

**Operational Excellence across Manufacturing and Quality Control -
A Guideline to Avoid Optimizing Silos in Pharmaceutical Production**

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The President:

Prof. Dr. Bernhard Ehrenzeller

Vorwort & Danksagung

Die vorliegende Arbeit entstand im Zuge meiner Tätigkeit als wissenschaftlicher Mitarbeiter im Bereich Produktionsmanagement am Institut für Technologiemanagement der Universität St.Gallen von 2018 bis 2021. Während dieses Zeitraums durfte ich umfassende Einblicke in die faszinierende Welt der pharmazeutischen Produktion im internationalen Kontext gewinnen. Neben der Zusammenarbeit mit zahlreichen Industrieunternehmen und deren Produktionsstandorten auf vier Kontinenten ist der kollaborative Austausch mit der U.S. Food and Drug Administration als absolutes Highlight einer intensiven und lehrreichen Zeit zu benennen.

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Abstract

Producing pharmaceutical goods is associated with numerous challenges nowadays: Steady drug shortages and product recalls go along with increasing regulatory requirements. Manufacturers are persistently forced to enhance effectiveness of their operations. At the same time, emerging global competition and tremendous price pressure from healthcare systems cause a strong need to increase efficiency.

Initial research shows that there seems to be no correlation between effectiveness in manufacturing operations and quality control of production sites. Applying the principles of Lean Management and Continuous Improvement to steer plants in the direction of becoming best in class is not new to pharma. However, the industry is lacking a comprehensive strategy along the value chain. Instead, empirically observable performance patterns lead to the assumption of optimized silos as a consequence of departmental improvement initiatives.

Operational Excellence is a management philosophy that paves the way to achieve superior performance by optimizing quality, delivery, and cost in a well-balanced manner. Additionally, it aims to introduce practices and deploy capabilities which enable an organization to continuously improve itself. The present thesis develops a management guideline to comprehensively approach Operational Excellence across pharmaceutical manufacturing and quality control. Thereby, it demonstrates the potential of interdepartmental alignment to conjointly improve effectiveness, efficiency, and compliance throughout production facilities.

The manifoldness of the research subject motivates a mixed-methods approach combining quantitative and qualitative techniques. Underpinned by the theoretical understanding of contingencies, constraints, and dynamic capabilities, an iterative research procedure is pursued. Three core research phases mutually stimulate each other: The studies start by deeply investigating the interrelation of performance between manufacturing and quality control based on benchmarking data. Furthermore, recommendations for managing capabilities across departments are drawn from literature revealing powerful levers beyond the current standard in the pharmaceutical industry. On top of that, proven successful practices applied by leading pharmaceutical companies are uncovered through a survey and subsequently detailed in individual case studies. Concludingly, implications are compiled and transferred into an actionable format. All findings add up to the overarching management guideline, which comes with specific instructions for implementation.

This dissertation makes an impact in practice and addresses an existing gap in theory at the same time. It enriches the current state of research with an object of consideration not priorly explored by scholars and unleashes improvement potentials in the industry. The findings constitute tangible benefits to the scientific community, pharmaceutical manufacturers, regulators, and patients.

Zusammenfassung

Die Herstellung von pharmazeutischen Produkten ist heutzutage mit einer Reihe von Herausforderungen verbunden: Lieferengpässe und Produktrückrufe gehen einher mit zunehmenden regulatorischen Anforderungen. Produzenten sind daher gezwungen die Effektivität der Produktion kontinuierlich zu steigern. Gleichzeitig erfordern vermehrter globaler Wettbewerb und Preisdruck der Gesundheitssysteme eine höhere Effizienz.

Erste Forschungsergebnisse zeigen, dass Effektivität in Produktion und Qualitätskontrolle nicht korrelieren. Während Konzepte zur kontinuierlichen Verbesserung bereits grundsätzlich in der produzierenden pharmazeutischen Industrie angewandt werden, fehlt es der Branche an einer ganzheitlichen Strategie zur Optimierung entlang der Wertschöpfungskette. Stattdessen resultieren isolierte, abteilungsspezifische Verbesserungsinitiativen derzeit in optimierten Silos, wie in den Kennzahlen ersichtlich ist.

Operative Exzellenz ist eine Management-Philosophie, die auf nachhaltige Leistungssteigerung durch die ausgewogene Optimierung von Qualität, Zeit und Kosten abzielt. Weiterhin werden Routinen und Praktiken implementiert, die es einer Organisation ermöglichen, sich kontinuierlich selbst zu verbessern. Die vorliegende Arbeit entwickelt einen Managementleitfaden, der die Integration von Exzellenzinitiativen innerhalb der pharmazeutischen Produktion und Qualitätskontrolle in einem umfassenden Ansatz anstrebt. Hierbei werden Potenziale zur abteilungsübergreifenden Verbesserung von Effektivität, Effizienz und Compliance aufgezeigt.

Das Forschungsvorhaben kombiniert quantitative und qualitative Forschungsansätze. Untermauert durch das theoretische Verständnis von Kontingenzen, Engpässen und dynamischen Fähigkeiten wird ein iteratives Vorgehen verfolgt: Der Leistungszusammenhang zwischen Produktion und Laboren wird anhand von Benchmarking Datensätzen eingehend analysiert. Ergänzend liefert wissenschaftliche Literatur Empfehlungen zum abteilungsübergreifenden Management von Fähigkeiten, die über den aktuellen Anwendungsstand in der pharmazeutischen Industrie hinausgehen. Weiterhin werden bereits bewährte Industriepraktiken zur ganzheitlichen Optimierung von Fertigung und Qualitätskontrolle identifiziert und anschließend anhand einzelner Fallstudien detailliert dargestellt. Schlussendlich erfolgt die Konsolidierung aller Implikationen in einem unmittelbar anwendbaren Leitfaden.

Die vorliegende Dissertation forciert die Praxis und adressiert gleichzeitig eine existierende Lücke in der Theorie. Hierbei bereichern die Studien den aktuellen Stand der Forschung um einen neuartigen Anwendungsfall und ermöglichen direkte Verbesserungen innerhalb der Industrie. Die Erkenntnisse liefern einen greifbaren Mehrwert für die wissenschaftliche Gemeinschaft, pharmazeutische Firmen, Regierungsbehörden und Konsumenten.

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List of Abbreviations

ANOVA	Analysis of Variance
API	Active Pharmaceutical Ingredient
APQ	Advancing Pharmaceutical Quality
ATL	Adherence to Standard Lead Time
ATS	Adherence to Schedule
BE	Basic Elements
CAPA	Corrective and Preventive Action
CDER	Center for Drug Evaluation and Research
cf.	confer
CI	Continuous Improvement
CMO	Contract Manufacturing Organization
CT	Contingency Theory
DP	Drug Product
DS	Drug Substance
DV	Dependent Variable
e.g.	exempli gratia
EH&S	Environment, Health & Safety
EMS	Effective Management System
FDA	Food and Drug Administration
FTE	Full Time Equivalent
GMP	Good Manufacturing Practice
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
iOOS	Invalidated Out Of Specification

IRSC	Informal Relationships and Social Capital
ISPE	International Society for Pharmaceutical Engineering
IV	Independent Variable
JIT	Just-in-Time
KPI	Key Performance Indicator
LH	Lower Half
MRQ	Main Research Question
No	Number
Lab	Laboratory
LTSI	Learning Transfer System Inventory
NAI	No Action Indicated
NGO	Non-Governmental Organization
OAI	Official Action Indicated
OEE	Overall Equipment Effectiveness
OM	Operations Management
OOS	Out Of Specification
OPEX	Operational Excellence
ORG	Industrial OPEX Research Group
OTIF	On-time Delivery in Full
PDA	Parenteral Drug Association
PPSM	Pharmaceutical Production System Model
PQS	Pharmaceutical Quality System
Q&A	Question and Answer
QBS	Quality Benchmarking Study
QC	Quality Control
QCEx	QC Lab Exchange Platform

QMS	Quality Management System
RBV	Resource-Based View of the Firm
R&D	Research and Development
SECI	Socialization Externalization Combination Internalization
SKU	Stock Keeping Unit
SI	Shared Identity
SME	Subject Matter Expert
SOP	Standard Operating Procedure
SRQ	Sub Research Question
TDC	Theory of Dynamic Capabilities
TH	Top Half
TOC	Theory of Constraints
TPM	Total Productive Maintenance
TPS	Toyota Production System
TQM	Total Quality Management
TR	Transfer of Routines
U.S.	United States of America
USD	US-Dollar
VAI	Voluntary Action Indicated
VM	Visual Management
WCM	World Class Manufacturing
WIP	Work-in-Progress
WHO	World Health Organization

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1 Introduction

“...and then, I moved to the dark side.”

Global Head of Laboratory Excellence illustrating the start in his current position after having led lean initiatives in manufacturing within the same pharmaceutical company for 13 years.

This thesis contributes to the subject area of Operational Excellence in the pharmaceutical industry. Continuously increasing effectiveness and efficiency in pharmaceutical production is key to ensure sustainable supply of affordable medicines in high quality (Sieckmann et al., 2018, p. 814).

Optimizing manufacturing operations, comprising formulation and packaging of drugs, has been the main focus of Operational Excellence and Lean Management programs in pharmaceutical production over the last decades. QC (Abbreviation Quality Control) labs are already considered one of the core levers besides manufacturing to achieve the objective of superior operational performance in the pharmaceutical value chain. Therefore, research with regard to Lean and Operational Excellence in QC labs has been trending, cf. contributions of Cherqaoui et al. (2018), Costigliola et al. (2017), Friedli et al. (2020) and Vijayshri et al. (2017). However, both theory and practice are lacking an integrative and comprehensive strategy to foster Operational Excellence across departments instead of solely optimizing manufacturing and quality control.

Chapter 1 introduces the motivation to conduct the present research and the set-up of the thesis. The background of the specific research problem and its grounding in the St.Gallen quality metrics research are outlined in chapter 1.1. Afterwards, chapter 1.2 presents the research strategy & design and chapter 1.3 expounds the subsequent thesis structure.

1.1 Origin & Relevance

Chapter 1.1 aims to provide the reader with a solid understanding of the research field the presented research contributes to. Therefore, background and context of the thesis topic are introduced in chapter 1.1.1 alongside with the main research objective. Subsequently, the relevance of the topic for both theory and practice is outlined in chapters 1.1.2 and 1.1.3.

1.1.1 Background & Research Objective

The research problem evolved during three years of researching quality metrics in pharmaceutical production under a collaborative grant with the U.S. Food & Drug Administration. This research can be summarized as an academic contribution to the FDA's (Abbreviation Food & Drug Administration) quality metrics initiative. Details of the initiative have been announced to industry in the draft guidance *Request for Quality Metrics* (2015) and the revised version *Submission of Quality Metrics Data* (2016). It aims to define a standardized set of metrics to be reported to the FDA by pharmaceutical manufacturers on a regular base. Consequently, the current state of manufacturing quality is more visible to regulators and informs further risk-based regulatory oversight strategies. On the other hand, additional freedom and reduced regulatory burden might be offered to establishments indicating a robust state of operations supported by their reported quality metrics. Findings on researching quality metrics have been published in three comprehensive reports after year 1 (Friedli et al., 2017), year 2 (Friedli, Köhler, et al., 2018), and year 3 (Friedli et al., 2019) of the project.

Various implications from the quality metrics research contributed to the conceptualization of the PPSM (Abbreviation Pharmaceutical Production System Model). It is a model to evaluate PQS (Abbreviation Pharmaceutical Quality Systems) which follows a holistic system approach and integrates several performance indicators and enabling factors. Following a comprehensive understanding of performance, the PPSM explicitly includes efficiency measures and is not limited to effectiveness. Guided by the PPSM the research team sought a balanced approach considering both single quality metrics and aggregated performance scores in their search for a system of suitable quality indicators. Operational Stability, Supplier Reliability or Cultural Excellence are examples for subject fields that have been operationalized and analyzed along the PPSM.

In the last development steps during the third year of quality metrics research, all categories of ICH Q10 were added to the foundation of the PPSM to ensure full compatibility. ICH Q10 is a reference model for quality systems conceptualized by a working group of specialists engaged in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH, 2008, p. 1). Figure 1 depicts the Pharmaceutical Production System Model.

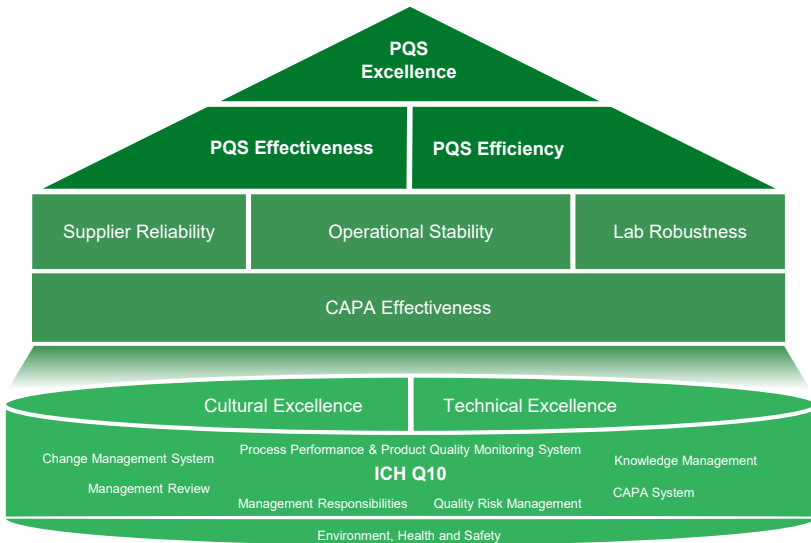


Figure 1: Pharmaceutical Production System Model (PPSM) (Friedli et al., 2019, p. 23)

Effectiveness of both pharmaceutical manufacturing operations and quality control is an integral part of the PPSM and depicted by the scores Operational Stability (manufacturing) and Lab Robustness (quality control). A detailed overview of the underlying metrics aggregated in these two scores is given in chapter 3.2.3.

Initially, the conceptualization of the PPSM specified Lab Robustness as an integral part of the higher aggregated layer of the PPSM, but due to several challenges PQS Effectiveness was solely calculated as aggregation of Supplier Reliability and Operational Stability. Hence, PQS Effectiveness can be seen as operations-focused measure along the quality metrics research. However, first analyses aiming to better understand the role of Lab Robustness in the overall quality system have been conducted and published in the final research report of the 2nd year of quality metrics research, cf. Friedli et al. (2018, p. 45).

The relation of PQS Effectiveness and Lab Robustness is shown in Figure 2. At the moment of analysis back in 2018, combined benchmarking datasets comprising both manufacturing and QC lab performance have been available from 19 production sites and are reflected in the scatter plot.

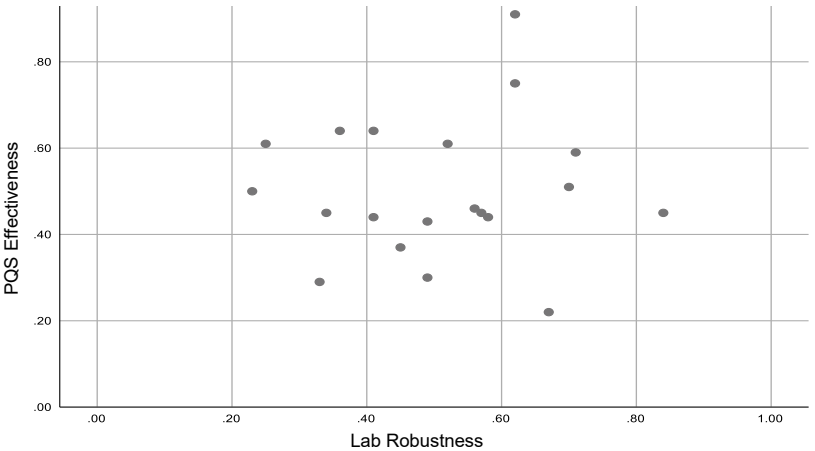


Figure 2: Relation of PQS Effectiveness and Lab Robustness (Friedli, Köhler, et al., 2018, p. 47)

As the number of available benchmarking datasets increased since 2018, an additional analysis performed utilizing the databases early 2020 is provided in Figure 3. At his point of time, the analysis has been based on 28 combined benchmarking datasets comprising both manufacturing and QC lab performance. Furthermore, Operational Stability instead of PQS Effectiveness is chosen to depict effectiveness in manufacturing. Thus, Supplier Reliability’s impact on the performance scoring is debarred to assess manufacturing operations narrower and exclude the impact of purchasing and supplier management.

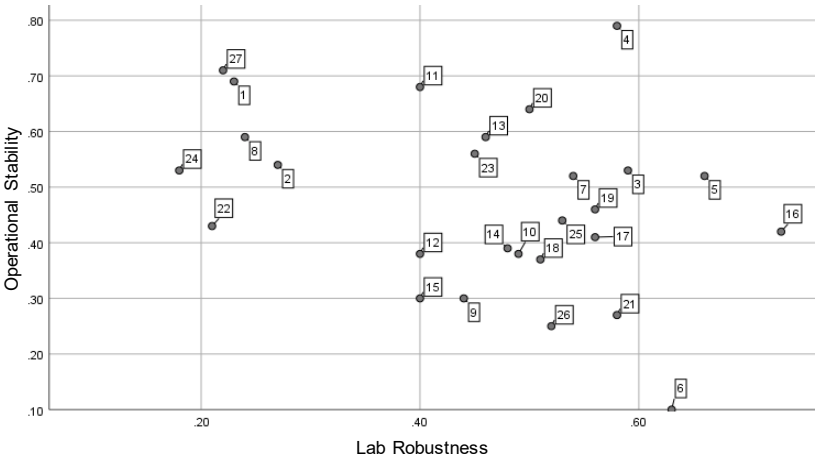


Figure 3: Relation of Operational Stability and Lab Robustness

Figure 3 confirms the general trend observed in 2018, cf. Figure 2: There seems to be no correlation between effectiveness of manufacturing operations and effectiveness of quality control. Thus, very well performing QC labs in production sites with less effective manufacturing operations are identified as well as the other way around. While individual outliers would be in expectation, neither the St. Gallen research team nor the FDA suspected such a diverse performance pattern between manufacturing and quality control in production sites. Especially, as a positive relation between OPEX capabilities and effectiveness could be shown for both manufacturing (Friedli, Köhler, et al., 2018, p. 29 f.) and QC labs (Friedli, Köhler, et al., 2018, p. 42).

This thesis takes on the phenomena described above and strives to deeply investigate the interrelation between performance of manufacturing and quality control in pharmaceutical production sites. The work is not limited to provide reasoning for initially observed inconsistencies in effectiveness. It includes to assess the level of excellence across both department from various angles and in a comprehensive manner by analyzing efficiency and capabilities in addition. Furthermore, recommendations for approaching Operational Excellence cross-departmentally and optimizing performance across manufacturing and quality control are developed.

1.1.2 Theoretical Relevance

Driving forward Operational Excellence in pharmaceutical production is of strong interest for industry, mainly approached by practitioners and still a relative new priority compared to other industries. Hence, OPEX in Pharma is rarely discussed in academia. This particular research area is predominantly driven by the division Production Management at the Institute of Technology Management, University of St.Gallen. The research team published numerous journal articles and four comprehensive books on Operational Excellence and Quality Management, see Friedli et al. (2006; 2010; 2013; 2018). However, other scholars have pointed out the relevance and importance of OPEX in Pharma from an academic perspective, cf. articles on the subject matter published by Birkie et al. (2018), Garza-Reyes et al. (2018), Haleem et al. (2015), Jaiganesh and Sudhahar (2015), Muse et al. (2016), Nenni et al. (2014) or Pavlović and Božanić (2012).

While the majority of researchers focus on manufacturing operations when studying OPEX in pharma, a few published articles were dedicated to the application of Lean Management and Operational Excellence in QC labs and underpin the theoretical relevance, cf. Barbarite and Maslaton (2008), Cherqaoui et al. (2018), Costigliola et al. (2017) or Vijayshri et al. (2017). Furthermore, Köhler (2019) published a comprehensive thesis on performance measurement and Operational Excellence in QC labs. In his work Köhler (2019, p. 172) pointed out that the integration of

performance measurement in manufacturing and quality is an important further research step to understand the crucial role of QC labs in full.

Cross-departmental alignment of Continuous Improvement strategies and Lean Management along the value chain are acknowledged and recommended for successful optimization of organizations by scholars (Bhasin & Burcher, 2006, p. 67; Comm & Mathaisel, 2000, p. 119 f.). The strong impact of intraorganizational relationships on operational performance was demonstrated by Tuominen et al. (2000, p. 139 ff.), while Nguyen et al. (2018, p. 123 ff.) evaluated the relation between cross-functional knowledge sharing and the level of both motivation and performance within firms.

Current academic literature does not offer any dedicated research on comprehensively managing Operational Excellence across manufacturing and quality control in pharmaceutical production (cf. chapter 2.2). Thus, the carried-out research is highly innovative and expands the existing theoretical knowledge base. At the same time, relevance to academia is proven by the research interest scholars show in the general subject fields Operational Excellence and cross-functional alignment of Lean Management.

1.1.3 Practical Relevance

Unlike other industries, the pharmaceutical industry plays a unique role in the global economy. It does not produce luxury goods but lifesaving medicines. Thus, it is crucial and tremendously relevant for the whole society. (Cueni, 2018, p. 2) In addition, pharmaceutical companies contribute significantly to the economy by fostering innovation and offering attractive job opportunities to highly skilled labor. According to Interpharma (2019, p. 7) revenue earned by the pharmaceutical companies leads to significant growth: Every franc spend on pharmaceutical products in Switzerland generates direct reinvestment of almost two francs. Pharmaceutical research and manufacturing are of major economic significance.

Beyond the commitment to research and develop new medicines, pharmaceutical companies need to ensure availability of their medicines to patients. (Durrant, 2001, p. 2) Hence, production and supply of quality products is of highest priority. This often comes along with logistical and regulatory challenges. Pharmaceutical producers lack of incentives to manufacture less profitable drugs leading to instable supply of these products. In other cases, imperfect Quality Management Systems have been identified as root causes for drug shortages by the FDA (2019b, p. 6). Johnston and Holt (2014, p. 218 ff.) present an overview of substandard medicines due to inadequate manufacturing and quality control causing threats to patients. The above described incidents reoccurred in the context of both branded and generic products over the last years and are a persistent problem of the global pharmaceutical industry. Besides the obvious risk these poor quality products pose to human

health, manufacturing quality issues cause 37 % of drug shortages preventing stable supply of essential drugs. (FDA, 2019a)

Continuous Improvement and Operational Excellence are important levers to increase manufacturing quality and prevent drug shortages. That is why providing incentives for process enhancement and ensuring an environment that allows Continuous Improvement is also a priority for regulators (Yu & Kopcha, 2017, p. 358). Quality improvements through CI tools -such as increased process capabilities due to Six Sigma efforts- are directly associated with efficiency gains resulting in cost saving and therefore highly relevant to industry (Yu et al., 2016, p. 541 f.).

Different to other industries, pharmaceutical companies belatedly discovered Continuous Improvement and the principles of Operational Excellence (Friedli & Werani, 2013, p. 27). Caused by increasing pressure to increase efficiency in production due to the challenging market environment (EY, 2020, p. 21), driving forward Operational Excellence has been a huge priority in pharmaceutical production in the recent past and still is today.

Similar to the academic world (cf. chapter 1.1.2) OPEX and CI initiatives in practice were limited to manufacturing in most cases (Friedli, Lembke, et al., 2013, p. 42). However, leading pharmaceutical companies such as Novartis (Scharton-Kersten et al., 2016, p. 5 ff.), Pfizer (DeWit, 2011, p. 72 ff) or Eli Lilly (Longden, 2011, p. 14) perceived the potential of Continuous Improvement in quality control and started lean lab initiatives in the recent past. An ever-growing number of more than 15 pharmaceutical companies in the St.Gallen QC Lab Exchange Platform (cf. chapter 1.2.5) during the years 2018, 2019 and 2020 clearly indicates the importance of OPEX in quality control to practitioners nowadays. In addition, the FDA quality metrics initiative (cf. chapter 1.1) certainly acts as additional booster for Performance Management and Operational Excellence in quality control labs: One of the proposed quality metrics to be continuously reported to the regulator iOOS (Abbreviation Invalidated Out Of Specification) directly addresses quality control's performance.

