and quantitative measures and that those measures should be connected to overall strategy (Nudurupati et al. 2011; Bititci et al. 2012; Gopal and Thakkar 2012).

One of the main challenges occurring when trying to implement strategic goals is that the achievement of those goals is often hard to measure. For example if strategically knowledge sharing and collaboration are important for a production network, setting goals and measuring the achievement of those goals based on data

is very difficult. Often, defined measures are just a proxy for the overall goal dimension (e.g. number contributions to a knowledge database or number of collaborative meetings held). These measures do not cover the identification with those strategic performance dimensions sufficiently.

One of our former project partners, the PharmaCorp Ltd., implemented a target and incentive system that addresses performance dimensions besides financial performance dimensions. These performance dimensions are hard to grasp and measure. The dimensions, which were equally binding for all production sites, had a focus on site as well as network level. The performance dimensions were:

- Corporate Support
- Culture
- Integration
- Structures for fostering continuous improvement
- Processes for process innovations
- People engagement
- Management Commitment

These performance dimensions are further broken down into specific performance success factors and underpinned with performance measures and targets where possible. However, not all dimensions are measurable. Therefore, the sites are asked to formulate and describe the degree of goal achievement. This description of goal achievement along with the performance in measurable dimensions is regularly reviewed and discussed between the sites and network management. In this discussion the network management reviews these self-assessments and contrasts the sites' evaluation with their own assessment reports. The performance of the different sites is compared to the performance of all other sites and a ranking is transparently communicated by central network management.

The important learning from this example is that performance does not always have to be measured with current quantitative performance measures in all performance dimensions. Instead a performance measurement and management systems can serve as a basis for internal interaction, discussion and learning. This is in line with recent contributions to scientific literature (cf. Micheli and Manzoni 2010; Bititci et al. 2012). A performance measurement and management system can serve as means of communication for production strategy. By setting performance dimensions strategy is communicated. The evaluation and comparison against other sites in the network allows deriving rewards based on the individual achievement of the sites in goals that are set above site level and are possibly hard to measure.

Summary and Implications for Pharmaceutical Companies

This article provided readers with some insights into the topic and current challenges of global manufacturing networks. The introduced management frameworks provide operation managers as well as top management with easy to

use approaches for the illustration and discussion of coordination aspects in their manufacturing networks. These frameworks will help addressing the strategic and operational challenges that arose with the evolution of manufacturing networks. In this chapter, the application of these frameworks is illustrated with some examples from previous projects and field experiences gathered in the course of the last years. However, the transfer of these frameworks into pharmaceutical manufacturing networks has not been done, yet. The most beneficial aspect of these frameworks is the fact that they can be used to clearly describe, illustrate and communicate manufacturing strategy and its application. The definition of site roles and the assignment of connected competences and tasks sharpen the vision of manufacturing networks and allow the establishment of collaboration above site level within manufacturing networks. It will be mandatory for the pharma industry to go a step further in its strive for continuous improvement and introduce a manufacturing network management, optimizing from a network perspective. The existing OPEX structures are in the driver seat for taking over this responsibility as they already have to balance site and corporate objectives globally.

References

Bartol KM, Srivastava A (2002) Encouraging knowledge sharing: the role of organizational reward systems. J Leader Organ Stud 9(1):64–76

Bititci US, Garengo P, Dörfler V, Nudurupati S (2012) Performance measurement: challenges for tomorrow. Int J Manag Rev 14(3):305–327

Brandenburger AM, Nalebuff BJ (1996) Cooperation, 1st edn. Currency Doubleday, New York

Braz RGF, Scavarda LF, Martins RA (2011) Reviewing and improving performance measurement systems: an action research. Int J Prod Econ 133(2):751–760

Chew WB, Bresnahan TF, Clark KB (1990) Measurement, coordination and learning in a multiplant network. In: Kaplan RS (ed) Measures for manufacturing excellence. HBS Press, Cambridge, pp 129–162

Diethelm R (2013) Der Süden ist der neue Motor der Weltwirtschaft. *Tages-Anzeiger*, 15 March, p. 10 (Accessed 15 Mar 2013)

Feldmann A, Olhager J (2009a) Bundles of site competences in defining plant roles. Working paper. Linköping University, Department of Management and Engineering, Linköping

Feldmann A, Olhager J (2009b) Plant roles and decision-making in manufacturing networks. Paper presented at the 16th international annual EurOMA convergence, Göteborg, 14–17 June 2009

Ferdows K (1997) Making the most of foreign factories. Harv Bus Rev 75(2):73–88

Friedli T, Thomas S, Mundt A (2013) Management globaler Produktionsnetzwerke. Hanser, Munich

Gopal PR, Thakkar J (2012) A review on supply chain performance measures and metrics: 2000–2011. Int J Productivity Perform Manage 61(5):518–547

Harre J, Moya-Quiroga R (2012) Footprints into the future. McKinsey

IFPMA (2012) The pharmaceutical industry and global health, Facts and figures 2012. IFPMA, Geneva

Luo Y (2005) Toward coopetition within a multinational enterprise: a perspective from foreign subsidiaries. J World Bus 40(1):17–90

Malik K (2013) Human development report 2013: The rise of the global south - human progress in a diverse world. United Nations [S.l.], New York

Manyika J et al (2012) Manufacturing the future: the next era of global growth and innovation. McKinsey Global Institute, McKinsey Operations Practice. McKinsey & Company, San Francisco

Maritan CA, Brush TH, Karnani AG (2004) Plant roles and decision autonomy in multiplant networks. J Operations Manag 22:489–503

Marr B, Schiuma G (2003) Business performance measurement: past, present and future. Manag Decis 41(8):680–687

Micheli P, Manzoni J (2010) Strategic performance measurement: benefits, limitations and paradoxes. Long Range Plann 43(4):465–476

Mundt A (2012) The architecture of manufacturing networks – integrating the coordination perspective. Dissertation, University of St.Gallen, St.Gallen

Nudurupati S, Bititci U, Kumar V, Chan F (2011) State of the art literature review on performance measurement. Comput Ind Eng 60(2):279–290

Taticchi P, Tonelli F, Cagnazzo L (2010) Performance measurement and management: a literature review and a research agenda. Measuring Bus Excellence 14(1):4–18

Vereecke A, Van Dierdonck R (2002) The strategic role of the plant: testing Ferdows's model. Int J Operations Prod Manag 22(5):492–514

Vereecke A, Van Dierdonck R, De Meyer A (2006) A typology of plants in global manufacturing networks. Manag Sci 52(11):1737–1750

Viñals J (2012) Global financial stability report: restoring confidence and progressing on reforms. International Monetary Fund (IMF), Washington, DC

Vokurka RJ, Davis RA (2004) Manufacturing strategic facility types. Ind Manag Data Syst 104 (6):490–504

Yu-Chung H, Shi-Ming H, Quo-Pin L, Mei-Ling T (2005) Critical factors in adopting a knowledge management system for the pharmaceutical industry. Ind Manag Data Syst 105(2):164–183

Zhan J (2012) World investment report 2012: towards a new generation of investment policies. United Nations, Geneva

Appendix

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7, © Springer-Verlag Berlin Heidelberg 2013

Benchmarking Project
Operational Excellence in the Pharmaceutical Industry

Pharmaceuticals Questionnaire

The project

Since 2004, the Institute of Technology Management at the University of St.Gallen (ITEM-HSG), Switzerland and the Transfer Center for Technology Management at the University of St.Gallen (TECTEM), Switzerland are conducting an international research project in the Pharmaceutical Industry in the field of Operational Excellence. This continuous benchmarking project deals with the implementation of Lean Thinking and other basic principles of Operational Excellence in the Pharmaceutical Industry. The results provide participating companies with the opportunity to position their production sites against a broad range of pharmaceutical production sites and show possibilities to improve productivity, quality and reduce lead time by implementing principles of Lean Manufacturing. Therefore, the survey analysis will provide a solid basis for conclusions for the participating sites. The following questionnaire is part of this project and aims to collect data from pharmaceutical sites worldwide.

Your commitment

Your participation is vital to the success of this unique study. Filling out the questionnaire takes about 60 minutes. The time to collect the data (e.g. performance indicators) differs from company to company.

Your benefits

The questionnaire and corresponding personalized analysis have been developed in cooperation with leading pharmaceutical companies under supervision of Professor Dr. Friedli. This will:

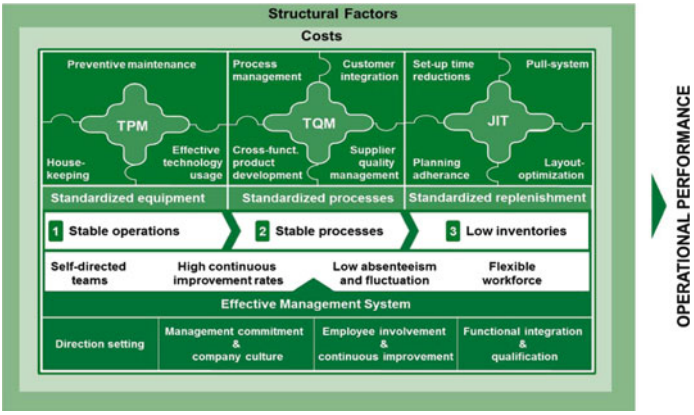
- help you to position your operational performance against approximately 150-200 other production sites.
- show you the extent of the implementation of Lean Manufacturing practices at your production site.
- and provide you insight into the most successful companies worldwide with regard to performance and enablers.

The confidentiality of the data

The benchmarking project will be conducted according to the International Benchmarking Code of Conduct, that ensures ethical activities of all participants. The company data will be handled with upmost discretion. Company-specific data will not be used without prior approval of the respective company.

Thank you very much for your participation !

Please find below our overall OPEX model that has been used to structure this survey!