M. May (2014, p. 1) points out that the critical role of QC labs needs to be recognized. As instrumental for both testing of all incoming raw materials and release of produced batches, labs are crucial for the entire pharmaceutical value chain. That is why quality control needs to be understood as part of the overall production value stream rather than as separate department by both manufacturing and quality control staff. So, analyzing cross-departmental relationships and viewing the laboratory in its broader context is another important aspect of lean lab transformation besides optimizing operations inside the lab. (M. May, 2014, p. 2)

Driving an end-to-end approach along the value stream and achieving an integrated flow including all relevant departments has been identified as one of the major challenges OPEX executives are currently facing across industries (Bajaj & Reffell,

2018, p. 5). This observation is also true for pharmaceutical production: Attention on increasing effectiveness and efficiency in QC labs grows besides the legacy focus on optimizing manufacturing. Regrettably, the initiatives for both departments are set-up according to their individual priorities and targets rather than part of an integral approach along the pharmaceutical value chain. Thus, fostering Operational Excellence across manufacturing and quality control is the next step to overall excellent production and a key priority, as the statements (cf. appendix A.1) of pharmaceutical managers gathered in unstructured interviews demonstrate. During early stages of the research, these unstructured interviews have been continuously conducted as a side activity to project meetings with pharmaceutical representatives to initially explore the presumed relevance of the topic.

As elaborated above in detail, the present research is highly relevant for practice. Pharmaceutical manufacturers, regulators and patients all benefit from an integrative approach to Operational Excellence across manufacturing and quality control.

1.2 Research Strategy & Design

Chapter 1.2 outlines the research strategy in detail. First, the conceptual background and the underlying theories applied to the research project are introduced in chapter 1.2.1. Subsequently, the research questions, which will guide the research project, are derived and elaborated in chapter 1.2.2. Chapter 1.2.3 condenses the different subject fields of this research in a concept map. After that, the chosen research approach and the corresponding procedure structured in five research phases are elaborated within chapter 1.2.4. Finally, chapter 1.2.5 presents the data gathering strategy to guarantee sufficient quantitative empiricism and to ensure access to pharmaceutical SMEs (Abbreviation Subject Matter Expert) for conducting qualitative research.

1.2.1 Paradigm, Conceptual Background & Research Theories

Pragmatism is one of the dominant philosophies of science and acknowledges that theory can never deliver a fully accurate picture. Reality is far too complex to allow theories to completely understand all aspects of a real-world phenomena. (T. J. Watson, 2013, p. 21) As this research project investigates an existing problem and is motivated by practice, it follows pragmatism as general paradigm how to understand and apply theory for both ontological and epistemological purposes.

The present thesis is positioned in the research discipline business administration. According to Ulrich (1982, p. 6, 1984, p. 168) business administration is understood as applied social and management science. It strives to develop and design social systems. Thus, ensuring practical relevance and delivering impact to practice are key objectives of studies in this field of research. Occurring phenomena are not only observed but changed by management research. Even if driven by practice,

management research must not lack of a theoretical perspective. (Ulrich, 1984, p. 168 f.)

Research theories offer different lenses to researchers allowing them to consciously control and shift the focal plane while analyzing certain aspects of complex phenomena and issues. Following a certain theory is helpful to draw attention on particular aspects of data and support analysis with guidance or high-level frameworks. (Reeves et al., 2008, p. 631) That is the reason why usage of theory is applied in this thesis and various theories have been initially evaluated for their ability to support the research project.

Due to the manifoldness of the research topic (cf. chapter 1.1.1) and the diversity of research streams contributing to the subject area (cf. chapter 2.1) three established research theories are chosen. They act as conceptual background of the overall research project in a combined and supplementing way. Hence, rather than choosing one theory that is strictly followed through the entire thesis, tailored support of subparts is ensured by partly applying the appropriate theory. This approach of using multiple theoretical perspectives has been previously applied by Abes (2009, p. 141 ff.) or Lewis and Grimes (1999, p. 672 ff.) revealing comprehensive theoretical guidance for their research projects. On top of that, Gassmann et al. (2016, p. 40) even state that use of multiple research theories is highly encouraged in the context of business and management research. Figure 4 summarizes the three chosen theoretical perspectives applied in the present thesis.

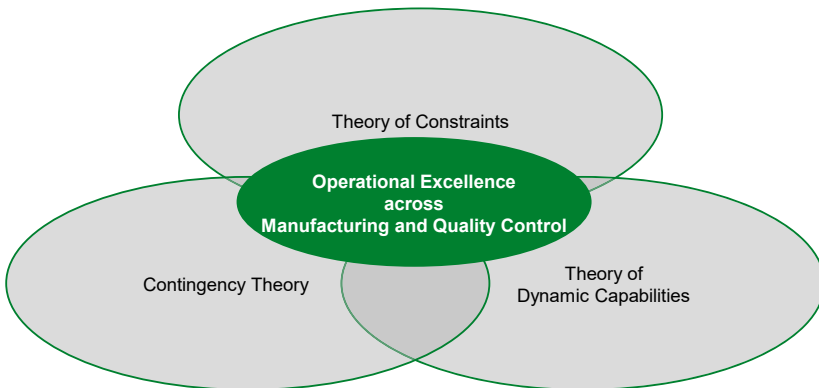


Figure 4: Conceptual Background Comprising Multiple Theories

Unlocking and exploiting the benefits of underpinning practically driven research with theory (cf. Reeves et al., 2008, p. 631), various research steps in subsequent chapters are guided by the three theories: Developing data gathering instruments (cf. chapter 3.3.1), drawing particular attention on certain aspects during systematic literature review (cf. chapter 4.3), considering the individual context of case studies

when interpreting (cf. chapter 5.1.2), and holistically combining multifarious findings (cf. chapter 6) all tremendously profit from their common theoretical grounding. In the following the three theoretical perspectives enriching in this thesis are briefly introduced while explaining their selection in the light of OPEX across manufacturing and quality control.

Theory of Constraints

TOC (Abbreviation Theory of Constraints) was initially published and further developed by Goldratt in the mid-1980s and 1990s. Based on a holistic approach the theory underpins that the overall status of performance is determined by the constraints companies have to deal with instead of the highest performing person or part. (Goldratt, 1990, p. 5 ff.) While the initial purpose of TOC was to provide a tool to optimize production timetables, it grew more and more to a holistic approach incorporating broad aspects of business. This resulted in an overall theory for running organizations. (Goldratt, 1988, p. 447 ff.) Nowadays, TOC is understood as a system methodology assisting people and organizations in understanding problems, developing solutions and implementing those (Mabin & Balderstone, 2003, p. 569). It comprises integrated management tools such as performance measurement and problem solving (Spencer & Cox, 1995, p. 1502).

Rahman (1998, p. 337) summarizes the basic concept of TOC in two main points: Firstly, every system has at least one constraint limiting to achieve higher performance. Therefore, the existence of constraints should be understood as positive as it is an opportunity for improvement. Thus, TOC does not only provide the researcher with a lens, it also proposes working principles aiming for Continuous Improvement, formalized in a five step approach to elevate system constraints (Rahman, 1998, p. 337 f.). The theory applies and promotes the foundations of system thinking. Secondly, it recognizes that due to complex interrelations every system is much more than the sum of its parts. This fact may result in limitations of performance caused by the system or system's elements. (Mabin & Balderstone, 2003, p. 570) Overall, TOC transfers the general perspective of seeing a chain just as strong as its weakest link into a management paradigm (Tulasi & Rao, 2012, p. 334).

Usage of TOC is broadly established in OM (Abbreviation Operations Management) and the theory was successfully applied to past projects in the domain. (Boyd & Gupta, 2004, p. 350; M. C. Gupta & Boyd, 2008, p. 991). Beyond general Operations Management, scholars chose TOC for supporting Lean, Six Sigma and Continuous Improvement projects as well as Quality Management activities (Dettmer, 1995, p. 77 ff.; Jacob et al., 2009, p. 5 ff.; Nave, 2002, p. 73 ff.; Wolniak et al., 2017, p. 171 f.). K. J. Watson et al. (2007, p. 387 f.) point out that TOC techniques help to increase output while decreasing cycle time and inventories in production. TOC is more than a pure research theory. It brings structured guidance for achieving improvements and the techniques have been applied in practice as well. Leading

companies across industries such as Amazon, Delta Airlines, Ford Motor Company or General Electric achieved significant improvements through deployment of TOC. Even nonprofit and governmental institutions like United Nations or the Israeli Air Force make use of TOC principles. (K. J. Watson et al., 2007, p. 387)

Because of its proven track record in Operations, Lean and Quality Management the theory of constraints is chosen as one of the theoretical perspectives for the present thesis. Fostering Operational Excellence across manufacturing and quality control requires an integrative approach along the pharmaceutical value chain. This objective can highly benefit from TOC's principles of understanding performance as a consequence of the sum. Furthermore, the profile of TOC as a management paradigm that proposes techniques and tools to steer organizations in the direction of improvement suits both research topic and research objective very well.

Contingency Theory

CT (Abbreviation Contingency Theory) dates back to Fiedler (1964, p. 158 ff.), who developed the basis of the theory in the 2nd half of the last century. It is established for studying organizational design following the paradigm that the most effective organizational design is given if the structure fits the contingencies (Donaldson, 2006, p. 19). Contingencies comprise the environment of an organization, the organizational size and the organizational strategy summarized as any variables moderating the impact of an organizational characteristic on organizational performance. Organizational structure needs to be designed in a way that it fits all contingencies of environment, size and strategy best. (Donaldson, 2001, p. 1 ff.) Furthermore, the preferable approach to structuring and managing an organization is always dependent on the specific case. Proven successful organizational structures are not necessarily transferable and promising for other organizations since many factors impact the individual effectiveness (Islam & Hu, 2012, p. 5159).

CT's popularity as one of the major lenses to view organizations in OM is increasing in response to the general trend of drawing insights from business and management theories for operations (Sousa & Voss, 2008, p. 698). Very fundamental OM positions such as Skinner's (1969, p. 136 ff.) manufacturing strategy, which explores the necessity for a good fit between production systems and organizations' priorities, already included contingency perspectives.

Individual matches of the particular organizational context need to be considered when striving for generalized excellence in Operations and Quality Management (Sousa & Voss, 2001, p. 383 f.). The contrast of universal applicable success factors and the need to tailor approaches from a contingency point of view is further discussed in the context of Continuous Improvement and Lean Production implementation (Netland, 2016, p. 2442 f.). Chavez et al. (2013, p. 567 ff.) researched the association of internal lean maturity with higher operational performance from a CT point of view and found that contingency variables moderate the relation between

internal lean practices and performance. Industry clock speed, described as the rate of change that is endogenous of an industry, has been tested as one variable impacting the relationship between implementation of internal lean practices and delivery performance. The study revealed that lean practices positively affect delivery performance in case industry clock speed is low. (Chavez et al., 2013, p. 567 ff.)

CT offers valuable insights and supplements the usage of TOC in this thesis. Differences in organizational structure and organizational strategy may contribute to the phenomenon of varying operational performance across manufacturing and quality control. Applying CT will support the research in studying those relations. Furthermore, successful application of CT in the fields of Lean Production and Quality Management (see above) provide confidence that CT is auspicious in the context of the present research project.

Theory of Dynamic Capabilities

TDC (Abbreviation Theory of Dynamic Capabilities) evolved from Barney's (1991, p. 99 ff.) resource-based view of the firm, which states that valuable, rare and non-substitutional resources allow firms to generate and sustain competitive advantages. RBV (Abbreviation Resource-Based View of the Firm) follows one of the most popular research streams in strategic management going back to Porter's (1985, p. 11 ff.) pioneering perceptions: Identifying levers to achieve superior performance.

TDC was initially published in the 1990s and predicates that companies need to dynamically respond to their changing competitive environments through building, renewing and deploying internal capabilities (Teece & Pisano, 1994, p. 538 f.). The first part of the theory's title *Dynamic* is characterized by changing business environments, evolving new technologies and future competition. *Capabilities* constitute of strategic management abilities that provide, adapt and reconfigures internal and external resources, skills and competencies to fulfill the demands of the business environment. (Teece et al., 1997, p. 515) As dynamic capabilities also represent direct and indirect processes of a firm, TDC is more an organizational lens rather than RBV's formal modelling strategy (Eisenhardt & Martin, 2000, p. 1106 f.).

TDC has previously been used by scholars to conduct research in operations and production management. Bititci et al. (2011, p. 1 ff.) explored the relation between managerial processes and dynamic capability building, Macher and Mowery (2009, p. 41 ff.) routed differences in operational performance to dynamic capabilities in semiconductor manufacturing. Cepeda and Vera (2007, p. 426 ff.) investigated knowledge management processes to develop dynamic and operational capabilities. Going beyond a general perspective of Operations Management, TDC has also been successfully applied in Lean Management and Continuous Improvement research. Anand et al. (2009, p. 444 ff.) conceptualized a framework of unifying Continuous Improvement approaches and organizational infrastructure to sustain

dynamic capabilities. Witcher and Chau (2007, p. 5 ff.) combined the two lean tools Hoshin Kanri and Balanced Scorecard with its focus areas strategy deployment and performance measurement to an integrative dynamic capability for strategic management.

TDC complements the theoretical background of the previously described research theories TOC and CT. It is used to highlight the existing level of OPEX capabilities in manufacturing and quality control labs as part of this work with a special focus on the organization's ability to deploy, disperse and sustain these capabilities across departments. While a resource-based view would generally support the investigation of differences in maturity between departments too, TDC is chosen due to its narrow focus on capabilities exhibiting a separate subcategory of resources. Furthermore, the theory's focus on dynamic trends suits the research project. Comprehensively approaching OPEX across manufacturing and quality control does not only comprise interdepartmental capability management, itself represents a capability of organizations. OPEX management is required to steadily reconfigure resources, skills, and competencies while reacting to a dynamic situation of changes in manufacturing areas and quality control laboratories of their production sites. Thus, the guideline for OPEX management to be developed is not a static concept.

1.2.2 Research Questions

Formulating research questions is fundamental to structure the research project. Besides delivering a solid grounding in theory, research questions need to be innovative to generate interest and deliver impact. In addition to the research interest, the nature of research questions further depends on project opportunities, publication objectives or fieldwork access. (Sandberg & Alvesson, 2011, p. 23 f.) Good research questions state the purpose of the research in form of a question, they provide guidance to the researcher what needs to be done and why (Lipowski, 2008, p. 1668 f.).

Based on the discovery of differences in performance across pharmaceutical manufacturing and quality control in previous research (cf. chapter 1.1) and the relevance for both theory and practice (cf. chapters 1.1.2 & 1.1.3) the MRQ (Abbreviation Main Research Question) of this thesis is derived. An initial literature review (cf. chapter 2.2) provides confidence that the question has neither been previously answered nor researched by other scholars. Four SRQs (Abbreviation Sub Research Question) break down the main research question in workable components and aspects to be researched in detail. Table 1 introduces the entire set of research questions.

Table 1: Set of Research Questions

MRQ	How to improve operational performance across manufacturing & quality control and avoid optimizing silos along the pharmaceutical value chain?	
SRQ	1	What are causes for performance differences and drivers for alignment across manufacturing and quality control?
	2	What are suitable strategies, approaches, and tools to overcome organizational barriers and dispense OPEX capabilities across departments?
	3	How do successful pharmaceutical production sites achieve excellent performance across manufacturing & quality control?
	4	How to consolidate uncovered causes for performance differences, identified strategies for cross-departmental alignment, and proven successful practices in a guideline for interdepartmental OPEX management?

MRQ – How to improve operational performance across manufacturing & quality control and avoid optimizing silos along the pharmaceutical value chain?

The question formulates the overall purpose of the research project. This thesis aims to identify suitable methods to optimize operational performance in manufacturing and quality control in an integrated and aligned manner by following an appropriate cross-departmental OPEX approach and strategy. Hence, the scope is not limited to understanding and providing reasons for performance differences between manufacturing & quality control (cf. chapter 1.1). The present research project additionally strives to transform the identified findings for this phenomenon into guiding principles how to increase performance along the pharmaceutical value chain. It targets to optimize holistically while transcending department specific improvements.

SRQ 1 – What are causes for performance differences and drivers for alignment across manufacturing and quality control?

The question intends to entirely understand the initial observed inconsistencies in performance between manufacturing and quality control. Previous research only compared the effectiveness of both departments within production sites using the aggregated scores of the Pharmaceutical Production System Model (Friedli, Köhler, et al., 2018, p. 47). This thesis carries out detailed analysis of the available performance data sets starting with a deep dive on the initial observations and identifying underlying indicators that drive the differences in aggregated effectiveness. The holistic investigation of performance differences is complemented by an efficiency perspective. Besides understanding the constituent elements of outcome performance, the implementation level of enabling practices in manufacturing and quality control is appraised. Implications are expected to support understanding whether differences in OPEX maturity exist across departments and if these differences correspond with the inconsistencies in effectiveness in case of occurrence. Lastly,

contextual factors such as the type of production or the geographic location are taken into consideration to understand affecting factors that are associated with performance differences across manufacturing and quality control in full.

SRQ 2 – What are suitable strategies, approaches, and tools to overcome organizational barriers and dispense OPEX capabilities across departments?

The question abstracts the observation of performance differences between manufacturing and quality control to a generic level of interdepartmental management. Since the exact research problem identified in pharmaceutical production has not been researched previously, general organizational strategies to foster alignment across departments and approaches for holistic Capability Management are studied. Findings from this research are assessed with regard to applicability to the specific problem of avoiding to optimize silos along the pharmaceutical value chain. Implications are adapted accordingly and supplement the creation of guiding principles to approach OPEX across manufacturing and quality control.

SRQ 3 – How do successful pharmaceutical production sites achieve excellent performance across manufacturing & quality control?

The question strives to provide detailed insights on how successful pharmaceutical establishments ensure alignment between manufacturing and quality control in practice. It considers organizational & strategic aspects such as the responsibilities for OPEX activities, prioritization, execution of improvement projects or the above-site structure to provide support and resources for this purpose. In addition, the individual background and history in launching and maintaining excellence initiatives plays an important role. Therefore, all undertaken efforts and actions to deploy and sustain OPEX practices across manufacturing and quality control are documented. This comprises all activities for cross-departmental optimization driven by either employees within the departments, above-department improvement staff at site, or corporate functions.

SRQ 4 – How to consolidate uncovered causes for performance differences, identified strategies for cross-departmental alignment, and proven successful practices in a guideline for interdepartmental OPEX management?

The question supports the integrated management of OPEX across manufacturing and quality control based on the outcomes of the three previous sub research questions. Implications are not only summarized but additionally consolidated and integrated in a guideline for OPEX management. Special attention is paid on the consistency and interplay of conclusions derived from the above described angles. Furthermore, the research question aims to compile consolidated observations and learnings in an actionable format for practitioners to ensure industry relevance of the entire research project.

1.2.3 Conceptual Framework

A conceptual framework is a significant component of scientific research and helps both the scholar and the reader to follow the project (Leshem & Trafford, 2007, p. 100). However, literature does not show a common understanding of how conceptual frameworks or research frameworks are compounded and for what purpose these frameworks are used. Some scholars suggest conceptual frameworks for linking theory with empiricism (Glatthorn & Joyner, 2005, p. 117; Rudestam & Newton, 2014, p. 6), while others use conceptual frameworks to introduce the methods applied or to structure the research process (T. May, 2011, p. 180).

Different to the proposals of the scholars referenced above, this thesis pursues a granular approach to outline the research design in its entirety. Instead of presenting research problem, theoretical grounding, research procedure, and the link to empiricism in one busy framework, components of the research design are elaborated step-by-step in dedicated chapters along the entire section 1.2 of the present dissertation: Relevant theories have already been introduced and linked to the research topic in the conceptual background (cf. chapter 1.2.1), while the research questions have also been detailed (cf. chapter 1.2.2). The methodological approach and research procedure are derived in the chapter to come (cf. chapter 1.2.4). Lastly, the data gathering strategy (cf. chapter 1.2.5) establishes the link to practice and provides confidence that the research design can build on sufficient access to industry.

Consequently, the conceptual framework presented in this chapter is intended to fulfill a certain aim and the scope is limited accordingly: It shall serve as a high-level picture of the area to be studied. For this purpose the conceptual framework is created in the form of a visual content map according to Maxwell (2012, p. 37). After having already introduced the research problem in all details during the previous chapters, the content map summarizes the different aspects of the research and their interdependencies. It provides a simplified overview and serves as visualization of the overarching research objective and the subject fields the research is positioned in. Therefore, the content map is depicted in Figure 5.

The map contains two main sections: Firstly, the inner circle section outlines the core subject of the project. This research aims to comprehensively optimize pharmaceutical manufacturing and quality control in relation to each other. Secondly, the three surrounding hexagons outside the circle summarize the influencing subject areas and constitute the research streams this thesis is positioned in. Based on research problem, objective, and questions stated, the project apparently relates to the research streams Operational Excellence, Organizational Strategy, and Capability Management. The connections to these subject fields are elaborated in detail when presenting the state of research along the three research streams in chapter 2.1.



Figure 5: Conceptual Framework in the Form of a Content Map

1.2.4 Research Approach & Procedure

According to Creswell (2014, p. 31 ff.) the decision for a research approach is informed by the topic of a study, the research problem addressed, philosophical assumptions of the scholar and procedures of inquiry. The chosen approach specifies or affects the methods of data collection, analysis, and interpretation.

Three different research approaches can be distinguished: Qualitative research, quantitative research, and mixed-method research. However, these three options should not be seen as discrete or exclusive. Usually, studies are classified based on their tendency of showing a quantitative or qualitative character, while mixed-method approaches incorporate elements of both areas. (Creswell, 2014, p. 31 ff; Newman et al., 1998, p. 9 ff.)

The present research project follows a mixed-method approach. It comprises both quantitative and qualitative phases conducted along the research process. A broad and deep understanding of interdependencies is needed due to the multifaceted aspects of the research problem. This objective can be achieved best by combining qualitative and quantitative research. Mixed-method research provides more comprehensive, valid and consistent results as it enables triangulation of findings from quantitative and qualitative perspectives (R. B. Johnson et al., 2007, p. 122 ff.).

Structuring research as an iterative learning process is one of the common approaches to conduct explorative research. It routes back to Kubicek (1977, p. 12 ff.), who initially proposed to combine the systematic creation of new knowledge with

existing findings from theory. The iterative nature of transforming theoretical knowledge in questions to practice, gathering empiricism, reflecting observations critically, and finally differentiating or abstracting findings from practice to create new theoretical knowledge, was further developed by Tomczak (1992, p. 84). Baumbach (1998, p. 13 ff.) and Gassmann (1999, p. 11 ff.) complemented the development of the iterative learning process. Gassmann (1999, p. 11 ff.) suggested its application especially for practice-driven case study research in business administration. Figure 6 shows the learning process, highlighting the iterative character of the research steps and visualizing the symbiosis of theory and empiricism to holistically draw conclusions from different data sources.

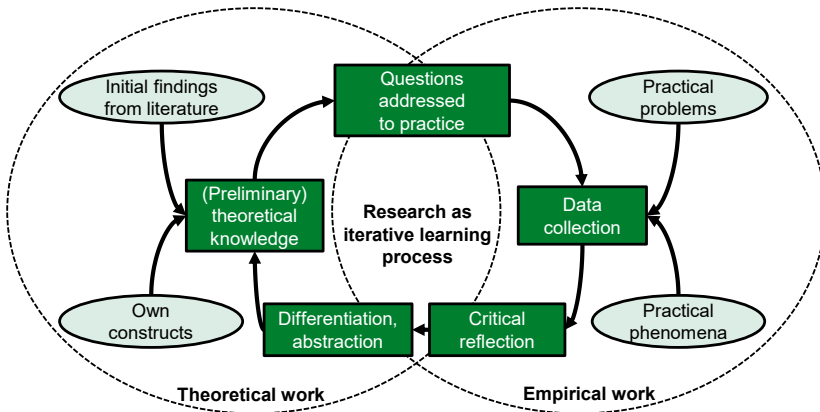


Figure 6: Research as Iterative Learning Process between Theory and Empiricism – Adapted from Baumbach (1998, p. 15) and Gassmann (1999, p. 13)

The research procedure of the present thesis as shown in Figure 7 builds on the iterative learning process. Recurring iterations between the core research phases 1, 2, and 3 follow the principles of Kubicek, Tomczak, Baumbach and Gassmann. In addition, the procedure is complemented by a sequential starting research phase (0) as well as a concluding research phase (4).

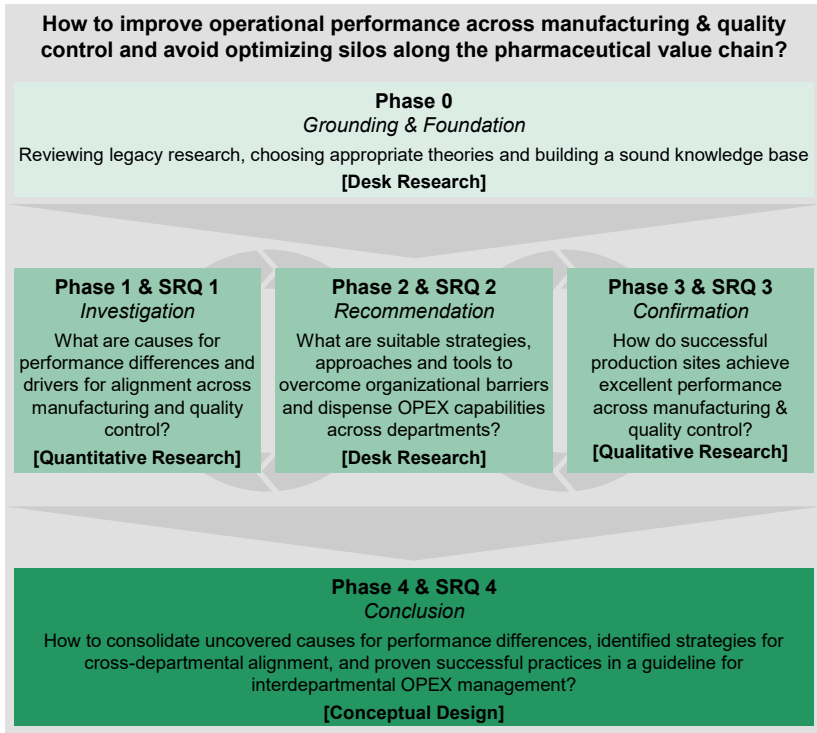


Figure 7: Research Procedure of the Present Thesis Comprising Five Phases

Moreover, the research procedure shown above provides an overview on the character and methodological approach of each research phase: Desk research, quantitative (empirical) research, qualitative (empirical) research, and conceptual design. The following outlines the procedure and describes all five phases in detail.

Phase 0 – Grounding & Foundation

The starting phase grounds the research project in existing literature and theory. As part of this phase an initial literature review is conducted to build a base of existing knowledge about the three research streams Operational Excellence, Organizational Strategy, and Capability Management. On this basis the current research gap is outlined. In addition, the research design as presented in this chapter, containing the theoretical background, research questions and conceptual framework is reviewed and finalized. Access to empiricism in accordance with the data gathering strategy (cf. chapter 1.2.5) is ensured.

Phase 0 is conducted as desk research. It serves as foundation for all subsequent phases 1 – 4.

Phase 1 – Investigation

Phase 1 investigates performance differences between manufacturing and quality control in detail. It contains detailed analyses of outcome performance indicators, OPEX maturity measures and structural context attributes of pharmaceutical production. Statistic methods such as regression analysis ensure objectivity and scientific validity of observations.

Phase 1 is conducted as quantitative empirical research. The identified drivers for performance alignment contribute substantially to the main research objective of compiling a general guideline for optimizing across manufacturing and quality control (phase 4). Furthermore, implications of phase 1 continuously stimulate the overlapping executed research in phases 2 and 3.

Phase 2 – Recommendation

Since the exact research problem of aligning operational performance in pharmaceutical manufacturing and quality control has not been researched previously, the recommendation phase aims to take knowledge from broader subject fields and to apply it to the specific object of concern researched in this thesis. Thus, concepts and approaches for cross-departmental management within production sites are studied. Phase 2 delivers implications drawn from the research streams Organizational Strategy and Capability Management and leads to explorative managerial recommendations how to optimize manufacturing and quality control holistically.

Phase 2 is conducted as desk research. Based on a systematic literature review existing models, approaches, and tools with proven potential for cross-departmental optimization are identified. In case of given applicability to pharmaceutical production, they are used to enrich the guideline for optimizing across manufacturing and quality control (phase 4) with new additions. Furthermore, implications of phase 2 continuously stimulate the overlapping executed research in phases 1 and 3.

Phase 3 – Confirmation

Phases 1 and 2 supply the overall research with several puzzle pieces that serve as individual parts of the solution. This research is based on pharmaceutical benchmarking data and literature from outside the pharmaceutical industry. Supplementary, phase 3 strives to confirm how to align manufacturing and quality control comprehensively by introducing existing industry successful practices. After identification of successful practices based on the outcomes of a survey-base study, proven role models' approaches how to optimize pharmaceutical manufacturing & quality control in an integrated way are presented in detail.

Phase 3 is conducted as qualitative empirical research. It contains a survey-based study and case study interviews with leading pharmaceutical production establishments. The identified case-specific concepts how to manage manufacturing and quality control holistically contribute to the main research objective of compiling a

general guideline for optimization across departments (phase 4). Furthermore, implications of phase 3 continuously stimulate the overlapping executed research in phases 1 and 2 and allow the triangulation of findings.

Phase 4 – Conclusion

The concluding phase of the research project summarizes all findings of the core research phases 1-3. It consolidates implications from researching the subject fields elaborated above based on quantitative empiricism, literature, and qualitative empiricism. Following SRQ 4 and the MRQ of the dissertation, these results are transformed into an actionable format that allows direct application by practitioners.

Phase 4 is conducted as conceptual design. It manifests the overall product of this thesis: A guideline to optimize operational performance across manufacturing and quality control in pharmaceutical production.

1.2.5 Data Gathering Strategy

A significant part of the present thesis builds on studying data from pharmaceutical production. While research phases 0 and 2 rely on academic literature, where access is guaranteed by the university's infrastructure, phases 1 and 3 require gathering empiricism from practice. Therefore, a data gathering strategy is needed and developed. It comprises four main data sources allowing access to both quantitative and qualitative empiricism. The following describes these four sources and their utilization along the research procedure.

Source 1 – St.Gallen OPEX Manufacturing & QC Lab Benchmarking

For more than 15 years the St.Gallen OPEX Benchmarking allows pharmaceutical manufacturers to report their operational data for benchmarking purpose. The benchmarking evaluation is conducted with regard to the later presented St.Gallen OPEX model (cf. chapter 2.1). It consists of various operational KPIs (Abbreviation Key Performance Indicator) in the three dimensions Total Productive Maintenance, Total Quality Management and Just-in-Time. Additionally, the Lean & Operational Excellence maturity of participants is assessed by 185 enabler questions with pre-defined and fully operationalized answer options on a 5-point Likert scale. To enable the set-up of meaningful peer-groups and interpretation of benchmarking results in the specific context of production sites, a set of structural factors such as the size, product and production portfolio of a site or its role in the company's production network is gathered as part of the study in addition. As an outcome of the benchmarking exercise all participating production sites receive a personalized result report highlighting identified strength & weaknesses in comparison to their dedicated peer group.

As the original St.Gallen OPEX Benchmarking demonstrates a focus on pharmaceutical manufacturing, a 2nd benchmarking program dedicated to measure

performance of quality control labs has been ramped-up in 2017. This benchmarking program gathers KPIs in the three main dimensions Productivity, Quality and Service along with the enabler implementation level and structural context following the established St.Gallen benchmarking methodology. Additionally, headcount and cost structure for both QA and QC are assessed. A summary of both benchmarking programs is provided in Figure 8.

Benchmarking Scope	Participation Benefits	Timeline
▪ Operational Excellence (OPEX) Benchmarking for Pharmaceutical Manufacturing (DS, DP Production & Packaging) and Quality Control Labs. ▪ Industry-tested holistic approach based on the St.Gallen OPEX Research. ▪ Assessment of both OPEX Metrics Performance and Maturity / Enabler.	▪ Personalized benchmarking report showing relative performance compared to tailored peer-group and High Performer. ▪ Participating with more than one site per companies enables to start capability transfer based on new transparency. ▪ St.Gallen benefits from data access for research purpose. However, confidentiality is ensured.	▪ Continuous evaluation allows industry to participate at any time. Benchmarking is performed compared to a recent selection of previous participants in the same peer group. ▪ A tailored project plan is developed for all participants according to their priorities. ▪ Standardized procedures minimize efforts for production sites and corporate sponsors.

Figure 8: Summary of St.Gallen OPEX Benchmarking Programs

As of March 2021, the St.Gallen OPEX manufacturing benchmarking database contains of detailed operational data from 385 production sites around the globe, while the QC lab benchmarking database comprises data from 111 quality control operations worldwide. Those datasets are directly available for analyses as part of the present thesis. Both benchmarking programs continue and the databases are expected to grow with additional participating pharmaceutical establishments in the months and years to come.

By now, there is an overlap of 35 production sites from 12 companies that completed both benchmarking exercises at the same point of time. The combined datasets are of special interest for the present research as they allow to study the performance of both departments manufacturing and quality control in direct comparison with one another.

Source 1, the St.Gallen Benchmarking databases, supplies the present research with quantitative empiricism. The data is used especially during phase 1 but informs phase 2 and 3 in addition following the iterative research procedure outlined in chapter 1.2.4.

Source 2 – Global Quality Benchmarking Study

Data source 2 leads back to the project *Quality Management Assessment & Surveillance* also focusing on benchmarking practices. The project was jointly executed with Dun & Bradstreet and funded by the U.S. FDA. It is tailored to research especially the current usage of quality management practices and their impact on outcome performance across the pharmaceutical industry. Figure 9 provides an overview of the study set-up.



Figure 9: Overview Global Quality Benchmarking Study

For this study, a streamlined OPEX & quality benchmarking questionnaire has been developed. The assessment contains a scientifically derived subset of legacy St.Gallen Benchmarking KPIs and selected enablers, that have been proven to meaningfully surrogating overall system’s stability and performance best. The overall objective was to conceptualize an assessment that is as slim and user friendly as possible but still comprehensive enough to deliver a solid and balanced overview of operational performance and quality maturity. 13 Key Performance Indicators in four dimensions, 18 maturity questions in three categories, and 5 contextual factors are gathered accordingly across pharmaceutical establishments.

Additionally, the conceptualized assessment module serves as basis to enrich the Assess, Aspire, Act, and Advance Framework of ISPE (Abbreviation International Society for Pharmaceutical Engineering) with a pre- and post- benchmarking instrument to evaluate and quantify improvements. The partnership with ISPE’s APQ (Abbreviation Advanced Pharmaceutical Quality) program is set up as long-term collaboration beyond the timeframe of the global quality benchmarking study. (ISPE, 2020; Ritz & Friedli, 2021a, p. 1 ff.)

Similar to the above outlined partnership with ISPE, the St.Gallen research team aims to support the PDA (Abbreviation Parental Drug Association) with the assessment module. Both institutions are currently evaluating the integration of the streamlined benchmarking to enable participants in PDA's quality culture program to link conclusions with operational outcome performance. (Ritz & Friedli, 2020, p. 1)

The study was announced to the public in May 2020 and collected operational data from 208 pharmaceutical establishments in 35 countries by end of 2020. As the set of KPIs contains two dedicated quality control measures besides manufacturing related indicators, the data gathered allows to analyze performance in manufacturing and quality control comprehensively. These observations can be put into perspective to the St.Gallen Benchmarking databases (source 1) to complement and broaden the analyses.

Source 2, the project Global Quality Benchmarking Study, supplies the present research with quantitative empiricism. The data is used especially in phase 1 but informs phase 2 and 3 in addition following the iterative research procedure outlined in chapter 1.2.4.

Source 3 – St.Gallen Industrial Research & Exchange Groups

Two industrial research & exchange groups are continuously operated following the fundamental objective of disseminating research to industry. The ORG (Abbreviation St.Gallen OPEX Industrial Research Group) focuses on discussing recent topics around Operational Excellence, especially related to manufacturing, whereas participants of the QCEx (Abbreviation St.Gallen QC Lab Exchange Platform) exchange on topics of Operational Excellence in quality control.

Both groups are established in industry and follow the same approach aiming to unite academic and practical knowledge: Specific exchange topics are jointly defined based on industry's priorities once per year and covered during a series of meetings throughout the year. Participating companies present challenges and successful practices related to the planned exchange topic at every meeting. The St.Gallen OPEX research team complements these inputs with recent research findings. Finally, joint workshop sessions foster knowledge exchange. Purposeful discussions bring together multiple perspectives on the topics from industry and academia. Figure 10 shows the set-up and contributing pharmaceutical companies in the 2020 editions of both groups.



Figure 10: Industrial Engagement in St.Gallen Research & Exchange Groups 2020

The industrial research & exchange groups are crucial for the present thesis as they allow to identify newest industry's successful approaches. At the same time these groups serve as a platform to actively present and challenge preliminary research findings. Industry's interests and expectations for joining the programs are perfectly aligned with the subject researched in the present thesis due to the topical focus of both groups. Furthermore, both exchange programs represent a unique access to industrial SMEs (Abbreviation Subject Matter Expert) who can be approached to conduct interview-based case study research.

Source 3, the St.Gallen research and exchange groups, supplies the present research with qualitative empiricism. The insights are used especially in phase 3 but inform phase 1 and 2 in addition following the iterative research procedure outlined in chapter 1.2.4.

Source 4 – Survey Study: Excellence across Manufacturing & QC Labs

The three data sources presented above all follow a twostep approach to gather data from both manufacturing and quality control department by department in a first step, before integrating both departments per analytics in a second step. That is why a dedicated survey study is conducted in addition. A comprehensive questionnaire has been designed and rolled-out across industry. It concerns companies' perception if there are differences between manufacturing and quality control in operational performance, level of maturity and status of compliance at their production

sites. In addition, the specific organization of and strategy to Operational Excellence is part of the questionnaire. Finally, participants should provide information about their approaches to deal with interdepartmental barriers and levers for alignment. Figure 11 summarizes the scope of the study and its main categories.

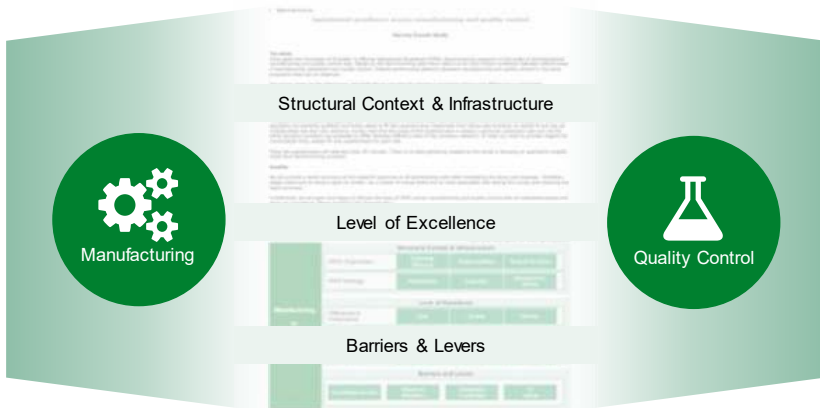


Figure 11: Survey Structure

Information gathered through the survey-based study complement the data foundation of the previously described sources. The collected insights on the degree manufacturing & quality control are already managed comprehensively are researched together with specific approaches to establish interfaces and interplay. On this basis, successful industry examples can be identified, selected, and even further detailed by subsequent interview-based case study research.

Source 4, the survey-based study on excellence across manufacturing and quality control, supplies the present research with qualitative empiricism. The insights are used especially in phase 3 but inform phase 1 and 2 in addition following the iterative research procedure outlined in chapter 1.2.4

1.3 Thesis Set-Up

The following section provides a summary of the thesis set-up aiming to guide through the subsequent passages. An overview of the content is given and visualized in chapter 1.3.1 alongside with a brief introduction to all dissertation chapters. Furthermore, a recap of the research schedule is presented in chapter 1.3.2. It depicts the time period in which the presented research was conducted and lists events that allowed for dissemination of intermediate findings to industry.

1.3.1 Structure & Content

This dissertation contains seven chapters which can be clustered in four main sections: Introduction of topic (chapter 1), Presentation of research field (chapter 2), Main Part (chapters 3, 4, 5, and 6) and Conclusion (chapter 7). Each chapter comprises multiple sections. Figure 12 depicts an overview of the overarching structure of the thesis.

Operational Excellence across Manufacturing and Quality Control – A Guideline to Avoid Optimizing Silos in Pharmaceutical Production				
1	Introduction	1.1 Origin & Relevance	1.2 Research Strategy & Design	1.3 Thesis Set-Up
2	State of Research	2.1 Introduction of Research Streams		2.2 Theoretical Gap – OPEX across Manufacturing and QC
3	Performance across Manufacturing and QC Labs	3.1 Methods		
		3.2 Analyses based on St.Gallen Benchmarking Databases	3.3 Analyses based on Global Quality Benchmarking Study	
		3.4 Implications for OPEX Management		
4	Approaches for Cross-departmental Collaboration & Optimization	4.1 Methods		
		4.2 Search Procedure & Outcomes	4.3 Review & Discussion	4.4 Findings & Applicability
		4.5 Implications for OPEX Management		
5	Proven Successful Practices in Pharmaceutical Production	5.1 Methods		
		5.2 Data Gathering & Sample Overview	5.3 Results, Discussion & Case Selection	5.4 Detailed Case Studies
		5.5 Implications for OPEX Management		
6	Guideline for OPEX Management	6.1 Overview & Structure		
		6.2 Modules & Recommendations	6.3 Application & Adaption	
		6.4 Summarized Outcomes & Anticipated Improvements		
7	Conclusion	7.1 Summary	7.2 Contributions	7.3 Limitations
				7.4 Future Research

Figure 12: Thesis Structure

In the following, all seven chapters are introduced to provide orientation for further reading. Each passage briefly outlines purpose, content, and contribution of the individual chapter to the research project.

Chapter 1 – Introduction

In addition to explaining the origin and legacy background of the research problem, chapter 1 grounded subsequent activities in theory. Research questions were derived alongside with a conceptual framework positioning the thesis at hand in three research streams. Furthermore, the procedure structuring all following research steps was outlined. Presenting the data gathering strategy provided confidence that sufficient access to empiricism has been ensured.

Chapter 2 – State of Research

Chapter 2 introduces the three research streams *Operational Excellence*, *Organizational Strategy* and *Capability Management* this dissertation is informed by and contributes to. Besides expounding the basic concepts of each research stream, special attention is paid on defining and clarifying terms used in the following chapters. Moreover, the existing theoretical gap is summarized based on an initial systematic literature review.

Chapter 3 – Performance across Manufacturing and QC Labs

After that, chapter 3 presents the outcomes of the first core research phase. It contains comprehensive quantitative analyses of benchmarking data gathered in the pharmaceutical industry and reveals cross-departmental patterns observed across production sites. Thereby, the section identifies metrics and maturity attributes correlated between manufacturing and quality control. Furthermore, associations of departmental scores, overall performance, and the compliance status of pharmaceutical production sites are investigated. Results allow to derive implications and inform the guideline for OPEX management.

Chapter 4 – Approaches for Cross-departmental Collaboration & Optimization

Chapter 4 extends the scope of research and incorporates knowledge from broader subject fields by an extensive desk research on cross-departmental collaboration and optimization. In order to do so, a systematic literature search is conducted and complemented by an in-depth review of promising articles. According to the aim of the corresponding research phase, practices applied beyond the pharmaceutical industry are identified and assessed for their applicability to Operational Excellence across pharmaceutical manufacturing and quality control.

Chapter 5 – Proven Successful Practices in Pharmaceutical Production

Subsequently, chapter 5 completes the empirical research by drawing implications for OPEX management based on a survey-based study among industry executives and SMEs. Observations allow to confirm findings of the earlier research phases

and to identify proven successful practices for comprehensively approaching Operational Excellence across manufacturing and quality control within pharmaceutical production sites. Based on this, the identified successful practices are individually detailed and explained in selected case studies while ensuring to consider their specific context of application.

Chapter 6 – Guideline for OPEX Management

Systemizing and summarizing all previously drawn implications, chapter 6 compiles the guideline for OPEX management and thus creates the overarching product of the thesis at hand. Accomplishing research phase 4 and addressing the latter SRQ, a structure of the guideline is derived and introduced first. After that, the guideline's modules are detailed and recommendations for practitioners stated within the different subject fields. On top of that, the need for specific adaption during implementation is emphasized and anticipated outcomes of application in practice are finally elaborated.

Chapter 7 – Conclusion

Chapter 7 concludes the overall research project. In addition to recapping answers to the initially raised research questions and thereby summarizing the results, contributions of this thesis to theory and practice are outlined. Supplementary, limitations of the findings and their generalizability are highlighted. An outlook on future research complements the chapter and rounds off the dissertation by introducing prospective opportunities.

Appendix

Lastly, the appendix of the thesis at hand provides supplementary material. It spotlights initial statements from industry on the relevance of the subject field and exhibits the interview guideline followed within research phase 3. Furthermore, the appendix contains all templates for data gathering, which have been used in the field along the research journey. Comprehensive definitions of terms and indicators are included in these questionnaires.

1.3.2 Timeline Recap & Continuous Dissemination

Establishing a basis to digest the subsequent chapters in the context of the time the thesis was written, a brief recap of the research timeline is provided in the following. The overall dissertation project was initiated in autumn 2018, completed in spring 2021, and the corresponding thesis finally submitted in June 2021. Within this period, the core research phases (cf. chapter 1.2.4) *Investigation*, *Recommendation* and *Confirmation* were executed in parallel before drawing up conclusions and compiling the implications in a guideline during phase 4. Individual research steps were performed in parallel to be able to respond to newly available data gathered

according to the data gathering strategy (cf. chapter 1.2.5) in an agile manner. Figure 13 provides a visual recap of the entire research project timeline.

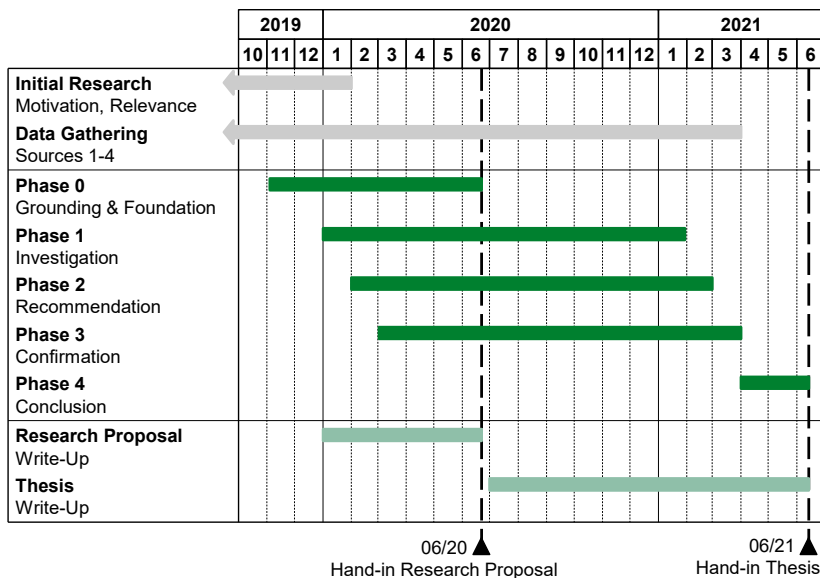


Figure 13: Thesis Time Frame

Intermediate findings have been continuously disseminated to academia and industry in the course of the entire research process. Preliminary results were presented at several conferences¹ in 2020, including Xavier Pharmalink in Cincinnati, ISPE Annual Meeting in Philadelphia, Pharma TechOps in Berlin, and LeanLab in Milano. Moreover, on-going project collaborations triggered regular exchange with the CDER (Abbreviation Center for Drug Evaluation and Research) of the U.S. FDA in Washington DC.

On this basis, feedback allowed to regularly evaluate the relevance of individual research steps. Learnings were directly considered in subsequent research activities according to the iterative research approach and helped to continuously sharpen the focus of the dissertation.

¹ Due to the COVID-19 pandemic, some of the conferences have been conducted in hybrid modes allowing remote attendance in addition to in-person presence or changed to full-virtual events. However, this did not diminish the benefits of disseminating intermediate findings of the research and gathering feedback from foreign researchers or industry experts.

2 State of Research

Reviewing relevant literature is essential for all research projects. A suitable review acts as sound base for any following analysis and consequently helps to enlarge existing knowledge. Furthermore, areas in need of additional research can be determined. As this thesis is motivated by an emerging issue (cf. chapter 1.1) it can highly benefit from exposure to theoretical basis. (Webster & Watson, 2002, p. 13 ff.)

The following chapter depicts the current state of the art in research and expounds insights from academic literature which are relevant for the examined research objective. Chapter 2.1 gives an overview of the three research streams Operational Excellence, Organizational Strategy, and Capability Management this thesis contributes to. Afterwards, the current state of literature concerning the particular research problem Operational Excellence across pharmaceutical manufacturing and quality control is studied in chapter 2.2. On this basis, deriving the existing theoretical gap complements the section and summarizes the conclusion drawn for the subsequent research steps.

2.1 Introduction of Research Streams

While the connection to the research stream Operational Excellence is apparent, this work is also informed by and contributes to broader subject areas of management research. The Organizational Strategy on corporate and site level is expected to play a crucial role for fostering and supporting cross-departmental alignment by providing a suitable organizational environment. Therefore, it is an essential part of the studies and supplements Operational Excellence as a second research stream with broader focus. Previous research found that the level of OPEX enabler implementation significantly differs between low performing and excellent plants (Friedli et al., 2019, p. 37). That is why building, sustaining, and dispensing capabilities is considered an important lever for driving forward performance in both manufacturing and QC labs. Hence, Capability Management serves as third research stream the present thesis is positioned in.