How to complete the form:

	Please enter text
	Please click the appropriate box(es)
☐	- multiple answers allowed
○	- only one answer possible

If you have any additional questions concerning the project please contact:

Transfer Center for Technology Management, University of St.Gallen (TECTEM)
Institute of Technology Management, University of St.Gallen (ITEM-HSG)
Dufourstrasse 40a
CH-9000 St.Gallen

Nikolaus Lembke
nikolaus.lembke@unisg.ch
Tel.: +41 (0)71 224 72 71
Fax: +41 (0)71 224 73 11

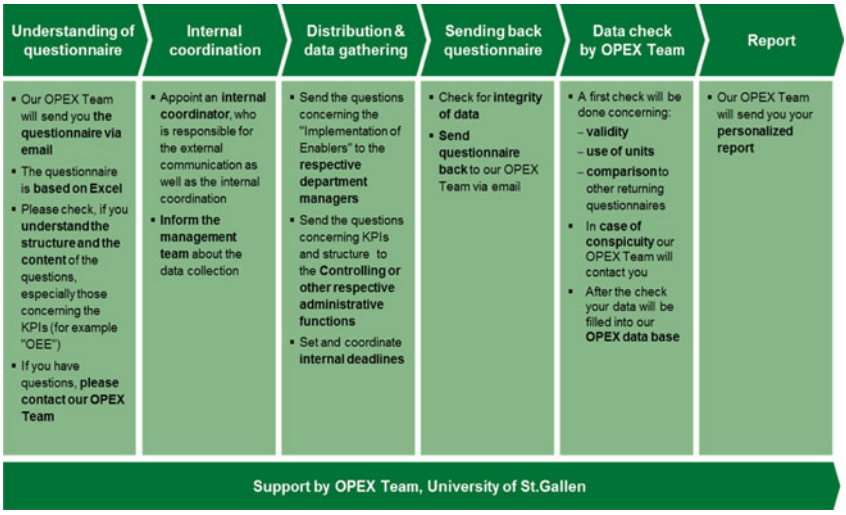
Daniel Bellm
daniel.bellm@unisg.ch
Tel.: +41 (0)71 224 72 69
Fax: +41 (0)71 224 73 11

To the questionnaire

http://www.opexbenchmarking.com

Data gathering

Please find below a figure showing you the optimal process of data gathering. This process ensures that every participant has the same understanding of the concept and the specific questions. Therefore, expressive and consistent conclusions can be drawn. Furthermore, the proposed proceeding helps you to coordinate the timeline for the data gathering process and to meet the schedule.



To the questionnaire

http://www.opexbenchmarking.com

General Information

	Contact information		
_01	Last name		
_02	First name (s)		
_03	Position or role		
_04	Company name		
_05	Production site		
_06	Telephone		
_07	Fax		
_08	E-mail		
_09	Address		

	Please fill in the year your data is valid for.		
_10	Year		

	Please fill in the currency the following answers are based on.		
_11	Currency		

proceed

YOUR COMPANY

A. Corporate Level

	How many production sites does your company have?		
A01	Number		

	What was your total sales in the last year?		
A02	**In millions**		

	Please fill in the cost structure of your company as a percentage of sales (approximate figures are sufficient).		
A03	R&D		
A04	Manufacturing costs		
A05	General & administration costs		
A06	Sales & marketing costs		
A07	Net profit		
A08	Total	**0%**	

	Compared to your competitors, indicate the development of your company on the following dimensions within the last 3 years.						
		Significantly lower		Average		Significantly higher	Don`t know
A09	Market share	○	○	○	○	○	○
A10	Sales growth	○	○	○	○	○	○
A11	Return on sales	○	○	○	○	○	○
A12	Launches of new promising products	○	○	○	○	○	○
A13	Share price	○	○	○	○	○	○

	Company type	
	Please indicate your company type (yes/ no). Multiple answers are possible!	
A14	Pharmaceutical company with R&D	○ yes ○ no
A15	Generics manufacturer	○ yes ○ no
A16	Contract manufacturer	○ yes ○ no
A17	Biotechnology	○ yes ○ no
A18	Miscellaneous	

Site Role

If your site is part of a manufacturing network, does the site have a specific role within this network? Multiple answers are possible!

A19	We have a manufacturing network.	○ yes	○ no				
		No competence		Average		High competence	Don`t know
A20	Launch site	○	○	○	○	○	○
A21	Special technology	○	○	○	○	○	○
A22	Special capacity size	○	○	○	○	○	○
A23	High packaging and production flexibility	○	○	○	○	○	○
A24	Access and entrance to markets	○	○	○	○	○	○
A25	Close to regional technology clusters	○	○	○	○	○	○
A26	Follow-the-customer	○	○	○	○	○	○
A27	Low cost site	○	○	○	○	○	○
A28	Securing of raw material sources	○	○	○	○	○	○
A29	Development site	○	○	○	○	○	○
A30	Back-up site (redundancy/ capacity)	○	○	○	○	○	○
A31	No special site role	○ yes	○ no				

proceed

YOUR SITE

B. Type of production site

	Planned improvements of the manufacturing strategy at your site					
	Indicate the degree of emphasis which your manufacturing plant places on the following ***future*** *activities.*					
		No activities planned		Activities planned	Key activities	Don`t know
	Increase of flexibility					
B01	Reduce cycle time	○	○	○	○	○
B02	Reduce set-up time and cleaning time	○	○	○	○	○
B03	Increase flexibility to respond to demand changes in volume	○	○	○	○	○
B04	Increase flexibility to respond to market needs for broad product mix (concerning package size, concentrations, flavors etc.)	○	○	○	○	○
B05	Increase flexibility to respond to shorter product lifecycles and higher number of product launches	○	○	○	○	○
B06	Accelerate new product introductions (scale-ups)	○	○	○	○	○
	Increase quality					
B07	Reduce process variance through statistical process control	○	○	○	○	○
B08	Increase supplier quality performance	○	○	○	○	○
B09	Reduce scrap rates	○	○	○	○	○
	Increase service level					
B10	Reduce lead time (lead time: time from raw material to finished goods incl. all kinds of process steps)	○	○	○	○	○
B11	Increase on-time delivery rate	○	○	○	○	○
	Reduce costs					
B12	Reduce stock	○	○	○	○	○
B13	Increase asset utilization (e.g. machines)	○	○	○	○	○
B14	Increase employee productivity	○	○	○	○	○
B15	Increase capital investment productivity	○	○	○	○	○

	Indicate how your production site is organized.	
B16	○ Cost-center	○ Profit-center

	Indicate the proportion of products manufactured at your plant (%) in the last year.				
		Synthetic products	Phytopharmaceuticals	Bio-technological products	Other products
B17 a-d	IP - protected products				
B18 a-d	Not IP - protected products				
B19 a-d	Contract manufacturing				
				Sum	0.00%

	Number of products in the last year		
B20	Number of different market products produced at your plant		
B21	Number of different formulations produced at your plant		
B22	Number of different SKUs produced at your plant		
B23	Number of different technologies/ platforms used at your plant		

	Procurement and supplier structure in the last year			
	*Supplier count: number of **active** suppliers both internal and external*			
		API	Excipients	Packaging material
B24 a-c	Number of active suppliers for…			
B25 a-c	Total amount purchased **(in millions)** of…			
B26	Overall number of active suppliers in the supplier base			
B27	Percentage of internal suppliers			
B28	Percentage of suppliers that deliver your site frequently			
B29	Frequently means on average every … days.			
B30	Number of orders placed with your suppliers			

	Sourcing by regions (primary the location of production, not the registered office/ in %) in the last year		
B31	Western Europe		
B32	North America		
B33	Eastern Europe		
B34	South America		
B35	Middle East		
B36	India		
B37	China		
B38	Rest of the world		

	Production structure		
		Unit	Measure
B39	Amount of API produced at your site in the last year	Kg	
B40	Percentage of API produced at your site that was processed for own production	%	
	Indicate the volume of bulk goods produced at your site in the last year.		
B41	Solid forms (tablets, capsules etc.)	Pieces	
B42	Liquids	Liter	
B43	Sterile liquids	Liter	
B44	Semi solid forms (creams etc.)	Kg	
	Indicate the total volume of bulk goods that was packed at your site in the last year.		
B45	Solid forms (tablets, capsules etc.)	Pieces	
B45 a	- thereof packed in blisters	Pieces	
B45 b	- thereof packed in bottles	Pieces	
B46	Liquids	Liter	
B46 a	- thereof packed in amps	Liter	
B46 b	- thereof packed in vials	Liter	
B47	Sterile liquids	Liter	
B47 a	- thereof packed in amps	Liter	
B47 b	- thereof packed in vials	Liter	
B48	Semi solid forms (creams etc.)	Kg	
	Indicate the number of packed units (boxes for sale) at your site in the last year.		
B49	Solid forms (tablets, capsules etc.)	Packed units	
B50	- average packaging size	Pieces	
B51	Liquids	Packed units	
B52	- average packaging size	Liter	
B53	Sterile liquids	Packed units	
B54	- average packaging size	Liter	
B55	Semi solid forms (creams etc.)	Packed units	
B56	- average packaging size	Kg	

	Batch & campaign structure in the last year			
		API	Formulation	Packaging
B57 a-c	Number of batches produced in the last year			
B58 a-c	Number of campaigns in the last year			
	Indicate the batch size range min to max			
B59 a/b	Formulation/ pelleting *(in kg)* min		max	
B60 a/b	Packaging units (*in units*) min		max	

	Vertical integration of manufacturing in the last year		
	Indicate the number of different process steps performed at your site (e.g. granulate, pelleting, packaging, etc. - e.g. 20% of the products run through 1 process step, the remaining 80% of the products run through 4-8 process steps, i.e. 20%/ 80%/ 0%)		
B61	Less than 4 operating procedures		
B62	4-8 operating procedures		
B63	More than 8 operating procedures		
	Please name the single process steps executed at your site by adding or deleting steps in the list provided.		
B64	Chemical API: Weighing, grinding, mixing, synthesis, filtration, crystallization, sieving, drying, centrifuging. Solids: Weighing, dispensing, kit preparation, sieving, blending, granulation, drying, compacting, coating, capsuling, primary packaging, end-packaging, labeling. Liquids: Weighing, dispensing, kit preparation, dose WFI, solution preparation, mix, filtration, wash/sterilize, filling & stopping, lyo-philization, capping, primary packaging, end-packaging, labeling.		