In order to present all three research streams a semi-systematic literature review is chosen as suitable approach in accordance with Snyder (2019, p. 335). The review does not aim to reflect available literature in its entirety but to establish a sound foundation from where in-depth research in later stages of the process can draw from. The results of the literature review are summarized in the subsequent sections and provide an overview of the subject fields Operational Excellence, Organizational Strategy and Capability Management. Implications from a full-systematic literature search on the specific research problem are presented in chapter 2.2. Moreover, another systematic literature review explicitly focusing on certain aspects within the

research streams is conducted at a later stage of the research process (cf. chapter 1.2.4).

2.1.1 Operational Excellence

According to Friedli et al. (2013, p. 24) Operational Excellence is recognized as the balanced management of cost, quality, and time while always focusing on the need of internal and external customer. Thus, it summarizes effectiveness and efficiency in production. Operational Excellence does not only comprise the current outcome performance. It also includes indications on how to achieve superior performance taking into account practices that allow an organization to continuously improve itself. Sustainable OPEX is not solely promoted by top management. It additionally requires routine employee engagement to maintain a culture of never being satisfied with the current status and strive for further improvements across the entire organization. (Ritz & Friedli, 2021b, p. 1)

The management philosophy Operational Excellence is informed by three main concepts that have played a crucial role in production management over the last decades: World Class Manufacturing, Lean Production, and Continuous Improvement. All three terms and the associated concepts are briefly presented as important foundations in the following.

Underlying Concepts

Hayes and Wheelwright (1984) introduced the term and concept of WCM (Abbreviation World Class Manufacturing). WCM comprises a set of practices recommended to manufacturers to achieve outstanding operational performance. The practices have been derived from an in-depth analysis of firms located in Japan, Germany, and the US. All identified practices can be summarized and clustered in 6 main dimensions that act as paradigms to strive for superior performance: (1) Workforce skills and capabilities, (2) Management technical competence, (3) Competing through quality, (4) Workforce participation, (5) Rebuilding manufacturing engineering, and (6) Incremental improvement approaches. Furthermore, the authors contribute to the still on-going debate on trade-offs vs. synergies in manufacturing voicing their opinion that clear priorities between the dimensions of competitive performance are needed. (Hayes & Wheelwright, 1984, p. 375 ff.; Flynn et al., 1999, p. 250 ff.) On that basis, the concept of WCM has been commented, challenged, and enriched by numerous scholars in the field of Operations Management, cf. Flynn et al. (1997, 1999), Schonberger (2007) and Voss et al. (1995) .

The famous book *The machine that changed the world* published by Womack et al. (1990) initiated the age of Lean Production and Lean Management. It summarizes best in class manufacturing practices identified as part of a far-reaching study conducted by the Massachusetts Institute of Technology. Based on a comprehensive literature review, Shah and Ward (2007, p. 791) define Lean Production as an

integral socio-technical system with the main objective to eliminate waste. Hence, Lean Production is characterized by integrating a broad range of management practices such as Just-in-Time, supplier management or usage of quality systems in a multidimensional approach for production. All management practices are expected to jointly create an optimized production system that produces high quality products according to the customer demand while limiting waste. (Shah & Ward, 2003, p. 129) Furthermore, Lean Production includes flexibility allowing to respond to varying demand with individual lot sizes. In addition to continuous flow, this flexibility forms a crucial competitive advantage of the TPS (Abbreviation Toyota Production System), which is a well-known role model for early Japanese Lean Manufacturing. (Krafcik, 1988, p. 45)

Following the philosophy of CI (Abbreviation Continuous Improvement) is at the same time an integral part and a crucial enabler of both concepts World Class Manufacturing and Lean Production. CI formalizes a culture of lastingly targeting improvements in all systems and processes of an organization (Bhuiyan & Baghel, 2005, p. 761). The Japanese term Kaizen is used synonymously to CI in literature (Chen et al., 2001, p. 19). In a comprehensive literature review Pettersen (2009, p. 129) found CI to be one of the only two aspects consistently mentioned as key element of excellent manufacturing practices across journal articles. It is seen as most important success factor for the early achievements of the TPS (Shingo, 1989, p. 16) and a key element of the modern approaches towards excellence (Sandell et al., 2013, p. 433 ff.). Fostering CI leads to significant improvements in manufacturing and is needed to unleash the potential of Lean Management. Thus, CI has evolved to a central management paradigm in different types of organizations. (Singh & Singh, 2012, p. 105) Employee involvement in Continuous Improvement activities and empowering the workforce to bring in individual skills and knowledge is key to sustain competitive advantages and an integral part of the CI philosophy (Schroeder & Robinson, 1991, p. 16). According to Dale (1996, p. 50) a well-defined CI process routinely measures progress of the administered activities. Effectiveness of CI can be measured by assessing changes in attitude and behaviors, improvements in performance indicators, and the alignment of CI projects with the company's overall strategy and priorities (Dale, 1996, p. 50). While improvements generally might also occur through radical changes or innovations, systematically planned and sustained achievements often result of numerous incremental improvements over time. (Bhuiyan & Baghel, 2005, p. 761 f.)

Utilization in Pharmaceutical Manufacturing and Quality Control

Pharma started comparatively late to systematically push improvements and to launch serious production excellence initiatives. Besides the special conditions for changes in a highly regulated production environment, comparably low cost pressure did not cause the same need for optimization to stay competitive as in other industries. (Friedli et al., 2014, p. 32)

However, in the early 2000s increasing pressure on drug prices as well as regulatory attention on process quality and optimization led to the rise of OPEX in pharma. This started causing manufacturers to develop along four different phases from Pre-OPEX to Integrated Operations Systems (Friedli & Werani, 2013, p. 33 f.). On this journey, leading pharmaceutical companies such as Abbott, Pfizer, Novo Nordisk, and Novartis launched comprehensive initiatives in the time frame from 2004 on (Friedli, Basu, et al., 2013). Moreover, the application of OPEX in pharmaceutical production was increasingly researched by scholars in recent years, see Birkie et al. (2018), Garza-Reyes et al. (2018), Haleem et al. (2015), Jaiganesh and Sudhar (2015), Muse et al. (2016), Nenni et al. (2014) or Pavlović and Božanić (2012).

As briefly introduced in chapter 1.1.2, the majority of academic research with regard to Operational Excellence is conducted by the division of Production Management at the Institute of Technology Management, University of St.Gallen. The research team compiles improvement programs for pharmaceutical production based on the St.Gallen Operational Excellence Model since it was initially published in 2006 (Friedli et al., 2006, p. 40 ff.). It is structured in a technical and a social sub-system acting as a framework to measure OPEX performance and maturity. Both sub-systems contain several elements reinforcing each other. Furthermore, the model supports management to derive and detail improvement actions based on the current level of performance and maturity. Figure 14 shows the entire model including all aspects and elements.

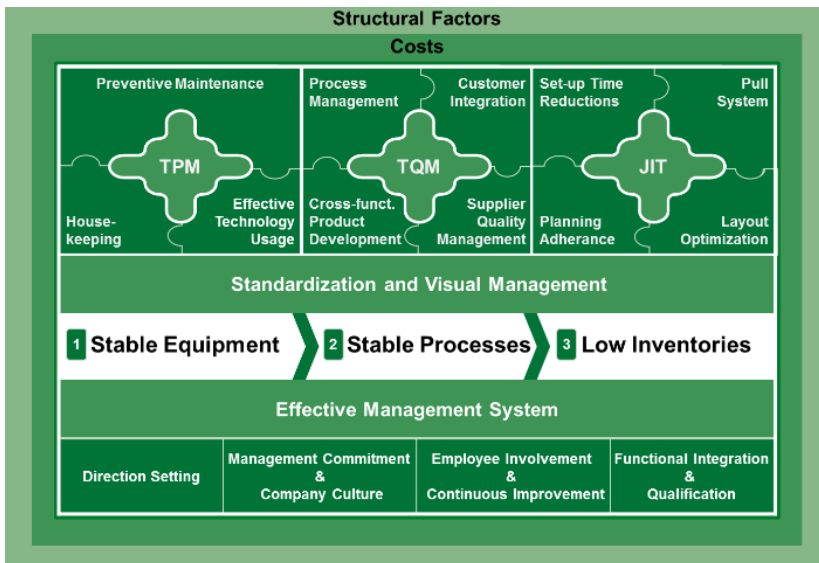


Figure 14: St.Gallen Operational Excellence Model (Friedli & Bellm, 2013, p. 16)

The technical sub-system summarizes three key aspects of Lean Production: TPM (Abbreviation Total Productive Maintenance), TQM (Abbreviation Total Quality Management), and JIT (Abbreviation Just-in-Time). While TPM aims to stabilize equipment, TQM focuses on decreasing process variability and JIT finally optimizes production system's efficiency by following the pull-principle and lowering inventories. All three aspects contribute with a set of practices and tools addressing a concrete lever to optimize production. However, companies are advised to follow the sequence TPM, TQM, and JIT when prioritizing and implementing improvement actions. Mitigating the risk of removing buffers and safeguards as part of JIT strategies requires robust equipment and processes first. Overall, the technical sub-system with its underlying indicators provides a framework to assess the performance of pharmaceutical operations comprising both effectiveness and efficiency. (Friedli & Bellm, 2013, p. 16 ff.)

Complementing the technical aspects of OPEX, the social sub-system allows to quantify the maturity in management and organization. The model's elements strive to engage and support employees in continuously improving direct and indirect processes as part of their day-to-day job. Four key categories Direction Setting, Management Commitment, Employee Engagement, and Functional Integration structure certain underlying social and technical enablers for Continuous Improvement. Additionally, transparent and aligned goal setting as well as an open feedback culture are recommended to foster motivation across the workforce. (Friedli & Bellm, 2013, p. 17 ff.)

Moreover, the St.Gallen Operational Excellence model highlights the crucial role of an effective management system serving together with standardization and visualization as the central layers of the system. Structural factors and cost complement the framework and need to be taken into account while setting objectives and defining priorities. Grounded in and motivated by the work of Ulrich (1984, p. 168 ff.), the St.Gallen OPEX model differentiates from other optimization frameworks by promoting a strictly system oriented perspective: Excellent manufacturing plants are characterized by achieving consistent high performance across both sub-systems and the different elements of the model rather than outperforming competitors in single KPIs. (Friedli & Bellm, 2013, p. 34)

Even if quality is not only considered in the St.Gallen OPEX model but also emphasized as crucial component of excellence in production, the model is designed to optimize manufacturing steps from formulation to packaging and not intended to be readily applicable to quality control. However, as mentioned in chapter 1.1.2, OPEX in quality control is recently of interest and extensively researched by Friedli, Köhler and Ritz. See articles published by the three authors: Friedli et al. (2019), Friedli, Köhler, et al. (2018), Friedli and Ritz (2020), Köhler (2019), Köhler et al. (2020) and Ritz and Friedli (2020, 2021a).

Optimizing QC labs is key to not only increase effectiveness and efficiency of quality control but also needed to support the entire pharmaceutical value chain. While specific lean techniques are already used in QC, there is no integrated approach to OPEX in QC labs. (Friedli & Köhler, 2020, p. 14) However, Greulich (2012, p. 3) acknowledged the need to measure lab's performance using appropriate indicators early on to explore opportunities for Continuous Improvement in all processes.

Köhler (2019) was the first to answer this call and developed a comprehensive approach for OPEX performance measurement in QC labs. The measurement model comprises the four performance dimensions Productivity, Quality, Service, and Cost Efficiency. Moreover, it follows the logic of the St.Gallen OPEX Model and includes 13 enabler categories in the three dimensions Management Commitment / Company Culture, Employee Involvement / Continuous Improvement, and Functional Integration / Qualification. These add an OPEX maturity perspective to the overall model. Besides that, the operating context of the specific QC lab is taken into account while interpreting performance results. Testing the model with benchmarking data, a general relationship between enabler implementation level and QC lab effectiveness can be shown. However, the correlation is highly dependent on the business context. Köhler's analyses do not allow any profound implications about efficiency and the interplay of QC labs with the overall pharmaceutical value chain. (Köhler, 2019, p. 46 ff.)

2.1.2 Organizational Strategy

The initial observation of performance differences between manufacturing and quality control (cf. chapter 1.1) leads to the subject field Organizational Strategy to foster cross-departmental optimization. In accordance with Gupta (2011, p. 511) Organizational Strategy includes all plans and activities to achieve the overarching objectives of an organization. Tailored to the presented research problem, the term Organizational Strategy will be utilized as a summary for its two aspects organizational structure and organizational design in the subsequent passages. Both terms are briefly clarified in the following as they are used overlapping and inconsistently across literature.

Organizational Structure & Design

Organizational structure describes the way organizations divide the workforce according to tasks and the coordination among these tasks (Mintzberg, 1979, p. 2). Based on this definition Mintzberg (1980, p. 322) further distinguishes between the following five organizational structure elements: Simple Structure, Machine Bureaucracy, Professional Bureaucracy, Divisionalized Form, and Adhocracy. All five elements comprise different parts of the organization, mechanism of coordination, design parameters and contingency factors. Daft (2015, p. 88) expounds organization structure as following: It comprises formal reporting relationships such as the

number of hierarchy levels and manager's span of control. Furthermore, organization structure defines the grouping of individuals into departments and the structure of departments in the entire organization. For Daft (2015, p. 88) this also includes systems to effective communication, coordination and integration of efforts across departments. The latter aspect is of particular interest for the present research (cf. chapter 1.2.2).

According to Stanford (2007, p. 5) organizational design describes carrying out business' purpose and strategy following six core principles (Stanford, 2007, p. 3 f.): (1) Organization design should be driven by the business strategy and the operating context. (2) It means a holistic understanding of the organization comprising structure, system, measures, and culture. (3) Design should address not only the present but the future. (4) Social interactions and conversations are key. (5) Organization design requires resources and invest. (6) Instead of a repair job, organizational design should be driven as a continuous and fundamental process. Stanford (2007, p. 6) concludes that organizational design strives to align units and organize work coherently in a way that is beneficial to the entire organization. Additionally, different organizational forms and their impact on cross-departmental collaboration are considered in the present research. Basic organizational models such as a flat structure, divisional hierarchy, functional hierarchy, product or geographic orientation, serve as examples for possible organizational set-ups. (Harris & Raviv, 2002, p. 853 ff.)

Organizational Strategy in the Context of Lean Management & CI

The importance of organizational aspects to support Continuous Improvement is acknowledged by Stone (2012, p. 121) as an outcome of a comprehensive literature review on Lean Management. Y. P. Gupta and Lonial (1998, p. 243 ff.) show a strong link between organizational manufacturing strategy and the achieved organizational performance based on a cross-industry study. Thus, management activities should focus on the alignment of organizational, business, and manufacturing strategies (Y. P. Gupta & Lonial, 1998, p. 259 f.). Faron (2012, p. 103 ff.) highlights the correlation between the point in time companies started applying lean tools and their organizational structure. While the majority of firms, which are just starting the lean journey, is organized functionally, companies which have started with lean implementation more than four years prior to the study, show a broader mix of organizational charts including matrix, process and team based organization forms (Faron, 2012, p. 110 f.).

Research on how to best introduce lean from an organizational perspective has been conducted by Wildemann and Baumgärtner (2006, p. 546 ff.). The authors illustrate various organizational approaches for implementation of Lean Management in their work: Personal responsibility of sites, introduction lead by dedicated staff or champions, and deployment by a functional department. Moreover, different strategies for lean introduction across a network such as simultaneously, sequential

or clustered along regions are elaborated. (Wildemann & Baumgärtner, 2006, p. 549 f.) While these concepts focus on the deployment and initial implementation of Lean Management, they do not consider sustaining a philosophy of Continuous Improvement or Operational Excellence in production sites and the respective departments over time.

Organizational Strategy in the Context of OPEX in Pharma

Lembke (2014, p. 103 ff.) developed a dedicated model for setting-up and organizing above-site OPEX support units. The approach offers and details two main organizational forms that can be chosen for the unit: Department or staff oriented. Furthermore, the main areas of tasks for the unit are defined as Enabling, Executing, Communicating, and Coordinating. The organizational structure is detailed within the aspects Span of control, Standardization, Centralization, and Hierarchical positions depending on the specific needs of the company applying the model. OPEX support units should be structured accordingly. Besides developing and introducing such an unit, two further use cases of the methodology are expounded: Discussing the need for central OPEX support and reflecting existing units. (Lembke, 2014, p. 127 f.) Lembke's model is tailored to provide a frame for structuring the organizational support of OPEX initiatives. The development of the model was also informed by pharmaceutical use cases. However, the present research problem of comprehensively managing OPEX across departments in general - or narrower across pharmaceutical manufacturing and quality control - is not addressed explicitly.

2.1.3 Capability Management

As briefly described in chapter 1.1, previous research on Operational Excellence in pharmaceutical production shows a relation between the level of enabler implementation and operational performance. This observation is true for both manufacturing (Friedli, Köhler, et al., 2018, p. 29 f.) and quality control (Friedli, Köhler, et al., 2018, p. 42). In the way measured and quantified, enabler implementation levels can be understood as indicators for the OPEX maturity of a department or production site (cf. chapter 1.2.5) and reflect underlying capabilities. A general correlation between capabilities and manufacturing performance was also observed in broader studies across industries, cf. Voss et al. (1995, p. 2 ff.). Thus, building and sustaining capabilities is a key lever for enabling and aligning excellent performance in production.

Adapted from Wissotzki (2015, p. 84) capabilities are understood as the ability of an organization to make use of available resources and information to support achieving a strategic goal by executing a defined and repeatable action or process. Specific functions or roles take responsibility for these actions to produce a desired outcome (Wissotzki, 2015, p. 84). Focusing more specifically on organizational capabilities, Grant (1996, p. 378) presents a hierarchy of different categories: Single-task capabilities, specialized capabilities, activity-related capabilities, broad functional

capabilities, and cross-functional capabilities. Cross-functional capabilities are of particular interest for the present research. Abilities which enable Continuous Improvement and Operational Excellence by applying appropriate tools and practices across departments, can be assigned to this category. In the same context, the term organizational practices is broadly used in literature. It is defined as organization's knowledge that evolved over time and is used for conducting a particular action (Kostova & Roth, 2002, p. 216). As definitions of both terms capabilities and practices indicate a tremendous overlap, they will be used synonymously in the subsequent passages.

Capability Building & Transfer

Building capabilities means integration of specialist knowledge into an organization (Grant, 1996, p. 377 ff.). Miller et al. (2002, p. 46) detail the strategy for systematically building capabilities in four dimensions: Leadership/Governance, Values/Culture, Structural Mechanism and Systems/Policies. Leaders need to prioritize and fund capability building. This also comprises to ensure availability of resources. A corporate culture of appreciating and celebrating newly generated knowledge motivates capability building. Dedicated functions or task forces should be set-up to establish a structured cross-departmental capability building, adapting, and sharing process. Furthermore, information systems can support planning and tracking capabilities per department or product. Moreover, such systems allow leveraging synergies between tools for knowledge management and recognition procedures that promote and reward employees based on present capabilities. (Miller et al., 2002, p. 46)

The majority of scholars focus on inter- and intrafirm networks when researching the transfer of organizational capabilities and practices, e.g. Maritan and Brush (2003, p. 945 ff.) or Tsai (2002, p. 179 ff.). Kostova and Roth (2002, p. 217 ff.) introduce a model for adoption of practices by subsidiary organizations of multinational corporations. The model comprises two dimensions: Implementation and Internalization. Implementation expresses the behavior or action caused by the transferred practice, while internalization is the process of employees familiarizing with and committing to the practice at the recipient subsidiary. Additionally, the authors point out that several interorganizational factors affect the adoption of practices: Institutional and relational context, dependence, trust, and identification. (Kostova & Roth, 2002, p. 218 ff.)

Challenges of sharing knowledge and capabilities across organization subunits are expounded by Hansen (1999, p. 85 ff.) and summarized as Search-Transfer Problem: Creating awareness of beneficial capabilities outside one's own unit requires a structured search process across the organization. This presupposes established communication channels and an existing cross-functional network. When the knowledge to be transferred across units is searched and identified, passing on

capabilities still faces two barriers: Willingness and ability to transfer. The willingness to transfer knowledge is especially determined by the source and can be limited due to internal competition or the intraorganizational atmosphere. Even if the source unit is willing to share capabilities and necessary resources are provided, the transfer might still exceed the existing competencies of the involved parties. Hence, the intermediaries are lacking the necessary ability and fail to facilitate the capability transfer successfully. (Hansen, 1999, p. 89 f.)

Operational Excellence Capabilities

A few articles explicitly address building, sustaining, and transferring capabilities related to Operational Excellence, Lean Management and Continuous Improvement. Anand et al. (2009, p. 444 ff.) utilize case studies to research how organizational learning can develop capabilities and practices to establish an infrastructure for Continuous Improvement. The scholars summarize their findings in two implications for managers: Firstly, pure training of employees regarding new processes and tasks is not sufficient. Successful introduction of new practices requires defined mechanisms for maintaining and sustaining the CI initiative as a whole. Secondly, strong interdependencies between different CI practices are observed. Hence, managing CI through certain selected practices may be ineffective. Instead, a system perspective is emphasized. (Anand et al., 2009, p. 458)

Longoni and Cagliano (2015, p. 1332 ff.) investigate the practice of strictly fostering employee involvement across functions. In addition to affecting performance in lean aspects TPM, TQM and JIT positively, the authors found that employee involvement also facilitates alignment of the Lean Management Strategy with environmental and sustainability goals of an organization. Jaca et al. (2014, p. 1755 ff.) highlight VM (Abbreviation Visual Management) as one of the key enablers to ease communication in shop floor management. Besides enhancing day-to-day organization of operations, usage of VM fosters active participation of the workforce in suggestion and improvement initiatives.

In a single case study Johnson (1997, p. 50 ff.) describes a structured process for leveraging Operational Excellence knowledge organization-wide within the company Texas Instruments. This process comprises standardized successful practice definitions as part of a maintained OPEX knowledge database, a supply/demand model for deployment, a defined network of facilitators, and supporting information systems.

A concrete example for transferring lean capabilities is presented by Maritan and Brush (2003, p. 945 ff.). The authors describe the introduction of flow manufacturing across different production plants along a standardized process. It comprises of the two phases pre-implementation and implementation. Both phases include a sequence of stages that provide defined implementation actions of the transfer process. An overview of the capability implementation process is given in Figure 15.

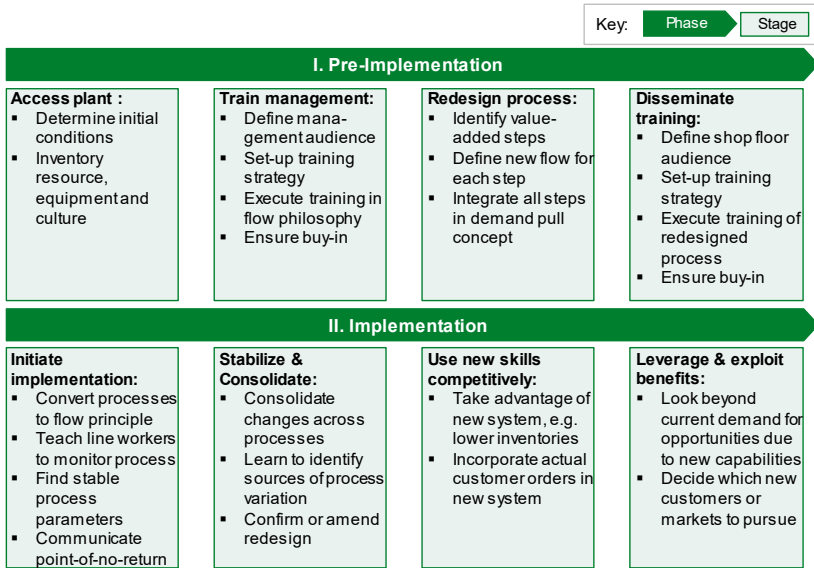


Figure 15: *Capability Transfer Flow Manufacturing – Adapted from Maritan and Brush (2003, p. 950)*

Above detailed process was applied to introduce flow manufacturing in four US plants of the case company's network in a sequential order. Learnings and capabilities were transferred from one plant to another. From these studies Maritan and Brush (2003, p. 957 f.) conclude a variety of conditions, which have to be acknowledged and accommodated to transfer practices successfully: The organizational structure of an establishment and its culture play a key role adding to operational characteristics such as production technology or product complexity. Furthermore, the heterogeneity of different organizations causes differences in effectiveness of successfully transferred capabilities case by case.

2.2 Theoretical Gap – OPEX across Manufacturing and QC

Research motivation and objective of the present thesis were introduced in chapter 1.1. Subsequently, a literature review on the specific research problem is conducted to explore an initial overview of the existing theoretical knowledge base in the subject field. Therefore, literature is systematically searched following a multi-step approach adapted from David and Han (2004, p. 42 ff.) and Newbert (2007, p. 125). This literature search and review methodology is explained in detail in chapter 4, which also presents the outcomes of an in-depth desk research conducted as part of research phase 2. The subsequently presented narrow literature review on the

initial research problem already follows this approach. Scope, chosen search criteria and defined focus of the initial literature search are summarized in the following:

1. Define scope of search to ensure quality and validity of results. Choose selection of literature types:
Only scholarly, peer-reviewed journals are considered.
2. Select data sources:
Due to easy access via the university's infrastructure and the broad range of represented journals the databases ProQuest and ScienceDirect are selected.
3. Ensure relevance with appropriate primary keywords encompassed in abstract or title of the paper:
"operational excellence" OR "lean management" OR "optimization" OR "continuous improvement"
4. Ensure relevance with supplementary industry or domain specific keyword encompassed in abstract or title of the paper:
"pharma"*
5. Ensure relevance with secondary topic specific keywords encompassed in abstract or title of the paper:
("manufacturing" OR "production") AND ("quality control" OR "lab")*
6. Consolidate outcomes from different databases and remove duplicates:
The described search reveals two duplicates that are removed as a result.
7. Ensure relevance by screening abstracts of all remaining articles for substantive context and empirical content. Exclude irrelevant articles:
Conducting the systematic literature search according to the details described above uncovers three hits. Due to the low number of only three articles all papers are considered for the final steps. No articles are excluded.
8. Confirm relevance by entirely reading all remaining articles for substantive context and adequate empirical content. Exclude irrelevant articles:
None of the three hits is finally deemed relevant. See subsequent explanation.

Conducting the systematic literature search described above led to following hits:

- a) Grimaldi et al., 2020. Life cycle assessment and cost evaluation of emerging technologies at early stages: The case of continuous flow synthesis of Rufinamide. *Journal of Advanced Manufacturing and Processing*, 2(2), 1–11.
- b) Paris et al., 2006. Near infrared spectroscopy and process analytical technology to master the process of busulfan paediatric capsules in a university hospital. *Journal of Pharmaceutical and Biomedical Analysis*, 41(4), 1171–1178.
- c) Sajjia et al., 2016. Statistical analysis of industrial-scale roller compactor “Freund TF-MINI model”. *International Journal of Pharmaceutics*, 513(1–2), 453–463.

Access to the articles is provided by the university’s infrastructure. Thus, a detailed full-text review of all articles is carried out. All three articles deal with the optimization of specific pharmaceutical manufacturing process steps such as synthesis (Grimaldi et al., 2020, p. 1 ff.), compounding of hard capsules by hospital pharmacists (Paris et al., 2006, p. 1171 ff.), and compaction of powders (Sajjia et al., 2016, p. 453 ff.).

Identified literature neither includes a holistic managerial perspective of Operational Excellence (as described in chapter 2.1.1) nor studies the cross-departmental optimization between manufacturing and quality control. Hence, none of the publications provide relevant implications for the present research problem, even if they match the defined search criteria and key words. For that reason, execution of a complementary backward search for identifying further related literature based on the identified articles’ references is refused. Similarly, no forward search is conducted.

The narrow research problem discussed in this dissertation evolved from practice and even the broader subject area of Operational Excellence in the pharmaceutical industry is researched by just a few scholars anyway. Thus, a lack of literature explicitly addressing the research problem was expected and confirmed by the systematic literature search. This result causes additional motivation to start academic studies. It provides confidence that there is a strong need to carry out the planned research. Based on the results of the semi-systematic literature review to introduce the research streams Operational Excellence, Organizational Strategy, and Capability Management in chapter 2.1 and the structured literature research on the specific research problem, the following theoretical research gap is derived:

Academic literature dealing with Operational Excellence in pharmaceutical production is heavily focused on manufacturing and complemented by a few studies

discussing its relevance for quality control labs. As of today, scholars study both departments solely and lack an integrated, cross-departmental perspective on Operational Excellence along the pharmaceutical value chain. Applicability of existing theories, models, and approaches from generally well-researched streams Organizational Strategy and Capability Management to aligning optimization across manufacturing and quality control has not been explored yet.

3 Performance across Manufacturing and QC Labs

Chapter 3 is focused on quantitative analysis aiming to research causes for intra-site performance differences and drivers for alignment between manufacturing and quality control. Thus, the following passages especially address SRQ 1 (cf. chapter 1.2.2) and present the outcomes of research phase 1 *Investigation* (cf. chapter 1.2.4).

The chapter is structured along analyses of Source 1 *St.Gallen Benchmarking Databases* and Source 2 *Global Quality Benchmarking Study* according to the previously formulated data gathering strategy (cf. chapter 1.2.5). After introducing the subsequently used methods in chapter 3.1, the two major passages 3.2 and 3.3 expound analyses of one data source each. Data of both sources is studied individually as the underlying databases evolved from different projects and represent independent samples. Previously presented and discussed analyses results are summarized in outcomes at the end of both chapters and finally transferred into implications for OPEX management in chapter 3.4. These implications inform the guideline (cf. chapter 6), which addresses the MRQ (cf. chapter 1.2.2) of this doctoral research.

3.1 Methods

Subsequent chapters discuss the quantitative analyses of benchmarking data from pharmaceutical production sites. For this purpose, statistical exploration of different benchmarking data points such as indicators and aggregated scores is conducted to derive data-backed conclusions for OPEX management. Applicable statistical methods are limited by the sample sizes available². In particular, three statistical methods will be used to research patterns across manufacturing and quality control: Descriptive statistics, correlation analyses, and linear regressions. All three methods are briefly introduced and described in the following chapters. Supplementary details are provided in appendix A.2.

Data organization, preparation and score calculation for all analyses described in the present chapter is performed in the spreadsheet software Microsoft Excel. All statistical analyses and tests are conducted in IBM SPSS, a software suite dedicated to statistics that also allows to directly plot and visualize results.

3.1.1 Descriptive Statistics

Scientific processes comprise the understanding of data sets to draw conclusions instead of presenting cases individually. Descriptive statistics describe what

² Data gathering is still on-going (cf. chapter 3.2.1). Increased samples might allow to challenge and confirm observations made in this thesis by methods such as ANOVA or cluster analyses in the future.

occurred in the sample. They help to extract and condense important characteristics of data sets by a simplified set of parameters. Furthermore, descriptive statistics can be used to compare multiple samples from different studies. (Mishra et al., 2019, p. 67; Potter, 2006, p. 97; Thompson, 2009, p. 57)

Literature distinguishes three major types of descriptive measurements: Frequency, central tendency and variability, cf. Mishra et al. (2019, p. 67) and Thompson (2009, p. 57). In addition to these, Kaur et al. (2018, p. 64) name measures of position as further category of descriptive statistics, while Mishra et al. (2019, p. 69) discuss determination of positions as part of variability and dispersion measures. Detailed explanations of each type of descriptive measurement are included in appendix A.2.

Different options to summarize data sets include tables, charts, and graphical plots such as scatter plots or box plots to display the outcomes of descriptive statistical analyses. These tools are used to observe trends in the subsequent passages. Compared to tables, plots pictorially convey multiple information and therefore allow for quick interpretation and understanding of the underlying data. Box plots are established straightforward visualizations to present the median, upper and lower quartiles as well as the minimum and maximum range of a data distribution. (Potter, 2006, p. 97 f.)

3.1.2 Correlation Analyses & Linear Regression

Correlation discusses the association or relationship between two or more quantitative variables. It can be measured with the help of correlation coefficients that allow to determine the direction and quantify the extent or strength of the relation. (Gogtay & Thatte, 2017, p. 78) In other words, correlation measures the degree of association between data rows. Changes in the magnitude of one variable are associated with changes in the magnitude of one or multiple other variables. This effect can either occur in the same (positive) or the opposite (negative) direction. (Schober et al., 2018, p. 1763)

Pearson correlation analysis measures the strength of a linear relationship between two variables. It can assume correlation values from $r = -1$ (perfect negative association) to $r = +1$ (perfect positive association). The closer correlation values are to zero, the more individual data pairs diverge from a linear relationship. Generally, coefficients $r < 0.5$ are interpreted as weak linear association, coefficients $r > 0.5$ and $r < 0.8$ indicate a moderate linear association, while coefficients $r > 0.8$ present a strong linear association. However, correlation coefficients always need to be individually interpreted in the context of the analyzed data set and the underlying phenomena. (Cleff, 2019, p. 90 ff.) The significance of correlations observed is usually tested in addition by conducting a t test hypothesizing that the correlation coefficient is zero. Thus, resulting p values indicate significance of the relation observed but do not inform about the strength of association of the two variables. Therefore, even if

the significance of a correlation is an important information, it should not be mixed-up with stating relevance of correlations observed. (Schober et al., 2018, p. 1765) Pearson correlation analyses require metric variables and are not applicable to nominal or ordinal scales (Cleff, 2019, p. 72). Additionally, Pearson correlation assumes independency of variables, linear relationships, and normal distributions. These pre-conditions should be tested and confirmed prior to the correlation analyses to ensure validity of results and implications. (Gogtay & Thatte, 2017, p. 80)

Spearman correlation analysis acts as non-parametric equivalent to calculating Pearson correlation coefficients and is primarily used in case the above-named assumptions are violated. Unlike Pearson correlations, Spearman calculations rank the indicators on the individual scales prior to assessing correlations. Therefore, it is a robust and valid indicator also for jointly analyzing metric and ordinal variables. (Gogtay & Thatte, 2017, p. 80) Spearman coefficients range from $\rho = -1$ to $\rho = 1$. Results should be interpreted analogously to the outcomes of Pearson analyses, paying special attention on clearly distinguishing observed correlation and causation. Furthermore – and different to regression analyses – both correlation coefficients do not indicate any dependence between variables but only show association of the data rows. (Gogtay & Thatte, 2017, p. 80; Schober et al., 2018, p. 1766)

Regression analysis allows to study the dependence of a response variable on a predictor and to estimate the impact of changes in the predictor on the value of the response. Like most statistical methods, regressions aim to summarize observed data in a simple, useful, and elegant way. Hence, as a study of dependence, it is a central part of quantitative research. Linear regressions form the basis for all further types of regression analyses. (Weisberg, 2005, p. 1)

Univariate linear regressions analyze the relationship between a DV (Abbreviation Dependent Variable) and an IV (Abbreviation Independent Variable) by formulating the linear relation equation. In addition to correlation analyses, cause-effect relations can be determined and linear regressions allow to research questions on the existence of relation, the strength of relation and the ability to predict changes in the DV while considering the conditions of analyses. (Uyanık & Güler, 2013, p. 234 f.)

Similar to correlation analyses, outcomes of linear regressions are only credible if the assumptions of the statistical methods hold true and prerequisites are met in addition to appropriate scale levels: The relation between DV and IV has to be linear, both DV and IV need to show characteristics of a normal distribution, little or no autocorrelation must exist as well as homoscedasticity referring to the standard deviation. (Urban & Mayerl, 2018, p. 169 ff.; Weinberg & Abramowitz, 2008, p. 393) In order to demonstrate validity of analyses and to ensure not to violate any of the criteria named, a set of technics and tests is performed prior or in parallel to the linear regression. These are introduced in appendix A.2.

3.2 Analyses based on St.Gallen Benchmarking Databases

As introduced in the data gathering strategy (cf. chapter 1.2.5), the University of St.Gallen is continuously operating the world largest academic-driven studies about Operational Excellence in the pharmaceutical industry: OPEX manufacturing benchmarking and QC lab benchmarking³. Both programs allowed the research team to build extensive databases containing of operational data from 385 pharmaceutical production sites and 111 quality control lab operations around the world. These benchmarking databases in general, and in particular the overlap of production sites having participated in both programs, serve as foundation for the quantitative analyses in the present thesis. Combined operational data from both manufacturing operations and QC labs is available for 35 production sites from 18 countries.

In the following, quantitative investigation of intra-site performance differences and alignment between manufacturing and quality control based on the St.Gallen OPEX benchmarking databases is expounded. Chapter 3.2.1 introduces the content of both benchmarking programs in detail and outlines characteristics of the sample used for subsequent analyses. Hereafter, chapter 3.2.2 describes the testing framework for all analyses based on the St.Gallen benchmarking databases and derives hypothesis. Introducing all aggregated scores used in the following, chapter 3.2.3 establishes the basis for subsequent statistical exploration. Chapter 3.2.4 elaborates all analyses conducted, presents, and discusses the research outcomes. Finally, chapter 3.2.5 summarizes the outcomes and draws conclusions for all hypotheses tested.

3.2.1 Data Gathering & Sample Overview

Pharmaceutical production sites around the globe are welcome to join the initiatives and compare their operational performance to peer facilities in order to prove existing strength and identify gaps for improvement. Both benchmarking programs follow a structured and standardized process to gather comprehensive operational data of pharmaceutical production sites.

During a joint kick-off meeting, the benchmarking procedure is introduced in detail to representatives of the participating facilities, including a live walk-through of the data gathering questionnaires. After having clarified all immediate questions, the industry contact person starts internal data gathering and to fill the benchmarking questionnaires. Depending on resources available on-site and priority assigned to the exercise, timeframes for initially completing the questionnaires range from four to eight weeks. In order to both support participants best and ensure accuracy of

³ The author significantly contributed to the two on-going benchmarking programs during his time as a Research Associate at the University of St.Gallen. He led the benchmarking process of around 20 manufacturing plants and 55 qc labs.

data provided, the researcher stays in close contact with the production site during the entire data gathering period. Ad-hoc support is guaranteed by regularly maintaining a shared Q&A template and offering supplementary calls to discuss details.

Additionally, comprehensive validation routines comprising outlier analyses as well as checks for sensitivity and internal consistency of the dataset are applied after receiving the completed questionnaires. Feedback is provided to participants based on the validation outcomes and starts an iterative process of double-checking, correcting, and confirming conspicuous data points. Finally, benchmarking reports are issued, results communicated, and implications discussed with site representatives in optional workshops. Thus, all final data sets used in the subsequent analyses are not only technically validated but additionally discussed with the corresponding production site to clarify all questions, observations, and initial inconsistencies as part of the regular benchmarking process.

Both benchmarking programs follow the same overarching concept. Content of the programs can be clustered in three major categories: Structural Factors, KPIs and Enabler. Structural Factors provide the operational context of a production site and allow to consider the specific environment while both setting-up a suitable peer group for benchmarking and interpreting the results. KPIs are metrics that allow to measure outcome performance in absolute numbers and ratios. Enabler are approaches, tools and methods expected to lead to better outcomes (Friedli, Lembke, et al., 2013, p. 35) and also represent efforts & resources already invested in CI. Measured on a fully operationalized 5-point Likert scale through a self-assessment, the degree of enabler implementation also indicates the current level of OPEX maturity in the plant or QC lab. Figure 16 visualizes the architecture of both benchmarking programs.

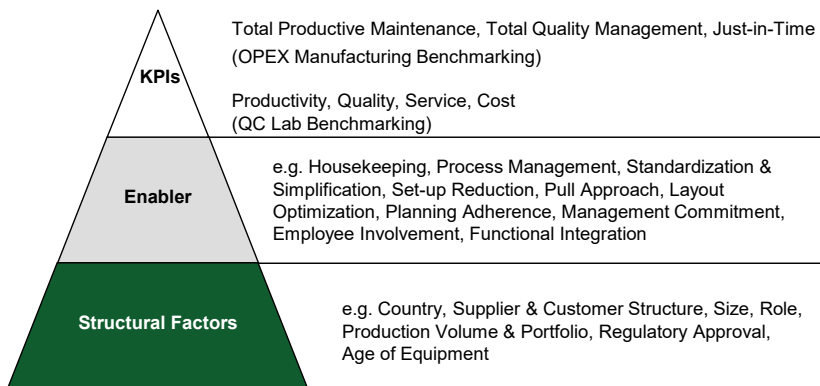


Figure 16: Architecture of St.Gallen OPEX Benchmarking Programs

Attributes within all three major categories are questioned for a 12-month period in both benchmarking programs. Thus, it is ensured to comprehensively assess the operational status of a production plant and leverage out batch-specific variations or seasonal effects during the data gathering. Subsequently, scope and content of the OPEX manufacturing and the QC lab benchmarking are introduced in detail alongside with an overview of the samples used for analyses in following sections of this thesis.

OPEX Manufacturing Benchmarking Database

The St.Gallen OPEX manufacturing benchmarking has been initially launched in 2005. Since then, the program is continuously offered to industry while at the same time regularly revising the benchmarking set-up to ensure up-to-date relevance. During all revisions, particular attention was paid on retaining comparability with the previously gathered datasets. In that way, the full sample of previously gathered datapoints can still be used for comparison even if additional items are added to the questionnaire.

The last major update of the program was rolled-out in 2017 and enables the St.Gallen team to clearly distinguish different production technology platforms to be more precise in research and industry support. All metrics collected afterwards are specific and exclusively represent performance within the technology platform. The majority of previously gathered benchmarking data sets were successfully assigned, converted in the new data format and are thus still available for use in the revised benchmarking.

Figure 17 provides an overview of the production technology platforms. In addition to the distinction of DS (Abbreviation Drug Substance) and DP (Abbreviation Drug Product) production, underlying technologies cover all common categories of pharmaceutical production. Moreover, the assessment allows for specific data collection along the manufacturing value chain and tailored assessment of formulation, primary and secondary packaging steps.

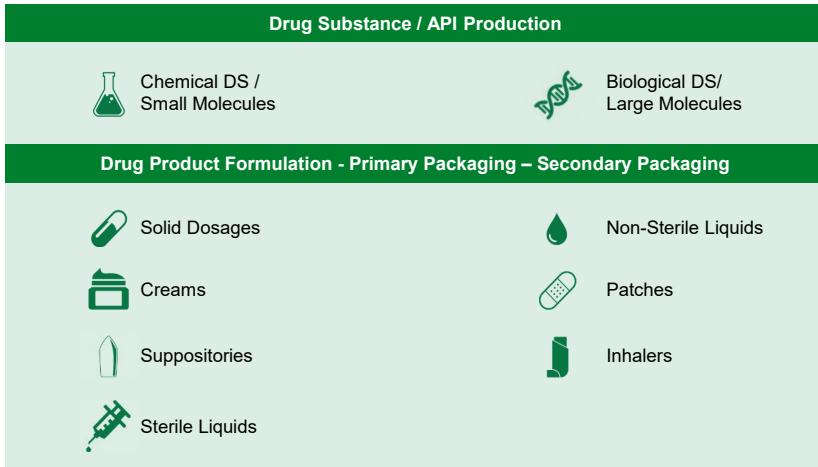


Figure 17: Production Technologies & Peer Group Overview

In addition to the above elaborated production technology platforms, a set of further structural factors per manufacturing site is part of the database. These structural factors include (among others) the location, size, and role of a production site in its company's network, its supplier and customer structure, inspection record of regulatory authorities, product portfolio and production volumes. Herein, the business nature of a site shall be highlighted as important indicator for complexity of operations and cost structure: Besides branded, research-driven pharmaceutical production sites, the database also comprises generic manufacturers and CMOs (Abbreviation Contract Manufacturing Organization) around the globe.

Operational metrics of the production sites are of particular interest for the quantitative analyses in this thesis. The OPEX manufacturing benchmarking database contains a balanced set of KPIs allowing to evaluate both effectiveness and efficiency of production per site. Thus, it is an operationalization of the St.Gallen Operational Excellence Model (cf. chapter 2.1.1) and the individual metrics can be clustered in the major categories of the model TPM, TQM, and JIT. While the more technical metrics within TPM, TQM and JIT are strictly questioned per production technology platform (leading to multiple submission of the same metric for different production areas in case of multi-purpose sites), the EMS (Abbreviation Effective Management System) metrics are assessed once and across the entire manufacturing plant. Depending on the nature of the individual data point, it can either be solely telling (such as *Right First Time* or *Scrap Rate*) or require normalization to consider the production volume (such as *Number of Deviations* or *Number of Priority Orders*). Figure 18 expounds a summary of all performance metrics included in the manufacturing benchmarking. As crucial part of the research strategy to ensure high quality data,

the metrics are not simply questioned in the benchmarking survey, but all come along with a detailed definition provided to participating production sites.

Total Productive Maintenance KPIs		Just-in-Time KPIs	
▪ Setup and Cleaning ▪ Dedicated Equipment ▪ Unplanned Maintenance ▪ Shift Model & Length, Line Staffing ▪ Overall Equipment Effectiveness (OEE) ▪ Maintenance Costs per Conversion Costs		▪ Order Lead Time ▪ Production Lead Time (Waiting, Production & QC/QA) ▪ Replacement Time to Customer ▪ Days on Hand (DOH) ▪ Service Level – Delivery (OTIF) ▪ Service Level – Supplier (OTIF) ▪ Forecast Accuracy ▪ Production Schedule Accuracy ▪ Priority Orders ▪ Production Freeze Period ▪ Number of Stockouts ▪ Cycle Time ▪ Material Turns (Raw Material; Work-in-Progress; Finished Goods) ▪ Changeover Time (Country, Format & Product Change) ▪ Number of Changeovers (Country, Format & Product Change)	
Total Quality Management KPIs			
▪ Yield ▪ Release time ▪ Deviations per Batch ▪ Deviation Closure Time ▪ Reoccurring Deviation ▪ Process Capability CPK ▪ Complaint Rate (Customer) ▪ Complaint Rate (Supplier) ▪ Right First Time ▪ Rejected Batches ▪ Mean Time between Failure ▪ Scrap Rate ▪ Number of Tests ▪ Critical TO Quality (CTQ) ▪ Quality Costs per Conversion Costs			
Effective Management System KPIs			
▪ Management Layers ▪ Management Span of Control ▪ Group work ▪ Functional Integration		▪ Quantity of Suggestions ▪ Quality of Suggestions per employee ▪ Employee Fluctuation ▪ Sick Leave	▪ Overtime ▪ Training ▪ Level of Qualification ▪ Level of Safety

Figure 18: Metrics St.Gallen OPEX Manufacturing Benchmarking

Benchmarking scoring follows a transparent assessment methodology: The position of the production site in comparison to its peers is determined by calculating percentile ranks of each metric within the benchmarking sample. Beyond a single metric comparison, the OPEX benchmarking informs production sites about overall OPEX performance and the status observed per category TPM, TQM, JIT, and EMS. Consequently, these aggregated scores always depend on the set-up of the specific peer-group and are therefore individually calculated when issuing a benchmarking report. That is why the benchmarking database itself only stores the metrics and disregards percentile ranks or aggregated scores included in the result reports.

Measuring the current status of OPEX maturity is a crucial addition to metrics to fully understand the current health of a production plant and identify levers for improvement. That is why the enabler maturity assessment is an integral part of the

St.Gallen OPEX manufacturing benchmarking. The benchmarking database contains of up to 185 maturity indicators assessed on a 5-point Likert scale per production site. Analogous to metrics, enabler questions follow the structure of the St.Gallen OPEX Model (cf. chapter 2.1.1) and cover the technical categories TPM, TQM and JIT but are not limited to those. Additionally, EMS related enabler questions and a section of Basic Elements (such as Standardization and Visualization) deliver insights about the social and managerial approaches to Operational Excellence of the individual facilities. Since the latest extension of the enabler landscape in 2019 (cf. Friedli et al., 2019, p. 24), all ICH Q10 elements are integrated and would also allow for a stand-alone Q10 maturity assessment. Figure 19 shows an example for enabler questions including the operationalized Likert scale.

Functional integration and qualification					
To what degree has your plant implemented a formal program to increase flexibility of operators?	○	○	○	○	○
	We do not seek to increase the proportion of cross-trained employees	We support employees who seek to cross-train on their own initiative	We provide ad-hoc training for some employees to become cross-trained	We have a formal program to cross-train employees	In addition to training, employees rotate to maintain their qualification

Figure 19: Exemplarily Enabler Question – Cross Training

The maturity levels measured using the qualitative self-assessment are transferred to an ordinal 5-point Likert scale and form an integral part of the site's data set in the benchmarking database. Thus, quantified enabler implementation levels are available for statistical exploration within the subject field of OPEX maturity or in relation with the metrics performance of production sites. The St.Gallen OPEX manufacturing benchmarking questionnaire incl. the full enabler assessment and definitions of all metrics is attached to this thesis (cf. appendix A.3).

At the time of analyses for this thesis, the St.Gallen OPEX manufacturing benchmarking database contained data of 385 production sites. 129 different pharmaceutical companies are part of the sample. Figure 20 visualizes the geographical split and the proportion of production sites per region.