	Innovation structure		
B65	Number of new drug introductions within the last 3 years ("new drugs" should be understood in the sense of new for the site)		
B66	Number of launched formats/ stock keeping units (SKU) at the site within the last 3 years		
B67	Number of inspections at site within the last 3 years from…		…regulatory body
B68			…headquarters
B69			…customer

	Age of production technology in the last year		
B70	Percentage of machines which are less than 3 years old		
B71	Percentage of machines that are between 3 and 5 years old		
B72	Percentage of machines that are between 6 and 10 years old		
B73	Percentage of machines that are older than 10 years		

	Level of automation in the last year		
B74	Percentage of machines that are manually operated		
B75	Percentage of machines that are operated with IT-support		
B76	Percentage of machines that are fully automated (without supervision)		

	Implementation of electronic batch records in the last year	
B77	Completely ○ ○ ○ ○ ○ Not at all	

	Customer structure in the last year		
B78	Overall number of customers		
B79	Percentage of internal customers		
B80	Percentage of customers delivered frequently		
B81	Frequently means on average every … days.		
B82	Number of orders received from your customers		

	Customers by regions (primary the location of delivery, not the registered office/ in %) in the last year		
B83	Western Europe		
B84	North America		
B85	Eastern Europe		
B86	South America		
B87	Middle East		
B88	India		
B89	China		
B90	Rest of the world		

	History of the plant	
B91	The plant is an original plant and was founded by the company itself	○ yes ○ no
B92	The plant was acquired during a merger or acquisition…	○ …within the last 3 years ○ …within the last 3-10 years ○ …more than 10 years ago

proceed

C. Cost and headcount structure of the plant

To ensure the comparability of the production sites it is important that you just fill in the figures that are related to the manufacturing part of your site. In case that you also have part of your R&D, Sales, Marketing etc. at your site, please list costs related to those functions under "Other costs".

	Please indicate the non-consolidated sales of your production site in the last year.		
C01	**In thousand**		

	Cost of Goods Sold (COGS) in the last year		
	On the income statement, the cost of purchasing raw materials and manufacturing finished products. Equal to the beginning inventory plus the cost of goods purchased during the last year minus the ending inventory.		
C02	**In thousand**		

	Cost structure in the last year				
C03	Please indicate the accounting principles on which the data is based (e.g. US GAAP).				
	The total of the following costs should add up to the COGS!				
	Name	Definition	Unit	Measure	
	Material costs				
C04	Direct material costs	Cost for raw materials and preliminary products.	**thousand**		
C05	Indirect material costs	Cost for operating supplies as well as services.	**thousand**		
	Labor costs				
C06	Direct labor costs	Cost for employees directly involved in manufacturing and quality labs (see also FTE structure below).	**thousand**		
C07	Indirect labor costs	Cost for plant employees whose time is not charged to specific finished products (see also FTE structure below).	**thousand**		
	Plant, property and equipment costs				
C08	Costs for machines & tools	Cost for machines, equipment, tools, spare parts including costs for depreciation, electricity for the machines etc.	**thousand**		
C09	Costs for property and plant	Cost for property and plant including costs of depreciation and other costs for electricity, water etc.	**thousand**		
	Other costs				
C10	Corporate allocations	Cost for corporate expenses charged to the plant.	**thousand**		
C11	Other costs	Cost for e.g. Sales & Clerical, Marketing, R&D located at the dedicated plant.	**thousand**		
			Sum	0.00	
C12	Maintenance costs	Total maintenance cost includes both - internally and externally- rendered services, also cost for spare parts and consumables used for maintenance.	**thousand**		
C13	Preventive maintenance cost	Cost for planned and condition-based maintenance activities.	**thousand**		
C14	Cost of quality	Overall costs for quality assurance (usually the total number from your cost center(s) QC/ QA).	**thousand**		
C15	Rework cost	Cost due to rework.	**thousand**		
C16	Destruction cost	Cost due to destruction.	**thousand**		

	Headcount structure		
	Please include all FTEs working at your site independent from being on your payroll.		
C17	***Direct labor***	***0***	
C18	Production labor	API production	
C19		Pharmaceutical production	
C20		Packaging	
C21	Quality control	Testing ("taking samples") incoming	
C22		Testing ("taking samples") product testing	
C23		Batch review and approval	
C24	***Indirect labor***	***0***	
C25	Quality control	Testing ("taking samples") management	
C26		Laboratories management	
C27		Environmental monitoring	
C28		Stability testing	
C29	Quality assurance	Validation of process, equipment and method	
C30		Quality planning	
C31	Maintenance	Reactive (Fire fighting)	
C32		Basic Care (e.g. lubrication, cleaning)	
C33		Preventive (calendar based exchange of parts)	
C34		Predictive (condition based exchange of parts)	
C35		Other	
C36	Other functions	Production management	
C37		Materials management (procurement and logistics)	
C38		Manufacturing engineering	
C39		EH&S (environment, health and safety)	
C40		IT-support	
C41		Miscellaneous (HR, finance, management)	
C42	***Overall number of FTEs at the site***	**0**	

	Employment structure		
C43	Percentage of FTEs permanently employed by the company		
C44	Percentage of FTEs temporarily employed by the company		
C45	Percentage of FTEs temporarily employed by a temp agency		

proceed

D. Total Productive Maintenance System

Please indicate to which degree the following statements apply to your plant!

	Preventive maintenance	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
D01	We have a formal program for maintaining our machines and equipment.	○	○	○	○	○	○
D02	Maintenance plans and checklists are posted closely to our machines and maintenance jobs are documented.	○	○	○	○	○	○
D03	We emphasize good maintenance as a strategy for increasing quality and planning for compliance.	○	○	○	○	○	○
D04	All potential bottleneck machines are identified and supplied with additional spare parts.	○	○	○	○	○	○
D05	We continuously optimize our maintenance program based on a dedicated failure analysis.	○	○	○	○	○	○
D06	Our maintenance department focuses on assisting machine operators perform their own preventive maintenance.	○	○	○	○	○	○
D07	Our machine operators are actively involved into the decision making process when we decide to buy new machines.	○	○	○	○	○	○
D08	Our machines are mainly maintained internally. We try to avoid external maintenance service as far as possible.	○	○	○	○	○	○

	Technology assessment and usage	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
D09	Our plant is situated at the leading edge of new technology in our industry.	○	○	○	○	○	○
D10	We are constantly screening the market for new production technology and assess new technology concerning its technical and financial benefit.	○	○	○	○	○	○
D11	We are using new technology very effectively.	○	○	○	○	○	○
D12	We rely on vendors for all of our equipment.	○	○	○	○	○	○
D13	Part of our equipment is protected by the firm`s patents.	○	○	○	○	○	○
D14	Proprietary process technology and equipment helps us gain a competitive advantage.	○	○	○	○	○	○

	Housekeeping	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
D15	Our employees strive to keep our plant neat and clean.	○	○	○	○	○	○
D16	Our plant procedures emphasize putting all tools and fixtures in their place.	○	○	○	○	○	○
D17	We have a housekeeping checklist to continuously monitor the condition and cleanness of our machines and equipment.	○	○	○	○	○	○

proceed

E. Total Quality Management System

Please indicate to which degree the following statements apply to your plant!

	Process management	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
E01	In our company direct and indirect processes are well documented.	○	○	○	○	○	○
E02	We continuously measure the quality of our processes by using process measures (e.g. On-time-in-full delivery rate).	○	○	○	○	○	○
E03	Our process measures are directly linked to our plant objectives.	○	○	○	○	○	○
E04	In our company there are dedicated process owners who are responsible for planning, management and improvement of their processes.	○	○	○	○	○	○
E05	A large percentage of equipment on the shop floor is currently under statistical process control (SPC).	○	○	○	○	○	○
E06	We make use of statistical process control to reduce variances in processes.	○	○	○	○	○	○
E07	For root cause analysis we have standardized tools to get a deeper understanding of the influencing factors (e.g. DMAIC).	○	○	○	○	○	○
E08	We operate with a high level of PAT implementation for real time process monitoring and controlling.	○	○	○	○	○	○

	Cross functional product development	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
E09	Manufacturing engineers (e.g. Industrial engineers) are involved to a great extent in the development of a new drug formulation and the development of the necessary production processes.	○	○	○	○	○	○
E10	In our company product and process development are closely linked to each other.	○	○	○	○	○	○
E11	Due to close collaboration between the R&D and the manufacturing department, we could significantly shorten our time for product launches ("scale-ups") in our plant.	○	○	○	○	○	○
E12	For the last couple of years we have not had any delays in product launches at our plant.	○	○	○	○	○	○
E13	For product and process transfers between different units or sites standardized procedures exist, which ensure a fast, stable and complied knowledge transfer.	○	○	○	○	○	○

	Customer involvement	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
E14	We are frequently in close contact with our customers.	○	○	○	○	○	○
E15	Our customers frequently give us feedback on quality and delivery performance.	○	○	○	○	○	○
E16	We regularly survey our customer`s requirements.	○	○	○	○	○	○
E17	We regularly conduct customer satisfaction surveys.	○	○	○	○	○	○
E18	On time delivery is our philosophy.	○	○	○	○	○	○
E19	We jointly have improvement programs with our customers to increase our performance.	○	○	○	○	○	○

	Supplier quality management	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
E20	Quality is our number one criterion in selecting suppliers.	○	○	○	○	○	○
E21	We rank our suppliers, therefore we conduct supplier qualification and audits.	○	○	○	○	○	○
E22	We use mostly suppliers that we have validated.	○	○	○	○	○	○
E23	For a large percentage of suppliers we do not perform any inspections of the incoming parts/ materials.	○	○	○	○	○	○
E24	Inspections of incoming materials are usually performed in proportion to the past quality performance or type of supplier.	○	○	○	○	○	○
E25	Basically, we inspect 100% of our incoming shipments.	○	○	○	○	○	○
E26	We jointly have improvement programs with our suppliers to increase our performance.	○	○	○	○	○	○

proceed

F. Just in Time System

Please indicate to which degree the following statements apply to your plant!