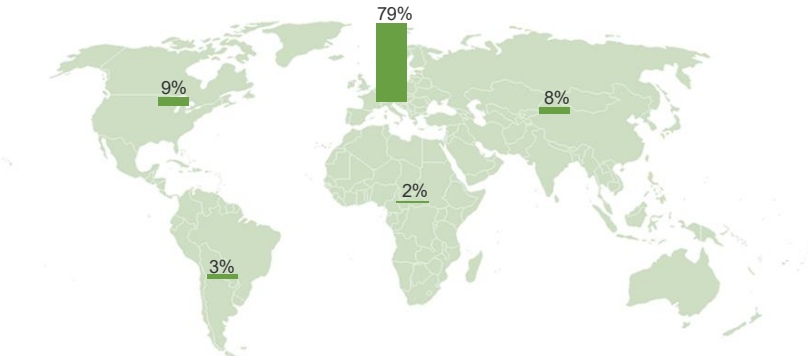


Figure 20: OPEX Manufacturing Benchmarking - Sites per Region

Moreover, the database allows access to operational performance measurements of a diverse set of different site types and business natures of pharmaceutical production. Figure 21 introduces the different production technologies as well as site types and sizes.

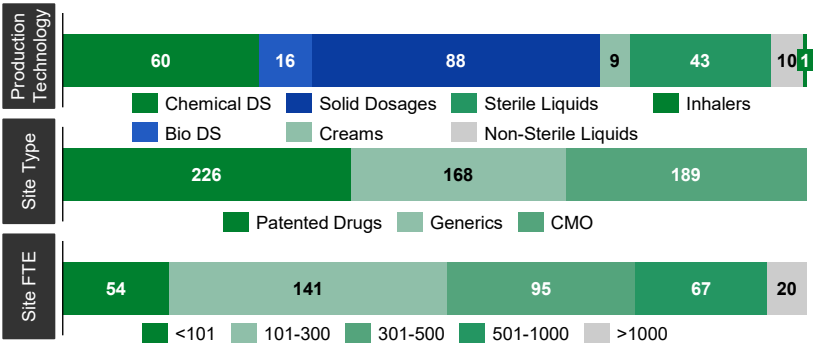


Figure 21: OPEX Manufacturing Benchmarking – Sample Set-up⁴

QC Lab Benchmarking Database

The St.Gallen QC lab benchmarking was launched in 2017 and is operated as a sister program to the OPEX manufacturing benchmarking. Two particular drivers motivated the research team to ramp-up this initiative to dedicatedly assess

⁴ Total number of sites differs between individual bars due to the completeness of the site-individual datasets. Depending on the production portfolio some sites cannot be distinctly assigned to one production technology and are therefore not represented in the first bar chart. Furthermore, sites may show characteristics of multiple site types, e.g. producing generic products and act as a CMO. Consequently, these sites contribute multiple times to the second bar chart of the figure.

laboratory operations: On the one hand, there was a tremendous industry pull for support in structurally identifying improvement fields to increase QC efficiency. On the other hand, FDA's quality metrics initiative and the published draft guidance (FDA, 2015, 2016) underpinned regulator's interest in quality metrics in both production and QC areas. See Köhler (2019, p. 34 ff.) for a comprehensive description of the QC lab benchmarking model and its development.

Following the overarching benchmarking architecture introduced above, the QC lab benchmarking database also collects structural factors with regard to each laboratory benchmarked. These include the region, the size of the QC unit and the entire production plant, and the product portfolio (among others). Additionally, two important QC-exclusive information are documented: (1) The degree of centralization, documenting what proportion of overall testing volume leads back to support the company network and is not caused by the local production on site. Centralized testing is often performed for stability testing or microbial environmental monitoring. (2) The proportion of individual test types indicating how large test volumes of different types of testing are within the benchmarked QC unit. Therefore, it is crucial to understand that the St.Gallen QC lab benchmarking was not designed to analyze single laboratories of a production site's QC department (such as solely looking at the incoming raw material lab or the microbiology lab) but always evaluates the entire QC unit at a production site comprising all laboratory operations in a combined site-wide assessment. Figure 22 summarizes the different test types considered.

Test types	
Drug Substance Testing	Drug Product Testing
Intermediates Testing	Packaged Product Testing
In Process Control	Microbial Environmental Monitoring
Raw Material Testing	Microbial Product Testing
Stability Testing	Component & Packaging Material Testing



Figure 22: Test Types QC Lab Benchmarking Database

In line with the program's purpose to break up the *black box*⁵ QC lab, all metrics gathered focus on the laboratory operations and can be clustered in three main performance dimensions: Productivity, Quality and Service. Cost shall not solely be understood as performance dimension as it heavily depends on the operating

⁵ In initial discussions with industry, this term was prominently used to describe the issue that OPEX initiatives in pharmaceutical production were mainly focusing manufacturing and driven by operations without considering and understanding QC as lever for improvement in the site-internal value chain.

context and location of a production site. However, selected cost indicators supplement the productivity measures to evaluate efficiency in a comprehensive and normalized manner. Further organizational metrics are included to quantify the managerial set-up of a QC laboratory. Numbers such as the average sick leave per employee or the number of days per year dedicated to training may also serve as indicators for the operating climate in the laboratory. Figure 23 provides an overview of the entire set of metrics used in the QC lab benchmarking.

Productivity	Quality
- Handled Samples - Number of Tests - Throughput Rate - Dedicated Equipment - Equipment Utilization Rate - Number of Samples per Run - Stock-time for Consumables - SOPs	- Analytical Right First Time - Lab Investigations - Invalidated OOS - Total OOS - Lab Deviation Events - Recurring Deviation - CAPAs Overdue - Customer Complaints Requiring Investigation - Product Re-Tests due to Complaints - Routine Product Re-tests - Annual Product Quality Reviews (APQR) - APQR On-Time Rate - Stability Reports - Change Controls Opened - Audits - Test Method Validations - Method Transfers
Service	
- Lead Time - Cycle Time - Release Time - Adherence to Schedule (ATS) - Adherence to Lead Time (ATL) / Testing On Time Rate (OTR)	
Cost	
- Maintenance Cost - Service Cost	- Depreciation Cost - Total Quality Control Cost - Total Quality Organization Cost
Organization	
- Span of Control - Reporting Layers - Qualified Technicians	- Employee Fluctuation - Cross-trained Analysts - Group Work - Training - Sick Leave

Figure 23: Metrics St.Gallen QC Lab Benchmarking

Volume-dependent metrics are normalized by either the number of tests (e.g. *Lab Deviation Events*) or headcount FTEs (Abbreviation Full Time Equivalent) to ensure meaningful interpretation of the individual data points. Key metrics of the performance dimensions Productivity, Quality and Service are assessed per individual test type (cf. Figure 22) first to allow specific comparisons, before aggregating performance across test types for each individual metric. Thus, the QC lab benchmarking database used for analyses in this thesis does not solely provide QC-wide performance levels but also insights about the underlying components. Transferring the performance per individual metric to percentile ranks within the peer-group and calculating dimension-wide scores, follows the same approach previously explained in the context of the manufacturing benchmarking program.

The maturity assessment of the QC lab benchmarking comprises 68 laboratory specific enabler questions in three major categories: (1) Maintenance & Quality System, (2) Planning & Steering System and (3) Management. Similar to the example provided in Figure 19, operationalized answer options on a 5-point Likert scale allow for an objective self-assessment. Results are stored in the QC lab benchmarking database and are available for the present research. While the unit of analyses is solely the QC lab operations, some subject fields evaluated are also questionable beyond QC, especially the social and managerial tools and approaches. These topics are similarly discussed for operations in the manufacturing benchmarking program. Hence, there is an overlap of maturity elements included in both benchmarking databases but assessed individually for manufacturing and quality control. The St.Gallen QC lab benchmarking questionnaire, its full enabler assessment and the definitions of all metrics is provided in appendix A.4.

At the time of analyses for this thesis, data sets of 111 QC labs from 26 countries were available in the St.Gallen QC lab benchmarking database. 31 different pharmaceutical companies are part of the sample. Figure 24 visualizes the geographical split and the proportion of production sites per region.

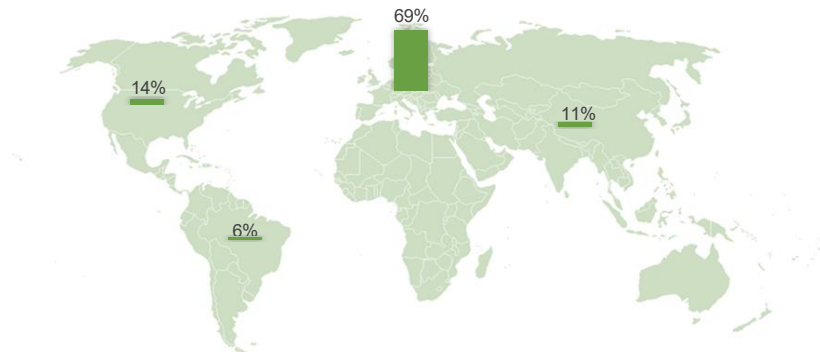


Figure 24: QC Lab Benchmarking – Sites per Region

Moreover, the database allows access to operational performance measurements of a diverse set of different QC lab operations. Figure 25 introduces the different QC unit sizes alongside with the further important structural factors test volume and degree of centralization.

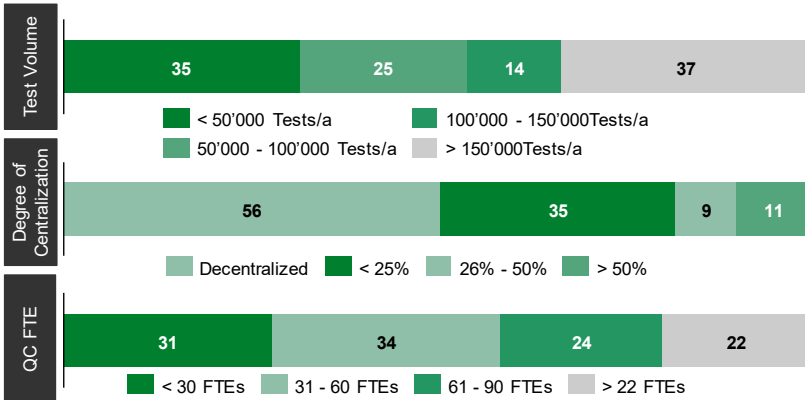


Figure 25: QC Lab Benchmarking - Sample Set-up

Combined OPEX Manufacturing and QC Lab Benchmarking Sample

Subsequent subchapters strive to quantitatively investigate the relation between performance in manufacturing and quality control based on the benchmarking data. For this reason, the overlap between both databases is extracted and forms an exclusive sample of combined data sets for analyses. The term *combined data set* hereby describes production sites having participated in both benchmarking programs within the same time period. All *combined data sets* add up to the *combined St. Gallen benchmarking database*.

For this selection of production sites, structural factors, departmental metrics & enabler implementation for both manufacturing and quality control operations are covered and allow interdepartmental research. Similar to the department-individual data sets, availability of data point combinations differs from analysis to analysis depending on the completion rates of the manufacturing and quality control assessments per production site.

At the time of analyses for this thesis, 35 combined data sets were available for the present research. This sample includes 12 companies and the production sites are located in 18 countries around the world. The geographical split is visualized in Figure 26. As a sub-sample of both databases, the distribution of sites across different regions is similar to the departmental manufacturing and QC lab benchmarking samples.

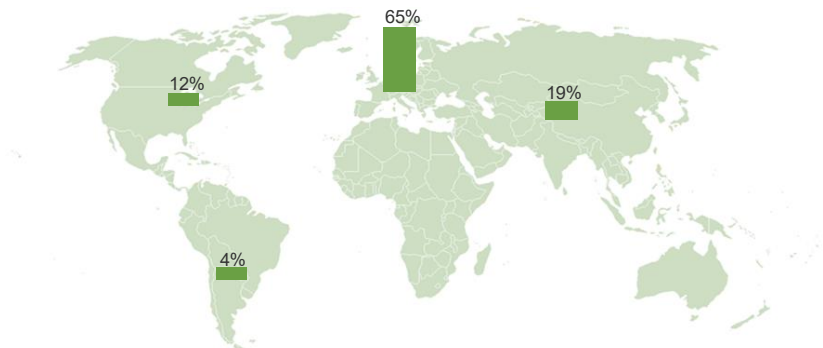


Figure 26: Combined St.Gallen Benchmarking Database – Sites per Region

Furthermore, and analogous to the individual databases, the combined sample represents a diverse setting of pharmaceutical production. It comprises a balanced set of different facilities representing both DS and DP operations within smaller and larger production sites. Production of patented drugs is represented alongside with generic products and contract manufacturing operations. Figure 27 further characterizes the combined benchmarking sample (consider footnote 4, Figure 21).

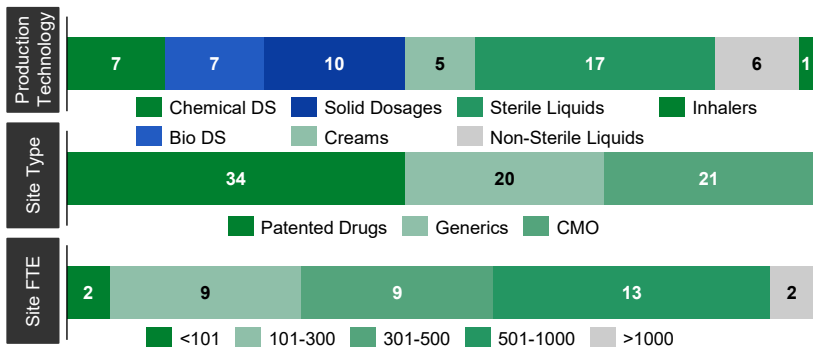


Figure 27: Combined St.Gallen Benchmarking Database - Sample Set-up

3.2.2 Testing Framework & Hypotheses

Following the aim of SRQ 1 (cf. chapter 1.2.2) a set of hypotheses is formulated to investigate performance patterns across manufacturing and quality control in detail. The analyses build on the initial observation of misalignment in effectiveness measured through Operational Stability in manufacturing and Lab Robustness in quality control (cf. chapter 1.1.1), examine the relation of underlying metrics and incorporate an efficiency perspective. Moreover, KPIs are set into relation with the

observable OPEX maturity in both departments measured through the level of enabler implementation. The structural context of the pharmaceutical production sites and their compliance status operationalized by inspection outcomes serve as additional dimensions and complement the framework. Based on the initial observations, all hypotheses assume there is no relation and strive to confirm or reject this presumed absence of associations based on the empirical data.

Overall, five hypotheses clusters are derived and situated in the basic architecture of the St.Gallen benchmarking programs (cf. chapter 3.2.1), which determines the sequence of different analyses. Figure 28 provides a summary.

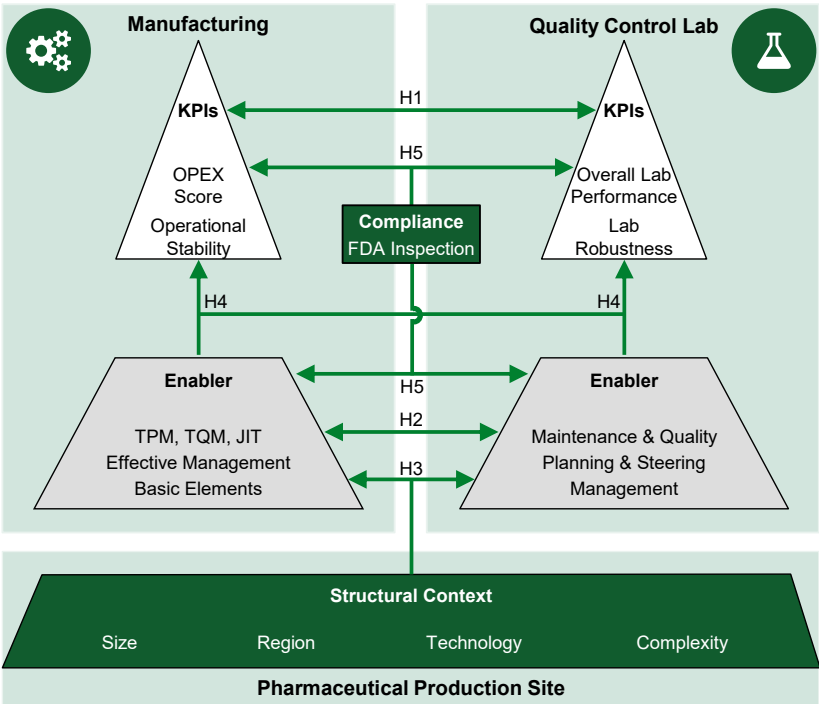


Figure 28: Hypotheses Cluster Overview

The first cluster H1 strives to test the relation of performance scores across manufacturing and quality control. In addition to a comprehensive validation of the initial observations on Operational Stability and Lab Robustness (cf. chapter 1.1.1) based on the newest benchmarking data available, the scope is extended to broader OPEX performance scores incorporating both effectiveness and efficiency across manufacturing and quality control. Moreover, the relation of all underlying metrics is approached individually to enhance the understanding of drivers for combined

performance, alignment, and misalignment of aggregated performance scores. Table 2 specifies four hypotheses accordingly.

Table 2: Cluster H1 – KPIs across Manufacturing and Quality Control

H1	The effectiveness and efficiency in quality control is not related to the effectiveness and efficiency in manufacturing
H1a	Lab Robustness in quality control is not related to Operational Stability in manufacturing
H1b	Underlying metrics of Lab Robustness in quality control are not related to underlying metrics of Operational Stability in manufacturing
H1c	Lab Performance in quality control is not related to OPEX Scores in manufacturing
H1d	Underlying metrics of Lab Performance in quality control are not related to underlying metrics of OPEX Scores in manufacturing

Subsequently, the relation of enabler implementation levels in manufacturing and quality control is researched following a 2nd cluster of hypotheses. Table 3 summarizes the different aspects. In addition to the relation of the aggregated OPEX maturity level per department, the benchmarking databases are analyzed concerning patterns across the main enabler dimensions TPM, TQM, JIT, EMS and Basic Elements in manufacturing alongside with the three enabler systems Maintenance & Quality, Planning & Steering and Management in quality control. The underlying enabler categories within each dimension are studied with special attention on implementation levels in categories, which are explicitly assessed in both departmental benchmarking programs such as Housekeeping or Visual Management.

Table 3: Cluster H2 – Enabler Implementation across Manufacturing and Quality Control

H2	The enabler implementation level in quality control is not related to the enabler implementation level in manufacturing
H2a	The overall enabler implementation level in quality control is not related to the overall enabler implementation level in manufacturing
H2b	The implementation level of individual enabler dimensions in quality control is not related to the implementation level of individual enabler dimensions in manufacturing
H2c	The implementation level of underlying enabler categories in quality control is not related to the implementation level of underlying enabler categories in manufacturing

Following the benchmarking architectures from KPIs and Enabler Implementation to Structural Factors, the third cluster H3 strives to test the relation between the structural context of production sites and their enabler implementation levels across manufacturing and quality control. For this purpose, the interplay of size, geographic region, production technology, and the portfolio complexity of pharmaceutical

production sites with cross-departmental enabler implementation is analyzed and discussed based on the benchmarking databases. Table 4 presents the four underlying hypotheses.

Table 4: Cluster H3 – Enabler Implementation and Structural Context

H3	The enabler implementation level across quality control and manufacturing is not related to the structural context of pharmaceutical production sites
H3a	The enabler implementation level across quality control and manufacturing is not related to the size of pharmaceutical production sites
H3b	The enabler implementation level across quality control and manufacturing is not related to the geographical region of pharmaceutical production sites
H3c	The enabler implementation level across quality control and manufacturing is not related to the production technology of pharmaceutical production sites
H3d	The enabler implementation level across quality control and manufacturing is not related to the portfolio complexity of pharmaceutical production sites

In a next step, hypotheses cluster 4 examines the interplay of enabler implementation and KPIs across both departments. While a positive relation between maturity and effectiveness KPIs was previously observed in manufacturing (Friedli, Köhler, et al., 2018, p. 29) and quality control (Köhler, 2019, p. 101), the relation of combined enabler implementation across both departments and KPIs has not been researched yet. Additionally, interdependencies between enabler implementation and the relation of departmental OPEX performance are investigated based on the combined benchmarking sample. Two hypotheses addressing this subject field are outlined in Table 5.

Table 5: Cluster H4 – KPIs & Enabler Implementation across Manufacturing and Quality Control

H4	The effectiveness and efficiency across quality control and manufacturing is not related to the enabler implementation level across quality control and manufacturing
H4a	Combined OPEX performance in quality control and manufacturing is not related to the combined enabler implementation level across quality control and manufacturing
H4b	The association of OPEX performance between quality control and manufacturing is not related to the combined enabler implementation level across quality control and manufacturing

Finally, analyses incorporate the perspective of compliance. Pharmaceutical productions sites are regularly inspected by health authorities and assessed for compliance with GMP and further regulations. Initial research (Friedli et al., 2019, p. 62 f.) showed tendencies of sites receiving favorable inspection outcomes performing better in KPIs. However, these observations were limited to selected metrics and enablers. As compliance issues lead to tremendous efforts and follow-up activities,

health authority surveillance in itself can cause a drive to mature in operations and quality control preventing regulatory issues. Assuming that approaching OPEX comprehensively across departments might drive inspection performance, the relation of combined enabler implementation and final FDA inspection outcomes is researched. Analogously, the relation of the compliance status and KPIs is tested. OPEX performance across manufacturing and quality control is expected to be impacted by regulators' surveillance. Furthermore, the relation of inspection performance measured through final inspection outcomes and the departmental OPEX performance is investigated. Table 6 presents the four hypotheses on enabler implementation, performance level, and compliance status forming cluster H5.

Table 6: Cluster H5 – Compliance Status, Enabler Implementation & Performance Levels across Manufacturing and Quality Control

H5	The enabler implementation and performance level across quality control and manufacturing is not related to the compliance status of pharmaceutical production sites
H5a	The combined enabler implementation level across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical production sites
H5b	The association of enabler implementation levels across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical production sites
H5c	The OPEX performance across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical production sites
H5d	The association of OPEX performance across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical productions sites

3.2.3 Score Development & Calculation

All benchmarking metrics and KPIs introduced in chapter 3.2.1 are questioned as absolute, individual data points as part of the St.Gallen benchmarking programs. Without further evaluation, this information in itself is expressionless and a pure description of the status measured. As the data is surveyed for a time-centric period and not evaluated against specific targets, it does neither allow implications concerning performance in the sense of achieving improvements, nor regarding the fulfillment of objectives. Hence, the research approach to evaluate performance and the aggregated scores calculated for this purpose are outlined in the following.

All measurements gathered per site are compared to other pharmaceutical production facilities in order to assess performance and ranked according to their relative performance in the specific indicator. This approach is applied to the research at hand and used in subsequent analyses. It is formalized by the calculation of

percentile rankings for each indicator within individual peer groups. For reasons of simplified handling in subsequent calculations and analyses, a decimal notation on a scale ranging from 0 to 1 is always used to handle the results of percentile rank calculations instead of the original percentage notation ranging from 0 % to 100 %.

Peer groups are defined based on the technology platform of establishments to ensure comparability across different operations. All departmental calculations are made separately within the OPEX manufacturing and QC lab benchmarking database, not limited to the combined sample to ensure robustness by sufficient peer group sizes. In that way, the status measured is transferred to relative performance for all indicators and allows interpretation on a metric scale from 0 (indicating lowest performance in the very indicator compared to the peer group) to 1 (indicating highest performance in the very indicator compared to the peer group) consistent across data points. Consequently, all indicators analyzed and displayed in chapter 3.2.4 refer to the percentile ranked, relative performance scores instead to the absolute measurements provided.

Unlike indicators, the observed OPEX maturity levels are measured against defined criteria on a fixed Likert scale through the set of enabler questions (cf. chapter 3.2.1). Consequently, the documented enabler implementation levels accurately represent the present level of maturity within the particular enabler attribute and allow interpretation with regard to the position within the scale even without ranking and arguing the production site's position compared to its peers. Comparability is ensured by utilizing the same reference scale across evaluations of different sites and the departmental benchmarking of manufacturing and quality control.

Unless highlighted otherwise, all analyses in chapter 3.2.4 discussing enabler implementation levels are performed at the level of enabler categories, which each comprises a set of enabler questions. These enabler category implementation levels are calculated as unweighted averages of implementation levels observed in the affiliated underlying enabler questions. Hence, enabler category implementation levels are presented on a metric scale ranging from 1 (indicating lowest maturity observed in all affiliated enabler questions) to 5 (indicating highest maturity observed in all affiliated enabler questions). Due to the calculation as unweighted averages across the implementation level observed in individual questions, the aggregated enabler implementation levels can show any decimal value between 1 and 5. They are not limited to the five ordinal scale values of the Likert scale used for all individual questions.

In addition to the data points from both benchmarking programs (cf. chapter 3.2.1), a set of aggregated scores is calculated to analyze relations and associations according to the hypothesis formulated (cf. chapter 3.2.2). Some of the scores are well-established and regularly used in the benchmarking programs, some have been developed and applied in the legacy St. Gallen FDA Quality Metrics Research

(cf. Friedli et al., 2017, 2019; Friedli, Köhler, et al., 2018), while others are newly derived for the research at hand. All scores entitled *combined* or *alignment* explicitly address the interplay of manufacturing and quality control, these scores are all exclusively compiled based on the combined benchmarking sample. Scores combining different metrics and KPIs are always formed based on the percentile-ranked, relative performance per indicator following the previously elaborated approach.

Subsequent passages introduce the aggregated indicators and scores, their components, and underlying calculations. Each table presents one aggregated score and all tables are structured in the same way from left to right: The first column names the score or indicator, all components are listed in the second column, the third columns provides the original measurement unit and the fourth column indicates whether higher or lower values on the original measurement scale are considered as higher performance in the aggregated score calculation. Descriptions are intentionally limited to naming the indicators, categories, and dimensions. Detailed definitions of indicators and an overview of all underlying enabler questions including the individual maturity levels are given in appendixes A.3 and A.4.

Manufacturing Plant Scores

In addition to the individual metrics and enabler category implementation levels gathered in the benchmarking, a set of aggregated scores is derived to quantify different aspects of performance in manufacturing. Names of some indicators, categories, and dimensions are either synonymously used in both benchmarking programs or do not clearly indicate the discussed department manufacturing or quality control. That is why all indicators, categorial and dimensional scores derived based on the manufacturing benchmarking database are marked with the index *P* in the analyses presented in chapter 3.2.4. It refers to *plant* and allows to easily identify data originated from the manufacturing benchmarking. The term *plant* is used instead of *manufacturing* to avoid the impression of a full departmental independence of performance measured: Even if indicators are questioned in the OPEX benchmarking program with a focus on manufacturing, some measures might also be impacted by lab's performance as a consequence of interaction along the site internal value chain.

At first, three dimensional performance scores along the main sections of the St.Gallen OPEX model (cf. chapter 2.1.1) are computed: TPM, TQM, and JIT. All three scores are calculated as equally weighted averages of the percentile-ranked decimal performance in the underlying indicators. They can range from 0 (indicating lowest aggregated dimensional performance compared to the peer group) to 1 (indicating highest aggregated dimensional performance compared to the peer group).

The TPM score represents effectiveness and efficiency of maintenance operations on site. It combines percentile-ranked performance in the four indicators presented in Table 7. In order to ensure insightfulness of the aggregated score, a 50 %

threshold applies: TPM scores are only calculated for production sites having provided at least two of the four indicators.

Table 7: TPM Score

Score	Indicator	Unit of measurement	Directional positive
TPM _p	Overall Equipment Effectiveness	%	Up
	Set-Up and Cleaning	%	Down
	Share of Unplanned Maintenance	%	Down
	Maintenance Cost / Conversion Cost	%	Down

Analogously, the TQM score quantifies operational performance in the subject fields of manufacturing processes and product quality. The score is calculated based on nine indicators. Applying the 50 % threshold as well, only TQM scores of data sets containing at least five of all nine TQM indicators are considered. Table 8 presents the score and its components.

Table 8: TQM Score

Score	Indicator	Unit of measurement	Directional positive
TQM _p	Deviations / Batch	No	Down
	Deviation Closure Time	Days	Down
	Right First Time	%	Up
	Share of Rejected Batches	%	Down
	Yield	%	Up
	Scrap Rate	%	Down
	Supplier Complaint Rate	%	Down
	Customer Complaint Rate	%	Down
	Quality Cost / Conversion Cost	%	Down

The JIT score represents the third main section of the St.Gallen OPEX model. It comprises nine indicators⁶ discussing especially planning and scheduling, handling of inventories and production times. Table 9 summarizes the score and its components. Fulfilling the 50 % threshold requires availability of at least five of the nine indicators. This leads to calculation of valid JIT scores taken into account for further analyses.

⁶ The JIT score used in the St.Gallen OPEX manufacturing benchmarking reports for participating establishments consists of ten indicators. Compared to this version of the score, performance in changeover times is excluded for the research at hand because of very limited data completeness in the combined benchmarking sample of production sites.

Table 9: JIT Score

Score	Indicator	Unit of measurement	Directional positive
JIT _P	Raw Material Turns	No	Up
	Work-in-Progress (WIP) Turns	No	Up
	Finished Good Turns	No	Up
	Order Lead Time	Days	Down
	Production Lead Time	Days	Down
	Forecast Accuracy	%	Up
	Production Schedule Accuracy	%	Up
	Replacement Time to Customer	Days	Down
	On-time Delivery in Full (OTIF)	%	Up

All three dimensional scores are once more aggregated and jointly represent the OPEX performance of a pharmaceutical production plant in a balanced way. Due to this manifoldness, the OPEX score gives a balanced indication of operational performance incorporating both an effectiveness and efficiency perspective. It is calculated as equally weighted average of TPM, TQM and JIT scores, cf. Table 10. In theory, the OPEX score can reach metric values from 0 (indicating lowest aggregated OPEX performance compared to the peer group) to 1 (indicating highest aggregated OPEX performance compared to the peer group), while very low and very high scores rarely occur in practice due to the apparent trade-offs between the different performance dimensions. The threshold for calculation is set to 100 % to underline the importance of the score's multidimensional balance. Hence, the OPEX score is only calculated for production sites that meet the score thresholds in all three underlying performance dimensions TPM, TQM, and JIT.

Table 10: OPEX Score

Score	Dimension Score	Unit of measurement	Directional positive
OPEX	TPM _P	%	Up
	TQM _P	%	Up
	JIT _P	%	Up

Different to the previously introduced aggregated scores, Operational Stability has already been initially discussed in chapter 1.1.1. The score narrowly focuses on effectiveness. It originates from the legacy St.Gallen research on FDA quality metrics and combines eight process quality related indicators across the main sections of the St.Gallen OPEX model. Addressing the importance of robustness and reliability of operations also highlighted in the ICH guidelines Q8, Q9 and Q10,

Operational Stability allows to evaluate the PQS. In the past, OS has been used in conjunction with quantified supplier performance levels to assess the risk of unfavorable quality and disruption of medicine supply. (Friedli et al., 2017, p. 21 ff.)

Operational Stability is calculated as equally weighted average of the decimal, percentile ranked performance in each of the eight underlying indicators. Results of OS score calculations can range from 0 (indicating lowest Operational Stability compared to the peer group) to 1 (indicating highest Operational Stability compared to the peer group). Applying a 50 % threshold for calculation ensures meaningfulness and credibility of the score. Table 11 summarizes all components.

Table 11: OS Score

Score	Indicator	Unit of measurement	Directional positive
OS	Overall Equipment Effectiveness	%	Up
	Share of Unplanned Maintenance	%	Down
	Deviations / Batch	No	Down
	Deviation Closure Time	Days	Down
	Share of Rejected Batches	%	Down
	Yield	%	Up
	Scrap Rate	%	Down
	Release Time	Days	Down

Similar to the above described aggregated scores summarizing indicators along the structure of the St.Gallen OPEX model, dimensional enabler implementation levels are calculated. OPEX maturity and the implementation of related enabling practices is evaluated for the three main sections of the model in addition to the dimensional outcome performance indicators. This allows to calculate aggregated enabler implementation levels for all dimensions TPM, TQM, and JIT. Additionally, two further maturity dimensions EMS and Basic Elements are assessed.

Consistent to the calculations of categorial enabler implementation levels, all dimensional enabler scores summarize the implementation levels based on the underlying individual enabler questions. Hence, scores are always calculated as equally weighted averages across all questions per dimension, rather than averaging the categorial enabler implementation scores. In that way, artificial over- or under-weighting of categories due to differentiating numbers of questions associated with the categories can be avoided. Aggregations result in dimensional enabler implementation scores on a metric scale from 1 (indicating lowest aggregated dimensional maturity assessed against the criteria formulated per single question in the 5-point assessment) to 5 (indicating highest aggregated dimensional maturity

assessed against the criteria formulated per single question in the 5-point assessment).

Table 12 outlines the aggregated TPM Enabler implementation score. It summarizes maturity levels observed in enabler questions across the three categories Preventive Maintenance, Technology Assessment & Usage, and Housekeeping. Following the St.Gallen philosophy to comprehensive optimization of production (cf. chapter 2.1.1) in a logical sequence, reaching and sustaining TPM maturity is particular important, not limited to improve maintenance operations itself. Moreover, ensuring stable and reliable equipment forms the basis for subsequent optimization of processes. It is also a much-needed prerequisite for lowering lead times and inventory levels to improve efficiency.

Table 12: TPM Enabler Implementation

Score	Category Enabler Implementation	Unit of measurement	Directional positive
TPM Enabler _P	Preventive Maintenance	Averages 1-5	Up
	Technology Assessment & Usage	Averages 1-5	Up
	Housekeeping	Averages 1-5	Up

Analogously, the aggregated TQM Enabler implementation score is calculated based on enabler implementation assessed within four categories. Table 13 provides an overview. TQM enablers are crucial for the research at hand: Besides Process Management, three of the four categories assessed discuss the overarching maturity of plants in managing interfaces with internal and external parties beyond operations.

Table 13: TQM Enabler Implementation

Score	Category Enabler Implementation	Unit of measurement	Directional positive
TQM Enabler _P	Process Management	Averages 1-5	Up
	Cross-Functional Product Development	Averages 1-5	Up
	Customer Involvement	Averages 1-5	Up
	Supplier Quality Management	Averages 1-5	Up

Introducing the next dimensional enabler implementation level, Table 14 presents the four underlying enabler categories summarized in the dimensional JIT Enabler implementation score. Approaches for production planning and scheduling are discussed in addition to evaluating the use of technical tools to support flow production.

Table 14: *JIT Enabler Implementation*

Score	Category Enabler Implementation	Unit of measurement	Directional positive
JIT Enabler _p	Set-Up Time Reduction	Averages 1-5	Up
	Pull Production	Averages 1-5	Up
	Layout Optimization	Averages 1-5	Up
	Planning Adherence	Averages 1-5	Up

Different to the technical dimensions, the aggregated EMS Enabler implementation score reveals insights on the maturity in managerial practices that are expected to support performance improvement. It is compiled based on four categories and crucial to understand the social components of OPEX. Table 15 indicates all components.

Table 15: *EMS Enabler Implementation*

Score	Category Enabler Implementation	Unit of measurement	Directional positive
EMS Enabler _p	Direction Setting	Averages 1-5	Up
	Management Commitment and Company Culture	Averages 1-5	Up
	Employee Involvement and Continuous Improvement	Averages 1-5	Up
	Functional Integration and Qualification	Averages 1-5	Up

Finally, the aggregated Basic Elements Enabler implementation score is calculated based on two categories covering the remaining components of the St.Gallen OPEX model as shown in Table 16. It summarizes practices, which cannot clearly be assigned to one of the previously discussed dimensions. Standardization and Simplification capabilities can enrich performance in almost all indicators, the same holds true for Visual Management.

Table 16: *Basic Elements Enabler Implementation*

Score	Category Enabler Implementation	Unit of measurement	Directional positive
Basic Elements Enabler _p	Standardization and Simplification	Averages 1-5	Up
	Visual Management	Averages 1-5	Up

In order to be able to analyze the overall enabler implementation level and investigate its association with KPIs and structural factors, an overarching implementation score is calculated across the five dimensions of the St.Gallen OPEX model and the

manufacturing benchmarking program. Table 17 provides an overview. The aggregation approach outlined above for the dimensional levels is also applied to the overall enabler implementation level: The score equally weights maturity across all enabler implementation questions of the questionnaire instead of averaging the dimensional enabler implementation scores. Consequently, it summarizes overall OPEX maturity on a metric scale from 1 (indicating lowest aggregated overall maturity assessed against the criteria formulated per single question in the 5-point assessment) to 5 (indicating highest aggregated overall maturity assessed against the criteria formulated per single question in the 5-point assessment).

Table 17: Overall Enabler Implementation Plant

Score	Dimension Enabler Implementation	Unit of measurement	Directional positive
Overall Enabler Plant	TPM Enabler Implementation _p	Averages 1-5	Up
	TQM Enabler Implementation _p	Averages 1-5	Up
	JIT Enabler Implementation _p	Averages 1-5	Up
	EMS Enabler Implementation _p	Averages 1-5	Up
	Basic Elements Enabler Implementation _p	Averages 1-5	Up

Quality Control Lab Scores

Aggregated quality control scores are developed and calculated to complement the set of individual indicators and enabler category implementation levels directly available from the QC lab benchmarking database. These allow broader and integrated analyses in the same way as the above presented aggregated manufacturing scores. Continuing to address the challenge of terms synonymously used in both departmental benchmarking programs, all indicators, categorial and dimensional scores derived based on the QC lab benchmarking database are marked with the index *L* in the analyses presented in chapter 3.2.4.

At first, four aggregated dimensional scores are compiled according to the pillars of the QC lab benchmarking program: Productivity, Quality, Service and Cost. All four scores are calculated as equally weighted average of the percentile-ranked decimal performance in the underlying indicators. They can range from 0 (indicating lowest aggregated dimensional performance compared to the peer group) to 1 (indicating highest aggregated dimensional performance compared to the peer group).

The aggregated Productivity score is a combined measurement summarizing different aspects of efficiency. It combines percentile-ranked performance in the three indicators presented in Table 18. Due to the normalization of all indicators by the number of FTEs, aggregated Productivity scores are comparable across different sizes of lab operations or varying test volumes. In order to ensure insightfulness of

the aggregated score, a threshold applies: Productivity scores are only calculated for QC lab operations having provided at least two of the three indicators.

Table 18: Productivity Score

Score	Indicator	Unit of measurement	Directional positive
Productivity _L	Handled Samples / QC FTE	No	Up
	Batches Processed / QC FTE	No	Up
	Tests / Direct QC FTE	No	Up

Analogously, lab process quality performance is summarized in the aggregated Quality score. Unlike the TQM score used in manufacturing, the aggregated Lab Quality score solely focuses on stability and effectiveness of testing processes. It does not allow any implications on quality of products produced. The score is calculated based on seven indicators and requires fulfilling a 50 % threshold. Only Quality scores of laboratory data sets containing at least four of the seven quality indicators are considered. Table 19 presents the score and its components.

Table 19: Quality Score

Score	Indicator	Unit of measurement	Directional positive
Quality _L	Lab Deviations / 1000 Tests	No	Down
	Share of Reoccurring Lab Deviations	%	Down
	Share of Lab CAPAs Overdue	%	Down
	Analytical Right First Time	%	Up
	Lab Investigations / 1000 Tests	No	Down
	Invalidated Out of Specification / 100000 Tests	No	Down
	Product Re-Tests due to Complaints	%	Down

Besides accurate process quality, timely release of batches according to schedules is crucial to ensure regular supply. That is why quantifying service performance of laboratories is approached by calculating a dedicated dimensional Service score. Thereby, both performance in absolute times and relative adherence to the schedule or standard lead times are considered. Table 20 summarizes the score and the underlying components. Meeting the 50 % threshold requires availability of at least three of the five indicators.

Table 20: Service Score

Score	Indicator	Unit of measurement	Directional positive
Service _L	Lead Time	Days	Down
	Cycle Time	Days	Down
	Test Release Time	Days	Down
	Adherence to Schedule	%	Up
	Adherence to Lead Time	%	Up

Lastly, performance in the fourth dimension of the QC lab benchmarking Cost is aggregated as presented in Table 21. In the context of lab specific benchmarking reports, the local currency of the assessed establishment is always used and cost data of its peer group converted accordingly. For the research at hand, the entire database is converted to USD to ensure comparability across different regions. Due to the small number of only two indicators, a 100 % threshold applies to ensure meaningfulness of the aggregated score.

Table 21: Cost Score

Score	Indicator	Unit of measurement	Directional positive
Cost _L	Total Quality Control Cost / FTE	USD	Down
	Total Quality Control Cost / Test	USD	Down

A conjunction of the four dimensional scores comprehensively quantifies performance of QC lab operations in a balanced way and forms the basis for an insightful overall lab performance score. Finally, this score is calculated as equally weighted average of Productivity, Quality, Service, and Cost scores and named LP. Table 22 summarizes the LP score set-up. Like the aggregated OPEX score in manufacturing, the LP score can reach metric values from 0 (indicating lowest aggregated lab performance compared to the peer group) to 1 (indicating highest aggregated lab performance compared to the peer group).

The threshold for calculation is set to 100 % to ensure to adequately consider trade-offs between effectiveness and efficiency in QC labs. Consequently, the LP score is only calculated for laboratories, which meet the score thresholds in all four performance dimensions Productivity, Quality, Service, and Cost.

Table 22: LP Score

Score	Dimension Score	Unit of measurement	Directional positive
LP	Productivity _L	%	Up
	Quality _L	%	Up
	Service _L	%	Up
	Cost _L	%	Up

In addition to the aggregated QC lab benchmarking scores, Lab Robustness is used for subsequent analyses according to the legacy St.Gallen research on FDA quality metrics, cf. Friedli et al. (2018, p. 37 f.). Contributing to the evaluation of quality system effectiveness also from a regulatory perspective, LR disregards efficiency and is heavily focused on performance in the dimensions quality and service.

LR is calculated as equally weighted average of the decimal, percentile ranked performance in each indicator included in Table 23. LR ranges from 0 (indicating lowest Lab Robustness compared to the peer group) to 1 (indicating highest Lab Robustness compared to the peer group). Similar to the Quality and Service dimension scores, a 50 % threshold for calculation applies.

Table 23: LR Score

Score	Indicator	Unit of measurement	Directional positive
LR	Lab Deviations / 1000 Tests	No	Down
	Share of Reoccurring Lab Deviations	%	Down
	Share of Lab CAPAs Overdue	%	Down
	Analytical Right First Time	%	Up
	Lab Investigations / 1000 Tests	No	Down
	Invalidated Out of Specification / 100000 Tests	No	Down
	Product Re-Tests due to Complaints	%	Down
	Adherence to Schedule	%	Up
	Adherence to Lead Time	%	Up

In addition to the dimensional performance metric scores, aggregated enabler implementation levels summarizing the maturity across underlying enabler categories for each QC lab data set are calculated. Mirroring the structure of the QC lab benchmarking program, aggregated enabler implementation is distinguished in three maturity dimensions: Maintenance & Quality, Planning & Steering, and Management System. While the first two dimensions mostly focus on the application of technical

practices, the latter addresses social capabilities of management in the context of OPEX in QC labs.

The approach for aggregating dimensional scores follows the logic introduced for dimensional aggregated enabler scores in manufacturing: All scores are calculated as equally weighted average across all questions per dimension, rather than averaging the underlying categorial scores to avoid artificial underweighting of categories comprising more question than others. Consequently, aggregations result in dimensional enabler implementation level scores on a metric scale from 1 (indicating lowest aggregated dimensional maturity assessed against the criteria formulated per single question in the 5-point assessment) to 5 (indicating highest aggregated dimensional maturity assessed against the criteria formulated per single question in the 5-point assessment).

As a first lab enabler dimension, the aggregated Maintenance & Quality enabler implementation score is calculated based on implementation averages in the five categories outlined in Table 24. While maintenance related categories show parallels to the aggregated TPM enabler implementation score in manufacturing, the lab quality related enabler categories are streamlined to routines positively impacting process quality.

Table 24 : Maintenance & Quality Enabler Implementation

Score	Category Enabler Implementation	Unit of measurement	Directional positive
Maintenance & Quality Enabler _L	Preventive Maintenance	Averages 1-5	Up
	Technology Assessment & Usage	Averages 1-5	Up
	Housekeeping	Averages 1-5	Up
	Process Management	Averages 1-5	Up
	Standardization and Simplification	Averages 1-5	Up

Table 25 presents the five enabler categories aggregated to the Planning & Steering enabler implementation score. The score comprises flow-related aspects alongside with managerial practices to optimize scheduling and leverage capacities.

Table 25: Planning & Steering Enabler Implementation

Score	Category Enabler Implementation	Unit of measurement	Directional positive
Planning & Steering Enabler _L	Set-Up Reduction	Averages 1-5	Up
	Pull Approach	Averages 1-5	Up
	Layout Optimization	Averages 1-5	Up
	Planning Adherence	Averages 1-5	Up
	Visual Management	Averages 1-5	Up

Additionally, the third and last aggregated QC enabler dimension score Management System summarizes maturity levels across three enabler categories. In addition to management practices, the contribution of analysts and further laboratory staff to the company culture is assessed alongside with the present level of qualification. Table 26 provides an overview.

Table 26: Management System Enabler Implementation

Score	Category Enabler Implementation	Unit of measurement	Directional positive
Management System Enabler _L	Management Commitment and Company Culture	Averages 1-5	Up
	Employee Involvement and Continuous Improvement	Averages 1-5	Up
	Functional Integration and Qualification	Averages 1-5	Up

Finally, all subject fields evaluated in the three aggregated dimensional lab enabler implementation scores are integrated once more to indicate the observed overall enabler implementation level according to Table 27. The overall lab enabler implementation score summarizes the present level of OPEX maturity in the lab operations on a metric scale from 1 (indicating lowest aggregated overall maturity assessed against the criteria formulated per single question in the 5-point assessment) to 5 (indicating highest aggregated overall maturity assessed against the criteria formulated per single question in the 5-point assessment). Individual maturity across all enabler implementation questions of the questionnaire is considered by equally weighting all questions regardless of the enabler category. In that way, unintended variance in the weight of individual questions for the aggregated overall enabler implementation score is avoided, as the analysis does not strive to state different levels of importance for selected enabler questions.

Table 27: Overall Enabler Implementation Lab

Score	Dimension Enabler Implementation	Unit of measurement	Directional positive
Overall Enabler Lab	Maintenance & Quality Implementation _L	Averages 1-5	Up
	Planning & Steering Implementation _L	Averages 1-5	Up
	Management System Implementation _L	Averages 1-5	Up

All aggregated manufacturing and quality control KPI scores introduced in the previous passages are subsequently used to test hypotheses formulated in clusters H1, H4 and H5 (cf. chapter 3.2.2). Furthermore, chapter 3.2.4 includes analyses of their underlying indicators across both departments.

Additionally, the set of aggregated enabler implementation levels and alignment scores outlined above is used in the following to test hypotheses formulated in clusters H2, H3, H4 and H5 (cf. chapter 3.2.2). Application of these aggregated scores complements the analyses basing on the individual enabler category implementation levels in chapter 3.2.4.

Structural Context Indicators

Three of the hypothesis formulated within hypotheses cluster H3 (cf. chapter 3.2.2) discuss the size of production site sizes, their geographical location and the production technologies on-site. Appropriate structural factors to test these hypotheses are directly available from the benchmarking databases and can be analyzed as categorical attributes given on nominal or ordinal scales: Site sizes are clustered in five groups distinguished by the total number of FTEs employed at site, four regional groups are compiled according to the continents Europe, North America, South America and Asia, and production technologies are considered by differentiating two groups producing drug substances or drug products⁷.

Differently, there is no measurement immediately available from the benchmarking programs to quantify portfolio complexity in manufacturing and quality control, which is discussed in the fourth hypothesis of cluster H3. That is why aggregated indexes quantifying the present level of portfolio complexity in manufacturing and qc lab operations based on structural information and indicators are developed.

Table 28 shows the plant complexity index derived based on data points available from the OPEX manufacturing benchmarking. It summarizes 12 indicators, that are first transferred to percentile ranks considering the optimization direction indicated. Afterwards, percentile ranks are aggregated by calculating their equally weighted average. Consequently, the plant complexity index can range from 0 (indicating lowest aggregated portfolio complexity in the sample) to 1 (indicating highest aggregated portfolio complexity in the sample).

⁷ Due to the limited sample size of combined benchmarking data sets, sites are only characterized by producing any types of DS or DP. Distinguishing more granularly between small / large molecule DS or sterile / non-sterile DP would decrease the number of sites per group dramatically and hinder analyses.

Table 28: *Plant Complexity Index*

Index	Indicator	Unit of measurement	Increased Complexity
Complexity Plant	Technology Mix	No	Up
	New Product Launches	No	Up
	New SKUs Launches	No	Up
	Process Steps	No	Up
	Share of Non-Dedicated Equipment	%	Up
	Number of Changeovers	No	Up
	Manufacturing Schedule Instability	%	Up
	Total Number of Employees	No	Up
	Management Layers	No	Down
	Share of Temporary FTEs	%	Up
	Share of Pre-Qualified FTEs	%	Down
	Share of Indirect FTEs	%	Up

Following the same calculation rules, the lab complexity index quantifies the aggregated level of QC portfolio complexity at the production sites. Table 29 shows the 13 underlying indicators from the QC lab benchmarking database.