	Set-up time reduction	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
F01	We are continuously working to lower set-up and cleaning times in our plant.	○	○	○	○	○	○
F02	We have low set-up times for equipment in our plant.	○	○	○	○	○	○
F03	Our crews practice set-ups regularly to reduce the time required.	○	○	○	○	○	○
F04	To increase the flexibility, we put high priority on reducing batch sizes in our plant.	○	○	○	○	○	○
F05	We have managed to schedule a big portion of our set-ups so that the regular up-time of our machines is usually not effected.	○	○	○	○	○	○
F06	Optimized set-up and cleaning procedures are documented as best-practice process and rolled-out throughout the whole plant.	○	○	○	○	○	○

	Pull production	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
F07	Our production schedule is designed to allow for catching up, due to production stoppings because of problems (e.g. quality problems).	○	○	○	○	○	○
F08	We use a pull system (kanban squares, containers or signals) for production control.	○	○	○	○	○	○
F09	We mainly produce according to forecasts.	○	○	○	○	○	○
F10	Suppliers are integrated and vendors fill our kanban containers, rather than filling our purchasing orders.	○	○	○	○	○	○
F11	We value long-term associations with suppliers more than frequent changes in suppliers.	○	○	○	○	○	○
F12	We depend on on-time delivery from our suppliers.	○	○	○	○	○	○
F13	We deliver to our customers in a demand-oriented JIT way instead of a stock-oriented approach.	○	○	○	○	○	○
F14	We mainly produce one unit when the customer orders one. We normally do not produce to stock.	○	○	○	○	○	○

	Layout optimization	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
F15	Our processes are located close together so that material handling and part storage are minimized.	○	○	○	○	○	○
F16	Products are classified into groups with similar processing requirements to reduce set-up times.	○	○	○	○	○	○
F17	Products are classified into groups with similar routing requirements to reduce transportation time.	○	○	○	○	○	○
F18	The layout of the shop floor facilitates low inventories and fast throughput.	○	○	○	○	○	○
F19	As we have classified our products based on their specific requirements our shop floor lay-out can be characterized as separated into "mini-plants".	○	○	○	○	○	○
F20	Currently our manufacturing processes are highly synchronized over all steps by one tact.	○	○	○	○	○	○
F21	Currently our manufacturing processes from raw material to finished goods involve almost no interruptions and can be described as a full continuous flow.	○	○	○	○	○	○
F22	At the moment we are strongly working to reach the status of a full continuous flow with no interruption between raw material to finished goods.	○	○	○	○	○	○
F23	We use "Value Stream Mapping" as a methodology to visualize and optimize processes.	○	○	○	○	○	○

	Planning adherence	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
F24	We usually meet our production plans every day.	○	○	○	○	○	○
F25	We know the root causes of variance in our production schedule and are continuously trying to eliminate them.	○	○	○	○	○	○
F26	To increase our planning adherence we share data with customers and suppliers based on a rolling production plan.	○	○	○	○	○	○
F27	We have smoothly leveled our production capacity throughout the whole production process.	○	○	○	○	○	○
F28	Our plant has flexible working shift models so that we can easily adjust our production capacity according to current demand changes.	○	○	○	○	○	○
F29	A smoothly leveled production schedule is preferred to a high level of capacity utilization.	○	○	○	○	○	○

proceed

G. Management System

Please indicate to which degree the following statements apply to your plant!

	Direction setting	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
G01	Our production site has an exposed site vision and strategy that is closely related to our corporate mission statement.	○	○	○	○	○	○
G02	Our vision, mission and strategy is broadly communicated and lived by our employees.	○	○	○	○	○	○
G03	Goals and objectives of the manufacturing unit are closely linked and consistent with corporate objectives. The production site has a clear focus.	○	○	○	○	○	○
G04	The overall objectives of the production site are closely linked to the team or personal objectives of our shop-floor teams and employees.	○	○	○	○	○	○
G05	Our manufacturing managers (Head of manufacturing, Site-leader etc.) have a good understanding of how the corporate/ divisional strategy is formed.	○	○	○	○	○	○
G06	Our manufacturing managers know exactly what the most important criteria for manufacturing jobs are (i.e. low costs, delivery, quality etc.).	○	○	○	○	○	○

	Management commitment and company culture	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
G07	Plant management empowers employees to continuously improve the processes and to reduce failure and scrap rates.	○	○	○	○	○	○
G08	Plant management is personally involved in improvement projects.	○	○	○	○	○	○
G09	There is too much competition and too little cooperation between the departments.	○	○	○	○	○	○
G10	The communication is made via official channels.	○	○	○	○	○	○
G11	The company has an open communication culture. There is a good flow of information between the departments and the different management levels.	○	○	○	○	○	○
G12	About innovations we are informed early enough.	○	○	○	○	○	○
G13	Problems (e.g. reclamations etc.) are always traced back to their origin to identify root causes and to prevent doing the same mistakes twice.	○	○	○	○	○	○
G14	The achievement of high quality standards is primarily the task of our QA/ QC departments.	○	○	○	○	○	○
G15	Our employees continuously strive to reduce any kind of waste in every process (e.g. waste of time, waste of production space etc.).	○	○	○	○	○	○
G16	Command and control is seen as the most effective leadership style rather than open culture.	○	○	○	○	○	○

	Employee involvement and continuous improvement	The statement applies to our plant...					
		not at all		partially		completely	Don't know
G17	We have implemented tools and methods to deploy a continuous improvement process.	○	○	○	○	○	○
G18	Our employees are involved in writing policies and procedures (concerning Site Vision down to Standard Operating Procedures).	○	○	○	○	○	○
G19	Shop-floor employees actively drive suggestion programs.	○	○	○	○	○	○
G20	Our work teams cannot take significant actions without supervisors or middle managers approval.	○	○	○	○	○	○
G21	Our employees have the authority to correct problems when they occur.	○	○	○	○	○	○
G22	Occurring problems should be solved by supervisors.	○	○	○	○	○	○
G23	Supervisors include their employees in solving problems.	○	○	○	○	○	○
G24	Our plant forms cross-functional project teams to solve problems.	○	○	○	○	○	○
G25	The company takes care of the employees.	○	○	○	○	○	○
	Please indicate which of the following statements are true for your work teams						
G26	We have organized production employees into teams in production areas. For each team there is one dedicated team member that is responsible for supervisory tasks.	○ yes	○ no				
G27	We have organized production employees into teams in production areas. For team leadership we have an additional supervisory level in our organization.	○ yes	○ no				

	Functional integration and qualification	The statement applies to our plant...					
		not at all		partially		completely	Don't know
G28	Each of our employees within our work teams (in case workers are organized as teams) is cross-trained so that they can fill-in for others when necessary.	○	○	○	○	○	○
G29	At our plant we have implemented a formal program to increase the flexibility of our production workers. Employees rotate to maintain their qualification.	○	○	○	○	○	○
G30	In our company there are monthly open feedback meetings.	○	○	○	○	○	○
G31	The information of these official feedback meetings is used systematically in further training.	○	○	○	○	○	○
G32	We continuously invest in training and qualification of our workers. We have a dedicated development and qualification program for our production workers.	○	○	○	○	○	○

proceed

H. Basic Elements

Please indicate to which degree the following statements apply to your plant!

	Standardization and simplification	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
H01	We emphasize standardization as a strategy for continuously improving our processes, machines and products.	○	○	○	○	○	○
H02	We use our documented operating procedures to standardize our processes (e.g. set-ups).	○	○	○	○	○	○
H03	Optimized operating procedures (e.g. shortened set-ups) are documented as best-practice processes and rolled-out throughout the whole plant.	○	○	○	○	○	○
H04	Standardized functional descriptions have reduced the period of vocational training for new employees.	○	○	○	○	○	○
H05	We use standardized machines and equipment (e.g. standardized machine design, standardized spare parts etc.) to achieve a high up time of our machines.	○	○	○	○	○	○
H06	By using standardized machines and fixtures we could significantly lower our material costs for spare parts.	○	○	○	○	○	○

	Visual management	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
H07	Performance charts at each of our production processes (e.g. packaging) indicate the annual performance objectives.	○	○	○	○	○	○
H08	Technical documents (e.g. maintenance documents) and workplace information (e.g. standardized inspection procedures, team structures) are posted on the shop floor and are easily accessible and visible for all workers.	○	○	○	○	○	○
H09	Charts showing the current performance status (e.g. current scrap-rates, current up-times etc.) are posted on the shop-floor and visible for everyone.	○	○	○	○	○	○
H10	Charts showing current takt times and schedule compliance (e.g. Andonboards) are posted on the shop-floor and visible for everyone.	○	○	○	○	○	○

	Reasons for launching Operational Excellence initiatives	The statement applies to our plant...					
		not at all		partially		completely	Don`t know
H11	To meet FDA regulations	○	○	○	○	○	○
H12	To implement Process Analytical Technology (PAT)	○	○	○	○	○	○
H13	To change from functional organization to process organization	○	○	○	○	○	○
H14	To increase cost awareness	○	○	○	○	○	○
H15	To increase employee involvement	○	○	○	○	○	○
H16	To increase employee empowerment	○	○	○	○	○	○
H17	To reduce lead times and inventory	○	○	○	○	○	○
H18	To change the quality focus from final product to process quality	○	○	○	○	○	○
H19	To initiate a cultural change for continuous improvement	○	○	○	○	○	○
H20	To introduce standardized methodologies for problem solving	○	○	○	○	○	○
H21	To launch a broader cost cutting program	○	○	○	○	○	○
H22	To improve final product quality	○	○	○	○	○	○
H23	To fulfill site targets between corporate and plant management	○	○	○	○	○	○

proceed

http://www.opexbenchmarking.com

I. Performance of the plant

Quality performance

	Name	Definition	Unit	Measure	Don't know
I01	Complaint rate (customer)	Number of justified complaints as a percentage of all customer orders delivered.	%		☐
I02	Yield	Average difference between 100% and real achieved output in pharmaceutical production due to material losses, weighting, sediments.	%		☐
I03	RFT	Total number of batches produced without document errors or exception reports as a percentage of the total number of batches produced.	%		☐
I04	Rejected batches	Number of rejected batches as a percentage of all batches produced.	%		☐
I05	Scrap rate	Average difference between 100% and real achieved output in packaging operations.	%		☐
I06	Complaint rate (supplier)	Number of complaints as a percentage of all deliveries received (from your supplier).	%		☐
I07	Release time	Average time from sampling to release of finished products including all waiting times.	Working days		☐
I08	Deviations	Number of deviations per month that arise from raw materials purchased, production components (equipment) and product/ process specifications.	Number per month		☐
I09	Deviation closure time	Average deviation closure time in days.	Working days		☐

Delivery performance

	Name	Definition	Unit	Measure	Don't know
I10	DOH	Average Inventory less write downs x 365 divided by the 'Cost of Goods Sold (COGS).	Days		☐
I11	Service level - Delivery (OTIF)	Perfect order fulfillment (percentage of orders shipped in time from your site (+/- 1 days of the agreed shipment day) and in the right quantity (+/- 3% of the agreed quantity) and right quality) **to your customer.**	%		☐
I12	Service level Supplier	Perfect order fulfillment (percentage of orders shipped in time to your site (+/- 1 days of the agreed shipment day) and in the right quantity (+/- 3% of the agreed quantity) and right quality) **from your supplier.**	%		☐

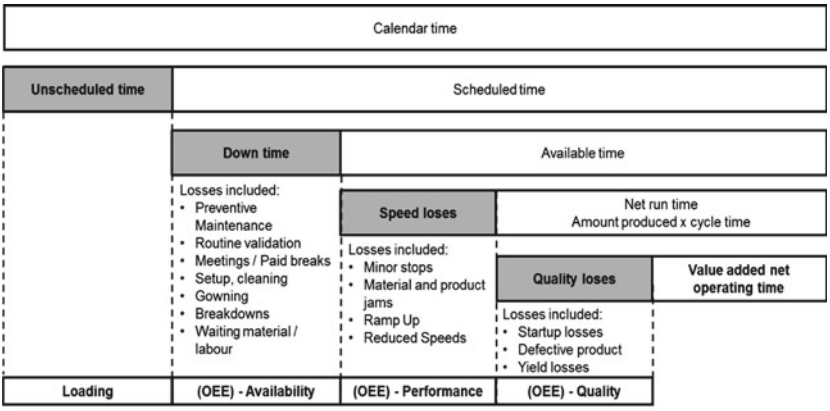
JIT performance

	Name	Definition	Unit	Measure	Don't know
I13	Forecast accuracy	Actual orders received compared to the annual sales forecast.	%		☐
I14	Production schedule accuracy	Number of released production orders as scheduled as a percentage of all production orders released within your freezing period.	%		☐
I15	Priority orders	Number of priority orders as a percentage of all orders produced.	%		☐
I16	Production flexibility upside	Freezing period in which you do not allow any changes of your production schedule.	Working days		☐
I17	Replacement time to customer	Response time for short-term delivery to the customer for goods not on stock (delivery time supplier and your production time).	Working days		☐
I18	Cycle time	Cycle time (from weighing to packaging). e.g. 30% of all products have a cycle time of 15-30 days. 70% of all products have a cycle time of more than 30 days.	< 15 days		☐
I19			15-30 days		
I20			> 30 days		
I21	Raw material turns	Annual cost of raw materials purchased divided by the average raw material inventory.	Number		☐

I22	WIP turns	Annual cost of raw materials purchased plus annual cost of conversion divided by the average work in process inventory.		Number		☐
I23	Finished goods turns	Annual cost of goods sold divided by the average finished goods inventory.		Number		☐
I24	Average order lead time	Average time between a customer placing an order and receiving delivery.		Working days		☐
			Waiting time	Production	QA/QC	Don't know
I25 a-c	Average production lead time	Average time *in days* from receiving the raw material to release of finished products in **API production.**				☐
I26 a-c		Average time *in days* from receiving the raw material to release of finished products in **pharmaceutical production.**				☐
			API	Formulation	Packaging	Don't know
I27 a-c	Average changeover time	Average time *in hours* spent between different products for setting up and cleaning the equipment.				☐
I28 a-c	Changeovers	Average number of changeovers performed per month including changing lots and changing formats.				☐

	TPM performance					
	Name	**Definition**	API	Formulation	Packaging	Don't know
I29 a-c	Setup and Cleaning	The time spend for setup and cleaning as a percentage of the scheduled time.				☐
I30 a-c	Dedicated equipment	The percentage of your equipment that is dedicated to one product.				☐
I31 a-c	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance works.				☐
			Mon - Fri	Sat	Sun	Don't know
I32 a-c	Shift-model	Number of shifts per day.				☐
I33 a-c	Shift length	Average length of one shift in hours.				☐

	Overall Equipment Effectiveness				
	If your are not sure an estimated answer is better than a field not completed!				
	in %	API	Formulation	Packaging	Don't know
I34 a-c	**Loading** = Scheduled Time / Calendar Time				☐
	*Scheduled Time - time during which the equipment was **scheduled or expected to operate** during the time period being analyzed* *Calendar Time - usually 365 days, 8760 hours*				
I35 a-c	**(OEE) Availability** = (Scheduled Time - Downtime) / Scheduled Time				☐
	*Scheduled Time - time during which the equipment was **scheduled or expected to operate** during the time period being analyzed* *Downtime - breakdowns (unplanned downtimes) + setup downtime*				
I36 a-c	**(OEE) Performance** = (Amount Produced x Ideal Cycle Time) / Available time				☐
	Amount Produced - the number of units produced during the time period *Ideal Cycle Time - the designed or optimum cycle time* *Available Time - the time the machine actually ran: scheduled time - downtime*				
I37 a-c	**(OEE) Quality** = (Input - Defects) / Input				☐
	Input - the number of units that were started through the process *Defects - the number of defective units (even if they were subsequently salvaged)*				
I38 a-c	**Overall Equipment Effectiveness** = (OEE) Availability x (OEE) Performance x (OEE) Quality	**0.00%**	**0.00%**	**0.00%**	



	Management System Performance				
	Name	**Definition**	**Unit**	**Measure**	**Don't know**
I39	Management layers	Number of management levels between production workers and the highest ranking manager at the site (e.g. Worker - Supervisor - Manager of the department - Site-leader = 4 Levels).	Number		☐
I40	Management span of control	The average number of employees directly reporting to middle management (supervisors).	Number		☐
I41	Group work	Percentage of production workers that are organized in self directed teams in terms of e.g. holiday planning and team meetings.	%		☐
I42	Functional integration	Number of production workers that are qualified to work on 3 or more technologies/functional areas as a percentage of all workers.	%		☐
I43	Suggestions (Quantity)	Average number of suggestions per employee in the last year.	Number		☐
I44	Suggestions (Quality)	Estimated total savings due to suggestions that were implemented.	**thousand**		☐
I45	Employee turnover	Employees leaving your site due to terminations, expired work contracts, retirements etc. as a percentage of all employees.	%		☐
I46	Sick leave	Total time of employees absent (e.g. sick leave) as a percentage of the total working time.	%		☐
I47	Overtime	Hours worked in paid overtime (excludes the overtime which is compensated with free time) in the last year as a percentage of the overall working time.	%		☐
I48	Training	Number of training days per employee (all kinds of training off- and on the job).	Days		☐
I49	Level of qualification	Number of workers without prior work related qualification/education as a percentage of the total number of workers at your site.	%		☐
I50	Level of safety	Reportable incidents due to accidents and safety on average per month.	Number per month		☐

You have completed the survey.

Thank you very much for your participation!

Please save the survey on your hard disk and email the file to

nikolaus.lembke@unisg.ch
daniel.bellm@unisg.ch

http://www.opexbenchmarking.com

About the Authors

Basu, Prabir K. Ph.D.

Pharmaceutical Manufacturing and CGMP Consultant

Prabir Basu is an independent consultant advising on pharmaceutical manufacturing and cGMP issues. From 2005 till June, 2013, Prabir was the Executive Director of the National Institute for Pharmaceutical Technology and Education (NIPTE) which is currently a non-profit organization supported by 13 leading universities in the U.S. NIPTE's goal is to address long-term fundamental research and education on the science of pharmaceutical development and manufacturing. As the Executive Director of NIPTE, Prabir built a strong relationship with the U.S. FDA and secured funding from the FDA for research and education programs to modernize drug manufacturing. Working with the U.S. FDA, Prabir was also able to secure a U01 Grant for NIPTE in 2011 worth up to $35 million over 5 years to improve drug manufacturing standards.

From 2004 to 2010, along with his role as Executive Director, NITPE, Prabir was also the Managing Director of the Pharmaceutical Technology Education Center at Purdue University's Discovery Park. In this role, Prabir, along with colleagues at Purdue and scientists from the industry, organized and offered various training courses on cGMP, Pharmaceutical Development and Manufacturing. Prabir, along with his colleagues at Purdue University also founded NIPTE at Purdue in 2005.

Prior to joining Purdue University, Prabir worked in the pharmaceutical industry (Pfizer, Pharmacia and Searle) for over 20 years in various capacities in research, development and manufacturing. During that period, Prabir had broad-ranging global senior management responsibilities for product development, manufacturing and outsourcing.

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7, © Springer-Verlag Berlin Heidelberg 2013

Prabir has a Ph.D. in Chemical Engineering from the University of California, Berkeley. Before joining Searle, Prabir briefly taught Chemical Engineering at the Indian Institute of Technology and worked for Unilever PLC (UK) in India for about 10 years. Prabir has co-authored over 50 journal and conference papers and 2 patents. He is a Fellow of the American Institute of Chemical Engineers.

Bellm, Daniel

Research Associate and Group Coordinator "Operational Excellence – Pharma", University of St.Gallen

Daniel Bellm is Research Associate at the chair of production management of the University of St.Gallen. As group coordinator he is responsible for the topic "Operational Excellence – Pharma". His research interests focus on the management of operational excellence programs and complexity management. He is currently working on his Ph.D.-thesis.

Daniel graduated in Business Engineering (Dipl.-Wi.-Ing.) at the Karlsruhe Institute of Technology (former University of Karlsruhe (TH), Germany). During his studies, Daniel worked at the Porsche AG (Germany), MTU Friedrichshafen (Germany), Porsche Asia Pacific Pte. Ltd. (Singapore), and Volkswagen Consulting (Germany).

Nuala Calnan

Regulatory Science Researcher, Pharmaceutical Regulatory Science Team, Dublin Institute of Technology (DIT), Ireland

Nuala has over 20 years experience in the pharmaceutical industry with a strong technical background in new facility design, start up and regulatory consultancy. Her industry roles include Leo Pharma, Elan, Wyeth BioPharma (Pfizer) and PM Group as Principal Life Science Consultant. Through these various roles she has developed a detailed operational knowledge of the pharmaceutical regulatory/cGMP environment and has been involved in preparing several facilities for FDA and IMB inspections.

In addition to her career experience Nuala has been involved with the ISPE since 1996 and has held committee positions at Irish affiliate, European and International Board level. She was a member of the Author Task Team which produced the ASTM E2500-07 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment. A member of the team which recently wrote the ISPE Guide for Science and Risk Based Approach for the delivery of Facilities, Systems & Equipment and the Good Practice Guide for Applied Risk Management for Commissioning & Qualification.

She holds a B.Sc. Eng and an M.B.A. and is currently working on her Ph.D. in Regulatory Science, researching the impact of the new science and risk based lifecycle approaches on the manufacturing sector of the pharmaceutical industry.

Crossman, Andy

Director of Network Performance Strategy, Pfizer

Andy Crossman is Director of Network Performance Strategy for Pfizer Pharmaceuticals Global Consumer Healthcare and External Supply Operating Units. He has 25 years experience in the industry. He is a trained Black Belt and expert in Organizational Change and Transformation. Andy has dual master degrees in International Relations and Business Management. He resides in Vermont. He has worked in nutritionals, biologics, pharmaceuticals and consumer businesses.

Davis, Richard

Senior Director – Network Performance Intelligence Lead, Network Performance, Pfizer Global Supply

Rich is currently the Network Performance Intelligence lead in the Network Performance group in Pfizer Global Supply. Rich is responsible for working with PGS leadership to identify, prioritize, and conduct external and internal benchmarking to find best-in-class practices, capabilities, and performance targets driving operational focus and continuous improvement. Rich also has extensive experience

in manufacturing; Environmental, Health and Safety; and business mergers, acquisitions, and divestitures at Pfizer prior to his role in Network Performance.

Rich holds B.S. degrees in Chemical Engineering and Material Science from the University of Connecticut as well as M.B.A.'s in Manufacturing Management and Environmental Management from Rensselaer Polytechnic Institute.

Diederich, Gert

CFO, hamelnpharmagmbh

Gert Diederich was born in Darmstadt, Germany, in 1951. From 1970 until 1977 he studied Industrial Engineering and Management at the Technical University of Darmstadt. He started his career first as Internal Auditor and then department controller at Degussa AG, Frankfurt. In 1985 he became CFO of Degussa s. a. – Group, San Paulo, Brazil. 1992 he transferred to ASTA Medica AG, the pharmaceutical division of Degussa, first after the German reunion heading the controlling department of the new acquired subsidiary Arzneimittelwerk Dresden, later the controlling of the group. In 2000 he moved to BOEHRINGER INGELHEIM Pharma GmbH & Co. KG as Director of accounting and controlling. In 2009 he changed to hameln group, first assuming the role of CFO than in addition the role of CEO for the subsidiary hameln pharmaceuticals. Today he is CFO of the hameln group with the responsibility for accounting, controlling, information systems, organisational development and human resources.

During his career Gert Diederich gained broad experience in organisational development in the pharmeceutical business and state-of-the art management methods especially in the management of change. Since the beginning of his career he participated in various optimisation and change projects with and without external consultancy using organisational methods and/or state-of-the art IS-systems. At hameln pharma he introduced the organisational and cultural change from a classic hierarchic orientation to process orientation using tools and principles of operational excellence and lean management.

Docherty, Paul

Founder and Executive Director, i-nexus

Paul Docherty started his career in Marconi, where he held a wide range of senior management roles covering manufacturing, IT, sales, product development, project management, Operational Excellence and corporate strategy as well as having P&L responsibility for the growth of a regional telecoms equipment business.

His deep understanding of the challenges of establishing robust business execution disciplines comes from his experience coaching senior management teams in over 100 global organizations and from leading the deployment of a substantial Operational Excellence program at Marconi.

Paul was the founder of i-nexus in 2001, and has spearheaded its rapid expansion into the leading provider of on-demand Strategy Execution software. Paul holds a M. Eng. in Computer Systems and Software Engineering from the University of York and an M.B.A. from the University of Warwick.

Dreamer, Steve

Former Head Global Pharma Engineering & Operational Excellence, Novartis AG

At Novartis, Steve was Head of Global Pharma Engineering (GPE) and Head of TechOps Operational Excellence. GPE is responsible for providing technical and project management for the major capital investments and programs. This includes developing new sites, expanding capacity, improving processes, major programs such as Continuous Manufacturing collaboration with MIT, Product Security, QbD& PAT.

The Operational Excellence program is responsible for embedding LEAN, POO, Six Sigma and other re-engineering processes throughout the organization.

Previously, Steve helped create the first Process Oriented Organization and was appointed the first Process Team Leader in Stein.

Steve has 33 years of pharmaceutical experience. He joined Novartis in 2002 with experience in manufacturing, engineering and quality areas for Johnson &

Johnson Biologics & Diagnostics, Schering-Plough and Abbott Laboratories. Steve holds Six Sigma black belt. He has a degree in Electrical Engineering from the University of Nebraska. Steve retired from Novartis in 2013.

Eriksson, Jesper Ph.D.

Operation Excellence Specialist, Pfizer

Jesper is a Certified Master Black Belt and is currently working with the transformation of the Strängnäs Site. He has a background as a process specialist for the manufacturing of biopharmaceutical drug substances and has previously been a project team leader for the development of manufacturing processes. Jesper holds a Ph.D. in Genetics from Stockholm University.

Eriksson, Karin

Communications Lead, Pfizer

Karin works in the site Strängnäs leadership team with responsibility for strategic communication. She is also manager for site Admin team and a member of a global communications team within Pfizer Biotech. Karin holds a B.A. in Political Science and Communication from Uppsala University.

Friedli, Thomas Prof. Dr.

Managing Director TECTEM, Vice Director Institute of Technology Management, University of St.Gallen

Since 2000 Professor Dr. Thomas Friedli is a member of the Faculty of the Institute of Technology Management at the University of St.Gallen (HSG). After graduating in Business Administration he wrote his Ph.D. thesis about management of collaborations at the University of St.Gallen. In 2004 Thomas Friedli became Privatdozent and Assistant Professor at the Institute of Technology Management. As an Associate Professor, today leads a team of 14 researchers as Head of the Chair of Production Management.

Thomas Friedli's main focus is the management of industrial enterprises. His area of expertise is strategic operations management, management of industrial services and operational excellence in the pharmaceutical industry.

He was an expert for the EU in the sixth framework programme and a consultant to several major global manufacturing companies. One of his recent books is "The Pathway to Operational Excellence in the Pharmaceutical Industry".

He is teaching in several executive programmes in St.Gallen, Salzburg, Fribourg and Aachen.

Furthermore, he was a batallion comander in the Swiss Army and is still an active colonel in the staff of the chief of the army.

Gejllan, Kirsti Ph.D.

Site Leader, Pfizer

Ph.D. in Pharmaceutical technology from University of Oslo, Norway. More than 25 years of experience from Pharmaceutical industry covering Discovery, Proof of Concept, Pharmaceutical Development including early clinical phase in Humans, Quality Operations and EHS in Manufacturing.

Has worked as a Leader and Manager since 1989. Since March 2010 Site Leader in Strängnäs Sweden and Managing Director of Pfizer Health AB since August 2010

Holistic Leadership engaging people and organizations delivering high valued business results. Honored with John Mitchel Quality Award 2006 in Pfizer for being

a change agent and a renewer of quality operations leadership. Site Strängnäs was also awarded with the Swedish National Change Management Award for 2013 for the best Transformational Project.

I have had the privilege to successfully generate experience and knowledge within Discovery, Proof of Concept, Development and Manufacturing. I have always worked in several multidisciplinary environments locally and globally. The context of change has been the theme of my working life and e.g. the process of merging Astra and Zeneca, therapeutic areas, factory organizations and different disciplines into a joint organization has given me insights about transformation processes including how to secure high performance through change.

I am team-oriented and cross-functional in my approach to challenges. I enjoy adding value by bridging between disciplines, and my platform is based on the opportunity to merge business-, technology- and people aspects with the purpose of improving quality of life for human beings. My leadership style is value driven and I get energized by working in teams towards a clear vision, specified goals and communicated expectations.

Götzfried, Matthias

Strategic Board Projects, Freudenberg Sealing Technologies

Before joining Freudenberg Sealing Technologies, Matthias was working as Research Associate and Group Coordinator "Operational Excellence" at the University of St.Gallen (Switzerland). The focus of his industry and research projects was the management of complexity in product portfolios and supply chain processes supporting companies to achieve Operational Excellence.

Matthias graduated in Technology Management (Dipl.-Ing.) at the University of Stuttgart (Germany). Further, he took part in the Master's program at Rose-Hulman Institute of Technology (USA) and graduated with a M.Sc. degree in Engineering Management. During his studies, Matthias worked at the Audi AG (Quality Management), Porsche Consulting GmbH (Process Optimization) and the Fraunhofer Society (R&D Management). In 2013, Matthias achieved his Ph.D. in "Business Innovation" at the University of St.Gallen.

Gütter, Saskia

Research Associate, University of St.Gallen

SaskiaGütter is a Ph.D. student at the Institute of Technology Management at the University of St.Gallen since March 2009. Her research concentrates on the challenges of manufacturing companies with a focus on the pharmaceutical industry, especially the implementation of integrated production systems as well as operational excellence. Furthermore, she is involved in research projects regarding global manufacturing networks and collaboration concepts.

Saskia Gütter graduated in industrial engineering focused on production management, production technology and quality management at the University of Technology Ilmenau (Germany). She gained practical experience at NETZSCH do Brasil Ind. e Com. Ltda (Brazil).

Hampton, David

Director, SSA & Company

David Hampton is a Director at SSA & Company, where he provides guidance for businesses implementing all aspects of Operational Excellence. The majority of his experience over the past 10 years of consulting has been in the BioPharma industry. His manufacturing experience includes Lean Six Sigma deployment, guiding clients in the design and implementation of Lean manufacturing systems and engaging employees at all levels in problem-solving. In Research and Development he has worked to improve throughput in Drug Discovery and reduce risks in Clinical Trials. He has also trained and coached employees in commercial areas.

David is an experienced keynote speaker at Operational Excellence conferences. His published work includes two articles for Drug Discovery Today and a book on Six Sigma in non-manufacturing environments.

David holds a Master of Engineering from the University of Cambridge.

Kumor, Joseph

Global Business Excellence Manager – Operations, AbbVie

At AbbVie, Joseph Kumor manages the Business Excellence team focusing on Operations. His team is primarily responsible for business process optimization initiatives driving improvements from a supply chain perspective together with all support functions.

Joseph has over 18 years of pharmaceutical experience at Abbott. As of January 1, 2013 Joseph is an employee of AbbVie which is a spin-off company of the former pharmaceutical proprietary products division of Abbott. He has experience in environmental health and safety, manufacturing, supply chain and logistics. Joseph has a bachelor's degree in Environmental Health from Illinois State University and a master's degree in Environmental and Occupational Health from the University of Illinois at Chicago.

Lamba, Sanjit Singh

Managing Director, President-Global Brands Business unit and Global Head – Procurement Strategy at Eisai India

Sanjit Singh Lamba is the Managing Director of Eisai Pharmatechnology & Manufacturing Pvt. Ltd., India a 100 % subsidiary of Eisai Co., Ltd, Japan. With more than 23 years of pharmaceutical industry experience, he has proven adaptability with multi-cultural corporate environment while working with multinational pharmaceutical companies including Pfizer, Merck Sharp and Dohme, Lupin and Ranbaxy in various disciplines including Global Manufacturing, Projects, Global procurement and Supply Chain Management, etc. Sanjit was instrumental in setting up Eisai's state of art Integrated Manufacturing and Research Complex in India which won the Facility of the year award for 2012 by ISPE and also named in the list of one of the "100 of the Most Inspiring people" in the life science industry by PharmaVOICE magazine, USA in August 2012.

He possesses a Master's degree in Pharmaceutical Technology and is currently pursuing his Ph.D. He has undergone a successful leadership programme at Kellogg School of Management, Northwestern University, USA. He is associated with professional bodies like Indian Pharmaceutical Association, International Society for Pharmaceutical Engineers (ISPE), Parental Drug Association (PDA) as President Elect – India Chapter and Drug Information Association (DIA).

Lembke, Nikolaus

Research Associate, University of St.Gallen

Nikolaus Lembke is research associate at the University of St.Gallen, Switzerland. At the Institute of Technology Management he concentrates on the challenges of manufacturing companies. His industry and research projects focus on operational excellence in the pharmaceutical industry and the further development of lean manufacturing in organizations.

Nikolaus studied at the University of Stuttgart (Germany) as well as at the Nanyang Technological University (Singapore) and graduated in Technology Management (Dipl.-Ing.). He gained practical experience at the Siemens AG, at the Audi AG, at the Fraunhofer Institute for Manufacturing Engineering and Automation, and at MBtech Consulting.

Liebetrau, Fabian

Research Associate and Group Coordinator "Global Production Networks", University of St.Gallen

Fabian Liebetrau is working in the group responsible for the topic global production networks at the chair of production management of the University of St.Gallen. His research interests include the management and optimization of global production networks, performance measurement in global production networks and complexity management. He is currently working on his Ph.D.-thesis.

Fabian graduated in Mechanical Engineering (Dipl.-Ing.) and Business Administration (Dipl.-Wirt.Ing.) from RWTH Aachen University. His studies included a stay at the Technion Israel Institute of Technology in Haifa. During his studies, Fabian worked at ThyssenKrupp (Galvanizing) and Siempelkamp (Casting).

Lützner, Richard

Research Associate, University of St.Gallen

Richard Luetzner is a research associate at the Institute of Technology Management at the University of St.Gallen (Switzerland) since February 2013. His research focus is the management of global manufacturing networks.

Richard Luetzner graduated in Information, Media and Technology Management at the University of St.Gallen after his management studies in St.Gallen and Maastricht (Netherlands). His study focus was on production management and business innovation. After and during his studies, Richard Luetzner gained practical experience in the automotive industry and the service sector.

Mänder, Christian

Research Associate, University of St.Gallen

Christian Maender is research associate at the University of St.Gallen (Switzerland). His research at the Institute of Technology Management concentrates on the challenges faced by the pharmaceutical industry. The focus on his industry and research projects is the management of operational excellence programs.

Christian graduated in mechanical engineering with a focus on production technique at the Karlsruhe Institute of Technology (former University of Karlsruhe (TH), Germany). He gained practical experience at Mercedes-Benz Malaysia Sdn. Bhd.

McColgan, Mark

Global Director Operational Excellence & Technical Services, Takeda Pharmaceuticals International

Mark McColgan is the Global Director Operational Excellence & Technical Services of Takeda Pharmaceuticals International. He is a Certified LeanSigma Master Blackbelt and holds a Master degree in engineering, with more than 20 years of industrial Continuous Improvement experience from automotive to chemicals. From 1996 on Mark was involved in supporting OPEX in the Pharmaceutical Industry working first for GSK, joining their OPEX core team working in the field of Lean and SixSigma. In 2009 Mark joined Nycomed. Nycomed and Takeda merged in October 2011.

Mejlvang, Kasper

Vice President, Operations, Novo Nordisk Production France

Kasper Bødker Mejlvang joined Novo Nordisk in 2002, starting as HR partner in Novo Nordisk production, Product Supply. Since then, he has worked in several leadership positions, primarily in the Novo Nordisk Product Supply organisation. In 2004 he was appointed Manager of Business Support for the Diabetes API production at the time the cLEAN® implementation was launched. From this position, he moved to R&D to help optimise the CMC area with the introduction of cLEAN® as a key part of the change effort. In 2006 he was appointed Vice President for R&D Services and CMC Business Support. In 2008 he moved back to the Product Supply organisation as Corporate Vice President for one of the Insulin Manufacturing areas. During this time, several optimisation efforts took place, most significantly the introduction of a new yeast strain improving insulin production yields significantly. From 2010–2013 he was Corporate Vice President of Global Support, which includes responsibility for the continued, global implementation of cLEAN® in Product Supply. Currently, he heads up Operations at Novo Nordisk Production in France to drive the capacity expansions of the site. Kasper holds a M.Sc. in Management from University of Bath, UK and an M.Sc. Psychology from University of Copenhagen, Denmark.

Morse, Ned

Partner and Managing Director, The Boston Consulting Group

Ned Morse is a Partner and Managing Director in the Atlanta office of The Boston Consulting Group. He is a core member of the firm's People and Organization practice. He is a veteran consultant with many years experience serving clients in large-scale change programs that have successfully engaged organizations from the C-suite to the front-line.

During his career Ned has worked with over 100 clients in the oil and gas, insurance, food service, food products, consumer packaged goods, health care, defense, semi-conductor, chemical, engineering, telecommunications, pharmaceutical, retail, and manufacturing industries. Prior to joining BCG, he served in senior leadership roles at Culture/Leadership Effectiveness Partners, the Hay Group, and Aubrey Daniels and Associates.

In October 2008, John Wiley & Sons published "SwitchPoints – Culture Change on the Fast Track to Business Sucess" co-authored by Ned, which highlights this type of work. It is the detailed account of how Canadian National Railway went from being already best-in-class to what one analyst described as "the railroad with no peer anywhere in sight" and stock performance 13 times better than every other competitor.

Ned is an active speaker and author, having written and/or delivered over 300 articles, speeches, and workshops. He earned his MBA from Wharton.

Niewiarowski, Pav

Global Innovation, Quality and Productivity (IQP) Champion

At Novartis, Pav is a Global IQP Champion, responsible for develop and driving Operational Excellence Programs throughout the organization. This includes developing Operational Excellence capabilities at all levels of the organization throughout the network of production sites and global functions, through the provision of training, coaching and deployment of operational excellence improvement programs in support of business objectives.

Previously, Pav developed the Operational Excellence program at one of Novartis manufacturing sites in the UK, having also held production management responsibilities there. He joined Novartis in 2004, having previously worked in operations management consulting, predominantly in the pharmaceutical sector. He started his career working deploying Six Sigma and in production management for General Electric in the UK. Pav has a degree in Manufacturing Engineering and Management from Loughborough University of Technology in the UK. He travels extensively as part of his global role for Novartis, whilst living in Surrey in the UK, with his wife and two children.

Pfahlert, Volker Dr.

Partner, Schuh & Company Complexity Management

Dr. Volker Pfahlert was born in Minden, Germany, in 1958. He is a citizen of Germany.

From 1978 until 1982, he studied pharmacy at the University of Braunschweig, Germany. He received his Ph.D. in Pharmacology in 1986. From 1988 until 1996 he was an Associate at Mckinsey & Company and served clients in several industries e.g. Pharmaceutical industry, automotive industry, food industry or leisure industry around the world.

Between 1996 and 2007, Dr. Pfahlert held a number of leading positions in the MedTech Industry at Roche Diagnostics in different European locations. Finally he took on the role of Head of Professional Diagnostics in Rotkreuz, Switzerland. In 2007, he transferred to Drägerwerk AG, Lübeck, Germany where he became CEO of Dräger Medical AG & Co. KG. Since 2008, he has been a Patner at Schuh & Co. Complexity Management AG in Würselen, Germany.

Dr. Volker Pfahlert has gained broad experience in the field of Operational Excellence and Change Management in the MedTech industry as well as in state-of-the art methods of corporate management and leadership.

During his time at Roche Diagnostics, Dr. Pfahlert was responsible for several large scale transformation programs or post merger integration aiming for process excellence to enhance the competitiveness of the respected business.

Reimers, Kai

Senior Director of Visual Control & Packaging, hamelnpharmagmbh

Kai Reimers was born in Hameln in 1977. He is of German nationality. From 1999 to 2002, he studied Business Informatics majoring in system integration at the University of Weserbergland Hameln. After taking his degree, he joined hameln pharmaceuticals ltd. in Gloucester, the British subsidiary of pharmahameln. Apart from working on process and organizational development tasks, he was responsible for the IT integration of the local IT system into the mainframe of hamelnpharma in Germany, in particular customizing SAP application.

In 2005, Kai Reimers started working for the IT unit of the hameln group. In this function, he led several process improvement projects in the pharmaceutical manufacturing environment. In 2010, he was put in charge of the Process and Organizational Development unit of the hameln group. In this role, he was responsible for the redesign of the organization of hamelnpharmagmbh. Over the years, Kai Reimers has gained broad experience in all methods and tools of Lean management, Operational Excellence and Change management.

In 2013, he was appointed Senior Director of Visual Control & Packaging, hamelnpharmagmbh.

Kai Reimers is a lecturer at the University of Weserbergland Hameln, teaching strategic business process management and the practical application of process modeling tools.

Sandell, Kim

Director of Operations Management & Operational Excellence, Pfizer

Kim joined Pfizer in Strängnäs, Sweden, in 1999. He is currently holding a position as Operation Excellence & Operations Management lead at the site. Kim has held a range of positions at the site starting as a process engineer, moving into project lead and quality support to projects. He then resumed responsibility for the manufacturing at the site until he joined the project team for construction of a new biotech facility at the Strängnäs site. In the project Kim was responsible

for starting up the new facility including tech transfer of two new process generations for the Drug Substance of Genotropin® and Somavert®.

Kim holds an M.Sc. in chemical engineering from the Royal Institute of Technology, Sweden and an M.B.A. from Reading University, Henley Business School, UK.

Schneider, Uli

Research Associate, University of St.Gallen

Uli Schneider is Research Associate at the University of St.Gallen (Switzerland). His research at the Institute of Technology Management focuses on the challenges within the pharmaceutical industry. The foci of his industry and research projects are the integrated optimization of manufacturing and complexity management.

Uli Schneider graduated in Business Administration and Mechanical Engineering at the Technische Universität Darmstadt in Germany, EcolePolytechnique and HEC Paris in France.

Prior to his assignment he worked for PwC as consultant for automotive and industrial clients in various restructuring and strategy projects.

Seller, Colin

Colin Seller is Vice President Strategy – Network Performance and API (Active Pharmaceutical Ingredients) for Pfizer Global Supply (PGS). During the past 5 years he has been responsible for leading the progress of PGS globally on its continuing journey to high performance as a best in class internal and external supply network. In addition, since March 2013, he has been responsible for the API network structural strategy.

Colin has been in technical and operational leadership roles in the Pharma industry for 25 years. During this time he has led substantial manufacturing sites and functional activities and has been responsible for leadership of significant change, driving operational performance improvements, step changes in financial performance and most critically, shifts in the capabilities and mindsets of people in these organisations.

Colin graduated in Applied Chemistry from Leicester Polytechnic.

South, Nick

Partner and Managing Director, The Boston Consulting Group

Nick South is a Partner and Managing Director in the London office of The Boston Consulting Group. He is a core group member of the firm's Health Care and People and Organization practices.

Nick's expertise in organizational topics includes organization design, change management and aligning people strategy to business strategy – especially performance management, talent management and capability building. He has worked extensively in the pharmaceutical sector, including implementing effective organizational structures for biopharma operations clients.

Prior to joining BCG, Nick worked for 4 years at corporate communications consultancy Burson-Marsteller, leading the corporate reputation team in London. Prior to this, Nick worked for 6 years for the Leader of the UK Liberal Democrats, Paddy Ashdown MP, as political adviser, press spokesman and finally his head of office.

Nick earned his M.B.A. from INSEAD and holds a Bachelor of Arts in Modern History from Oxford University.

Starke, Valentin

Director Business Excellence, Established Pharmaceuticals Division, Abbott

Since joining Abbott in 2008, Valentin has been leading the Business Excellence team which drives process simplification, standardization and savings for the company's Operations, Commercial and Quality organizations. The team operates with an end-to-end view including internal and external partners in the supply chain. Prior to joining Abbott, Valentin worked for General Electrics Healthcare as Master Black Belt, Plant Manager and Service Operations Manager.

Stigell Warnström, Maria

Operation Excellence Specialist, Pfizer

Maria is currently working with implementation of Lean, training and coaching Lean activities, as well as she is a process leader for continuous improvements. She has earlier been working with quality system design and Human Error Reduction for 10 years at Pfizer. She has a Fil. Mag in Chemistry from University of Stockholm.

Thomas, Simone

Research Associate, University of St.Gallen

Simone Thomas is working as a research associate at the Institute of Technology Management at the University of St.Gallen (Switzerland) since January 2010. Her research concentrates on the integrated management of plants in global manufacturing networks. One focus of her work is on network integration of the manufacturing plants through knowledge exchange.

Simone Thomas graduated in media and communications, economics and law at Johannes Gutenberg University Mainz (Germany). She gained practical experience at the German Embassy in Seoul and the Korean-German Chamber of Commerce and Industry.

Walkhoff, Uta

Owner and Founder, uwprocessconsulting

Uta Walkhoff studied industrial engineering and management and started her career 1990 at Boehringer Mannheim GmbH. She has more than 20 years of professional experience in Finance, Controlling and Business Process Management and was head of Business Excellence at Roche Diagnostics Germany until 2011. In this leading position she was responsible for various operational excellence projects and for the operational and organizational structure of this function.

Since 2012 she is owner of a consulting company which offers professional support and solutions for sustainable business process management. During this time UtaWalkhoff finished miscellaneous kind of Business Excellence projects with customers operating in different businesses.

Walter, Gideon

Partner and Managing Director, The Boston Consulting Group

Gideon Walter is a Partner and Managing Director in the New Jersey office of The Boston Consulting Group. He is a core member of the Health Care and Operations practices.

Gideon works extensively with biopharma clients focused on large scale transformations including elements such as strategy, operations and organizational design. This has included the global supply chain transformation and reorganization and the implementation of a lean/operational excellence program for leading biopharma companies.

Early in his tenure at BCG, Gideon was an ambassador in BCG's Copenhagen office and in the year, he contributed to the firm's Consumer and Operations practices.

Prior to joining BCG, Gideon held the position of VP – GM for Delia's Inc., a US multi-channel retailer. As GM of Delia's Direct, he oversaw marketing and supply chain functions for the company's business.

Gideon has an M.B.A. from Columbia Business School with a dual concentration in Finance and Marketing.

Werani, Jürgen Dr.

Member of the Board, Schuh & Company Complexity Management

Dr. Jürgen Werani was born in Vienna, Austria, in 1951. He is a citizen of Switzerland.

From 1971 until 1976, he studied pharmacy at the University of Graz, Austria. He received his doctorate in natural sciences in 1978. In 1998, he obtained a degree in Business Administration at the University of St.Gallen. In 2008, he received his Lean Expert qualification from the Lean Management Institute Germany.

Between 1979 and 1995, Dr. Werani held a number of leading positions in pharmaceutical manufacturing at Sandoz Pharma AG in Basel, Switzerland. There he finally took on the role of Head of Solids Production. In 1995, he transferred to Warner Lambert Company where he became Managing Director of the Gödecke AG Freiburg plant. In 1998, he joined Gödecke AG's Board of Management. From 2000 onwards, he was member of the Board of Management of Pfizer Germany GmbH. From 2003 to 2008, Dr. Werani was responsible for the implementation of the Operational Excellence Program in Europe which included its deployment to a total of 15 sites. Since 2008, he has been member of the Managing Board of Schuh & Co. Complexity Management AG in St.Gallen, Switzerland.

Dr. Jürgen Werani has gained broad experience in the field of Operational Excellence and Lean Thinking in the pharmaceutical industry as well as in state-of-the-art methods of corporate management and leadership. He is the author and co-author of reference books on these subjects, wrote numerous publications and is a sought-after speaker at congresses and seminars on corporate change management.

During his time at Pfizer Freiburg, Dr. Werani introduced the principles of Lean Manufacturing on a broad scale, thus helping to turn the site into a leading Lean Manufacturing production site in the pharmaceutical industry.

Since 2008 he has been leading several projects in different companies addressing Operational Excellence, Cultural Change and Leadership Development programs. He also acts as a mentor and coach for Executives and operational leaders.

Wright, Troy

Director, Business Performance and Operational Excellence Global Network Lead, Amgen

Troy is currently serving as Director of Business Performance and the Operational Excellence Global Network Lead. He has been responsible for the development and deployment of Amgen's Operational Excellence program since 2009. His organization's responsibilities include leading Amgen's Lean Transformation and Organizational Design and Capabilities programs as well as providing global Industrial Engineering services.

Troy began his career with Amgen in Colorado 13 years ago. Prior to his current role, he was a member of the Colorado Site Leadership Team and served as the Director of Operational Excellence and the Director of Site Engineering.

Troy holds an M.B.A. from the University of Colorado at Colorado Springs. He also attended the Colorado School of Mines where he earned a bachelor's degree in Chemical Engineering and Petroleum Refining Engineering with a minor in Economics & Business Management.

Ziegler, Reto M.

Research Associate, University of St.Gallen

Reto M. Ziegler is Research Associate at the Institute of Technology Management (University of St.Gallen, Switzerland). His research concentrates on today's challenges faced by the pharmaceutical industry, especially the cross-functional collaboration at the interface of development and production. Besides the pharmaceutical industry, he is an expert for process and organization optimization as well as outsourcing in the public sector.

Reto M. Ziegler graduated in Molecular Biology (M.Sc.) from the University of Basel (Switzerland). Previous to his research in St.Gallen, he gained practical experience in different research labs and in software engineering.

Index

T. Friedli et al. (eds.), *Leading Pharmaceutical Operational Excellence*,
DOI 10.1007/978-3-642-35161-7, © Springer-Verlag Berlin Heidelberg 2013

D