Table 29: *Lab Complexity Index*

Index	Indicator	Unit of measurement	Increased Complexity
Complexity Lab	Testing Technology Mix	No	Up
	Number of Products Tested	No	Up
	Number of Batches Tested	No	Up
	Number of Tests	No	Up
	Share of Non-Dedicated Lab Equipment	%	Up
	Lead Time	Days	Up
	Lab Deviations / 1000 Tests	No	Up
	Share of Reoccurring Lab Deviations	%	Up
	Reporting Layers	No	Down
	Share of Pre-Qualified Analysts	%	Down
	Employee Fluctuation	%	Up
	Total QC Employees	No	Up
	Share of Temporary QC Employees	%	Up

Furthermore, a combined complexity index is calculated in order to be able to not solely consider departmental portfolio complexity in manufacturing and quality control, but additionally take into consideration the entire production site. The combined complexity index is the equally weighted average of both departmental indexes, cf. Table 30. It ranges on a metric decimal scale from 0 to 1.

Table 30: Complexity Index Combined

Index	Departmental Index	Unit of measurement	Increased Complexity
Complexity Combined	Complexity Plant	%	Up
	Complexity Lab	%	Up

Additionally, a complexity alignment index is compiled. It comprises the same underlying indexes and acts as second cross-departmental index addressing complexity as depicted in Table 31. Unlike the combined complexity index, the alignment index does not summarize the level of complexity present at site but quantifies the differences in portfolio complexity across manufacturing and quality control. Therefore, multiple calculation steps are required: At first, the absolute difference between plant complexity index and lab complexity index is determined. Based on these deltas all production sites of the combined benchmarking sample are ranked accordingly calculating percentile ranks. Finally, percentile rank results are inverted and transferred to a decimal scale. Consequently, the complexity alignment index ranges from 0 (indicating lowest departmental alignment and highest difference in aggregated portfolio complexity between plant and lab in the sample) to 1 (indicating highest departmental alignment and lowest difference in aggregated portfolio complexity between plant and lab in the sample).

Table 31: Complexity Index Alignment

Index	Departmental Index	Unit of measurement	Increased Complexity
Complexity Alignment	Complexity Plant	%	Up
	Complexity Lab	%	Up

All complexity indexes are subsequently used to test hypothesis H3d alongside with the further structural context factors size, geographic region, and technology platforms. The categorial values of size, region and technology platform only allow for descriptive statistical analyses or to evaluate Spearman correlations in case of ordinality. Different to that, the complexity indexes are also available to test for Pearson correlation or perform linear regressions due to their metric scale.

Combined Scores across Departments

The present chapter of this thesis not solely aims to recognize relations between manufacturing and quality control based on the combined benchmarking sample. Additionally, it strives to understand interdependencies and interplay of both departments. For this purpose, combined cross-departmental scores are calculated following-up on the aggregated departmental measurements previously introduced.

A combined OPEX & LP Score allows to jointly analyze performance measured in the departmental benchmarking programs. It is calculated as the equally weighted average of the OPEX and LP scores per production site, cf. Table 32. Combined cross-departmental performance is quantified on a metric scale from 0 (indicating lowest combined performance compared to the departmental peer groups) to 1 (indicating highest combined performance compared to the departmental peer groups). A 100% threshold applies: The combined score is only calculated for data sets having met all underlying thresholds for calculation of the two aggregated departmental scores.

Table 32: Combined OPEX & LP Score

Score	Departmental Score	Unit of measurement	Directional positive
OPEX & LP Combined	OPEX	%	Up
	LP	%	Up

Analogously, the combined overall enabler implementation level is aggregated as presented in Table 33. Equal weight is assigned to both departmental enabler implementation levels. Consequently, the combined implementation level represents overall OPEX maturity across manufacturing and QC on a metric scale from 1 (indicating lowest aggregated overall maturity assessed against the criteria formulated per single question in the departmental 5-point assessments) to 5 (indicating highest aggregated overall maturity assessed against the criteria formulated per single question in the departmental 5-point assessments).

Table 33: Combined Overall Enabler Implementation

Score	Departmental Enabler Implementation	Unit of measurement	Directional positive
Overall Enabler Combined	Overall Enabler Lab Implementation	Averages 1-5	Up
	Overall Enabler Plant Implementation	Averages 1-5	Up

Finally, overall alignment scores are derived as additional cross-departmental measurements discussing the interplay of performance and enabler implementation levels. Unlike all previously discussed aggregated measurements, the alignment scores do not summarize the observed level of performance and maturity at site but

quantify the departmental differences in OPEX across manufacturing and quality control. Compiling the scores requires multiple calculation steps: At first, the absolute difference between manufacturing and quality control is determined for both the OPEX & LP scores as well as the overall enabler implementation levels. Based on these deltas, all production sites of the combined benchmarking sample are ranked accordingly by calculating percentile ranks. Finally, percentile rank results are inverted and transferred to a decimal scale.

The OPEX & LP Alignment score is outlined in Table 34. It is given on a scale from 0 (indicating lowest departmental alignment and highest difference in aggregated OPEX and LP scores in the sample) to 1 (indicating highest departmental alignment and lowest difference in aggregated OPEX and LP scores in the sample). Both underlying scores are required to calculate a meaningful alignment score. Hence, a 100% threshold applies again.

Table 34: OPEX & LP Alignment Score

Score	Departmental Score	Unit of measurement	Directional positive
OPEX & LP Alignment	OPEX	%	Up
	LP	%	Up

Analogously, the Overall Enabler Implementation Alignment Score and its components are depicted in Table 35. Different to the 1 to 5 scale used for the previously introduced aggregated enabler implementation levels, the combined overall enabler alignment score ranges from 0 (indicating lowest departmental alignment and highest difference in aggregated OPEX maturity between plant and lab in the sample) to 1 (indicating highest departmental alignment and lowest difference in aggregated OPEX maturity between plant and lab in the sample). The Overall Enabler Implementation Alignment Score is only calculated for complete datasets that allow to calculate both overall plant and lab enabler implementation.

Table 35: Overall Enabler Implementation Alignment Score

Score	Departmental Enabler Implementation	Unit of measurement	Directional positive
Overall Enabler Alignment	Overall Enabler Lab Implementation	Averages 1-5	Up
	Overall Enabler Plant Implementation	Averages 1-5	Up

The combined scores are subsequently utilized to incorporate an integrated, cross-departmental perspective for testing hypotheses of clusters H3, H4 and H5. In that way, comparisons of departmental patterns across the benchmarking programs are enriched by considering the cross-departmental interaction and interrelation assessable for the combined sample of production sites.

3.2.4 Results & Discussion

Analyses of the combined OPEX manufacturing and QC lab benchmarking sample are presented and discussed in the following. Results are outlined according to the testing framework defined and the sequence of five hypotheses clusters derived in chapter 3.2.2. Definitions of indicators and enabler attributes are provided in appendixes A.3 and A.4. All aggregated scores used in the following, underlying components and the calculation rules have been introduced in chapter 3.2.3.

Cluster H1 – KPIs across Manufacturing and Quality Control

The first cluster of hypotheses researches the relations of KPIs across manufacturing and quality control. Aggregated performance scores quantifying the measured levels of cross-departmental effectiveness and efficiency are analyzed alongside with dimensional indicators. Furthermore, underlying metrics in plant and lab are subsequently checked for correlations and associations.

In a first step, the relation of Lab Robustness and Operational Stability is analyzed following-up on the legacy observations motivating the overall research at hand: Inconsistencies in departmental performance quantified by these scores have been initially observed in 2018 and confirmed based on the databases at the starting point of the research journey early 2020 (cf. chapter 1.1.1). Both scores represent the departmental level of effectiveness. Figure 29 provides a scatter plot of LR and OS scores compiled based on the most recent combined benchmarking sample (cf. chapter 3.2.1).

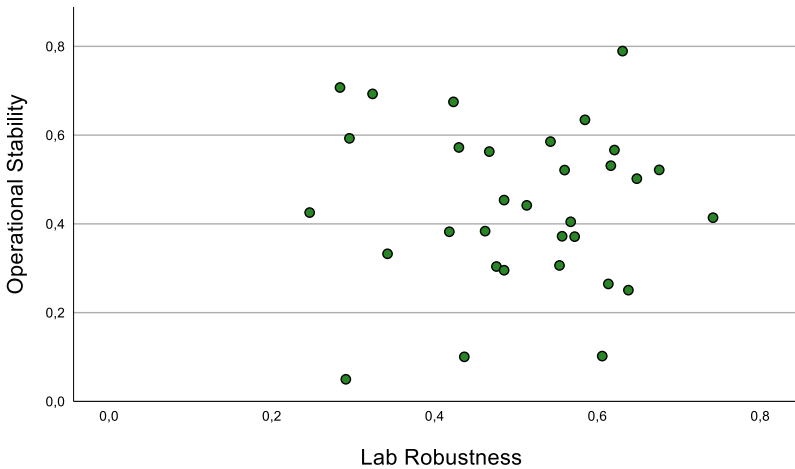


Figure 29: Scatter Plot of Lab Robustness and Operational Stability

Similar to the legacy analyses based on earlier versions of the benchmarking databases, no clear pattern across LR and OS can be observed from the descriptive statistic presented. There seems to be no relation between effectiveness in quality control and manufacturing.

Striving to confirm the absence of an association, a correlation analysis of Lab Robustness and Operational Stability scores is performed. Before conducting the analysis, both variables are assessed for the preconditions of credible Pearson correlation coefficients in order to determine the appropriate correlation method. Table 36 summarizes the results of Shapiro-Wilk tests for normal distribution of variables.

Table 36: Test for Normal Distribution Lab Robustness and Operational Stability

	Shapiro-Wilk Test		
	Statistic	df	Sig
Lab Robustness	.970	32	.249
Operational Stability	.977	35	.658

Significant levels $p > 0.05$ allow to assume normal distribution of LR and OS across the combined benchmarking sample. Q-Q plots of both variables do not reveal any indications for non-normal distributions. Assuming a linear relation of both variables, all preconditions for correlation analysis according to Pearson are fulfilled since both scores are calculated on a continuous metric scale. The results of the correlation analysis are presented in Table 37.

Table 37: Pearson Correlation Analysis of Lab Robustness and Operational Stability

	Operational Stability	
	r	-.018
	Sig (2-tailed)	.921
	N	32

The Pearson correlation coefficient $r = -0.18$ indicates almost no correlation of both variables. Consequently, outcomes of the legacy research are confirmed based on the enlarged, recent combined benchmarking sample: Lab Robustness in quality control is not associated with Operational Stability in manufacturing.

Subsequently, all underlying metrics of both aggregated departmental effectiveness scores are also assessed for cross-departmental relation. Before interpreting graphical visualizations of metric combinations, an initial correlation analysis of all KPIs contributing to Lab Robustness and Operational Stability is conducted. In order to determine applicability of Pearson correlation analyses, Shapiro-Wilk tests for

normal distribution of variables are performed beforehand. Results of the Shapiro-Wilk tests are presented in Table 38 for all components of Lab Robustness.

Table 38: Test for Normal Distribution of LR KPIs

	Shapiro-Wilk Test: Lab Robustness Components		
	Statistic	df	Sig
Lab Deviations / 1000 Tests	.945	34	.089
Share of Reoccurring Lab Deviations	.872	25	.005
Share of Lab CAPAs Overdue	.949	32	.139
Analytical Right First Time	.944	30	.119
Lab Investigations / 1000 Test	.970	35	.438
Inv. Out of Specification / 100000 Tests	.972	35	.512
Product Re-Tests due to Complaints	.812	30	.000
Adherence to Schedule	.932	30	.055
Adherence to Lead Time	.9956	29	.261

Outcomes of tests diverge across different KPIs: Normal distributions can be confirmed for the majority of indicators based on a non-significant Shapiro-Wilk result ($p > 0.05$) and the associated Q-Q plot. However, both variables Share of Reoccurring Lab Deviations and Product Re-Tests due to Complaints show characteristics of non-normal distributions and therefore do not allow to proceed with calculating correlation coefficients according to Pearson.

Similarly, all indicators contributing to Operational Stability in manufacturing are evaluated for normal distribution. A set of Shapiro-Wilk tests serves as starting point again and is completed with an in-depth review of the Q-Q plot per variable. Outcomes of the Shapiro-Wilk tests performed for all Operational Stability indicators are summarized in Table 39.

Table 39: Test for Normal Distribution of OS KPIs

	Shapiro-Wilk Test: Operational Stability Components		
	Statistic	df	Sig
Overall Equipment Effectiveness	.934	25	.105
Share of Unplanned Maintenance	.881	25	.007
Deviations / Batch	.925	28	.047
Deviation Closure Time	.892	33	.003
Share of Rejected Batches	.877	27	.004
Yield	.866	31	.001
Scrap Rate	.868	19	.013
Release Time	.932	26	.088

Most KPIs show a significant Shapiro-Wilk test result. Therefore, normal distributions cannot be confirmed. The comparably high number of non-normally distributed variables can lead back to determining performance by calculating the percentile rank for each indicator compared to the much larger departmental peer group first before extracting the combined database. Furthermore, the number of combined benchmarking data sets is limited to $n = 35$ in general. Depending on the completeness rate per indicator, the number of observations lies below this theoretically achievable maximum. Consequently, small and variant sample sizes are sensitive to outliers and do not allow for analyses requiring normally distributed data sets.

Since both sets of Shapiro-Wilk tests revealed non-normally distributed components of Lab Robustness and Operational Stability, non-parametric Spearman correlation analyses are preferred over calculating coefficients according to Pearson. Striving to ensure consistency and comparability of analyses across all KPIs in scope, Spearman correlation coefficients ρ are calculated for all combinations of LR and OS components. Analyses are performed accordingly and all combinations of LR and OS components are tested for cross-departmental correlations.

The SPSS output of all Spearman correlation analyses is given in Figure 30. Combinations revealing significant positive or negative correlations are highlighted in yellow. Additionally, all significantly correlated cross-departmental pairs of indicators deemed insightful for further interpretation based on an initial content review are encircled.

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		P OEE Score	P Unplanned Maintenance Score	P Deviation per Batch Score	P Deviation Closure Time Score	P Rejected Batches Score	P Yield Score	P Scrap Rate Score	P Release Time Score
L Lab Deviations/1000 Tests Score	Correlation Coefficient	.307	-.475	.377	-.399	-.039	.071	-.072	-.110
	Sig. (2-tailed)	.144	.016	.052	.021	.848	.710	.768	.602
	N	24	25	27	33	27	30	19	25
L Recurring Deviations Score	Correlation Coefficient	.349	-.081	.193	-.033	.209	-.002	.067	-.192
	Sig. (2-tailed)	.143	.735	.428	.877	.376	.992	.821	.461
	N	19	20	19	24	20	22	14	17
L CAPAs Overdue Score	Correlation Coefficient	-.118	-.015	-.242	.203	.162	.081	.056	-.034
	Sig. (2-tailed)	.601	.946	.245	.282	.438	.675	.821	.872
	N	22	22	25	30	25	29	19	25
L Overall RFT Score	Correlation Coefficient	.361	.306	.359	.079	.063	-.140	.292	.029
	Sig. (2-tailed)	.098	.177	.093	.689	.777	.494	.290	.899
	N	22	21	23	28	23	26	15	22
L Overall Invest/1000 Tests Score	Correlation Coefficient	.122	-.025	.117	-.119	.143	-.171	.201	-.175
	Sig. (2-tailed)	.560	.904	.553	.508	.478	.359	.409	.391
	N	25	25	28	33	27	31	19	26
L Overall Inv. OOS/100000 Tests Score	Correlation Coefficient	-.340	-.051	.058	-.089	-.026	-.253	-.142	-.324
	Sig. (2-tailed)	.097	.809	.769	.623	.897	.169	.561	.106
	N	25	25	28	33	27	31	19	26
L Product Re-Tests due to Complaints Score	Correlation Coefficient	-.017	.097	-.441	-.193	-.236	-.602	.018	-.237
	Sig. (2-tailed)	.942	.666	.031	.324	.291	.001	.949	.275
	N	21	22	24	28	22	26	15	23
L Average Adherence to Schedule Score	Correlation Coefficient	-.177	-.009	.367	-.080	.423	-.090	.318	-.148
	Sig. (2-tailed)	.442	.970	.078	.686	.050	.662	.214	.511
	N	21	21	24	28	22	26	17	22
L Average Adherence to Lead Time Score	Correlation Coefficient	.487	.026	.326	-.022	-.002	-.091	-.215	.242
	Sig. (2-tailed)	.025	.915	.139	.912	.992	.664	.441	.290
	N	21	20	22	27	22	25	16	21

Significant (p < 0.05)

Further considered

Figure 30: SPSS Output – Spearman Correlation Analyses of LR KPIs and OS KPIs

Table 40 summarizes the outcomes of the comprehensive set of Spearman correlations analyses conducted and the associated SPSS output in a consolidated manner. The selection of KPI pairs included in the table is limited to significant correlations only, what allows to present the comprehensive content in an easier digestible format.

Overall, the Spearman correlation analyses revealed six significant ($p < 0.05$) correlations between underlying metrics of Lab Robustness and Operational Stability. After an initial review of all six significant ($p < 0.05$) correlations, three out of the six identified pairs are considered as insightful and marked with circles in Figure 30 and Table 40. The additional three significantly correlated combinations are not found to be content-wise associated with each other, even if the data indicates correlations. Therefore, the not relevant combinations are excluded from subsequent discussions: Adhering to standard lead times in the laboratory cannot directly impact the Overall Equipment Effectiveness in manufacturing, which is calculated based on the scheduled equipment time and quantifies the degree of time losses due to breakdowns, speed losses, and quality losses (cf. appendix A.3). The same holds true for the relations of Deviations/1000 Tests_L and the Share of Unplanned Maintenance_P as well as Product Re-Test due to Complaints_L and Yield_P.

Table 40: Significant Correlations LR KPIs and OS KPIs

Further considered		Overall Equipment Effectiveness _P	Share of Unplanned Maintenance _P	Deviations/ Batch _P	Deviation Closure Time _P	Share of Rejected Batches _P	Yield _P
Deviations / 1000 Test _L	ρ		-.475		-.399		
	Sig		.016		.021		
	N		25		33		
Product Re-Tests due to Complaints _L	ρ			-.441			-.602
	Sig			0.31			0.01
	N			24			26
Adherence to Schedule _L	ρ					.423	
	Sig					.050	
	N					22	
Adherence to Lead Time _L	ρ	.487					
	Sig	.025					
	N	21					

All three combinations deemed relevant for further consideration are discussed subsequently in detail after having completed the initial analyses of additional aggregated performance scores. Lab Robustness, Operational Stability and the underlying KPIs discussed above solely focus on effectiveness and allow to determine cross-departmental dependencies with regard to this selected subject field. Broadening the scope of interdepartmental analyses, approaching performance more comprehensively and incorporating an efficiency perspective, relation of the overall performance scores applied in both benchmarking programs are investigated in the following. The OPEX score represents aggregated KPI performance in manufacturing and beyond, LP summarizes the aggregated KPI performance of QC labs based on the underlying indicators (cf. chapter 3.2.3).

Following the procedure to choose appropriate statistics for correlation analyses, preconditions for calculating Pearson's correlation coefficients are evaluated prior to analyses. The Shapiro-Wilk tests presented in Table 41 are performed to test both scores LP and OPEX for normal distribution.

Table 41: Test for Normal Distribution of LP Score and OPEX Score

	Shapiro-Wilk Test		
	Statistic	df	Sig
LP	.969	33	.465
OPEX	.926	20	.129

Non-significant results of the Shapiro-Wilk tests ($p > 0.05$) indicate a normal distribution of both variables. Findings are confirmed by the visual interpretation of the Q-Q plots. Both scores are compiled on a continuous metric scale and linear relation is assumed, no indications for non-linear dependencies can be recognized. Consequently, all criteria for credible results are met and the Pearson correlation coefficient of LP and OPEX scores is calculated. Table 42 reveals the result.

Table 42: Pearson Correlation Analysis of LP Score and OPEX Score

	OPEX	
	r	.405
	Sig (2-tailed)	.076
	N	20

The Pearson coefficient $r = 0.405$ indicates a positive correlation of both variables that is not significant according to the previously used level $p < 0.05$ but can be deemed significant at a level $p < 0.1$. Consequently, a positive association of performance in LP and OPEX scores is assumed being mindful of the significance level limited to $p < 10\%$. A linear regression is conducted to further investigate this positive relation observed, results are presented in Table 43.

Table 43: Linear Regression of LP Score (IV) and OPEX Score (DV)

	DV: OPEX						
	Model Summary				Coefficient		
	R Square	Adjusted R Square	F-value	Durbin-Watson	Standard. Coefficient Beta	t-value	Sig
IV: LP	.164	.118	3.535	1.562	.405	1.880	.076

A positive association of both variables is revealed by the linear regression. The Durbin-Watson test result $1.5 < d < 2.5$ indicates a non-critical level of autocorrelation. Moreover, the residual plot does not show any heteroscedastic pattern. Figure

31 presents a scatter plot of Lab Robustness and Operational Stability across the benchmarking sample including the linear regression line.

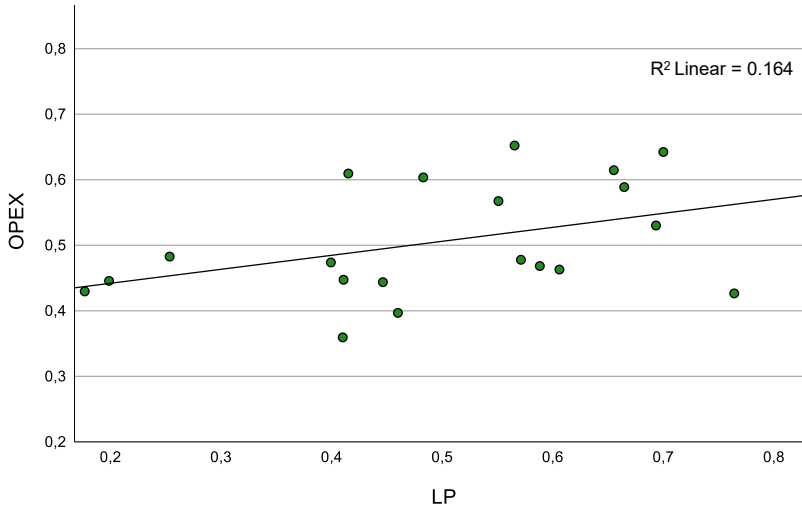


Figure 31: Regression Plot of LP Score and OPEX Score

In addition to the positive association of both variables, the linear regression reveals a degree of determination $r^2 = 0.164$. Hence, 16.4% of the variation in OPEX scores can be explained by the variation in LP scores of production sites. Different to the initial analysis comprising LR and OS, performance across manufacturing and quality control have been found to be associated with each other using the more comprehensive benchmarking scores.

Further investigating the relation of LP and OPEX scores, all underlying performance dimensions are individually evaluated for cross-departmental relations. Some performance dimensions might interact and act as driver for cross-departmental associations, while others are not related to each other. The analyses comprise the aggregated dimensional scores TPM_P , TQM_P and JIT_P calculated based on the manufacturing benchmarking sample as well as $Productivity_L$, $Quality_L$, $Service_L$ and $Cost_L$ summarizing the performance levels assessed in the QC benchmarking program.

Similar to the correlation analyses presented above, preconditions of Pearson correlation analyses are evaluated prior to calculating the correlation coefficients. For this purpose, Shapiro-Wilk tests for normal distribution are conducted across all dimensional performance scores. Table 44 summarizes the outcomes of the Shapiro-Wilk tests for all variables.

Table 44: *Test for Normal Distribution of OPEX Score Dimensions and LP Score Dimensions*

	Shapiro-Wilk Test: OPEX & LP Dimensions		
	Statistic	df	Sig
TPM _P	.956	27	.300
TQM _P	.968	30	.491
JIT _P	.964	23	.551
Productivity _L	.958	34	.219
Quality _L	.959	35	.217
Service _L	.966	35	.333
Cost _L	.966	33	.371

No significant test results can be observed. Furthermore, the Q-Q plots of all variables do not indicate any violation of normal distributions. As all scores are calculated on metric scales and linear relations are assumed, all criteria for conducting correlation analyses according to Pearson are met.

Table 45 provides a summary of the Pearson correlation analyses performed across all dimensional performance scores. It indicates the correlation coefficients between all scores and states the significance level of each correlation. Only two significantly correlated cross-departmental combinations of dimensional performance scores can be observed.

Table 45: *Pearson Correlation Analyses of OPEX Score Dimensions and LP Score Dimensions*

		OPEX	TPM _P	TQM _P	JIT _P
LP	r	.405	.105	.161	.471
	Sig	.076	.603	.412	.023
	N	20	27	28	23
Productivity _L	r	.193	.063	.135	.380
	Sig	.415	.756	.486	.073
	N	20	27	29	23
Quality _L	r	.162	.104	-.053	.506
	Sig	.496	.606	.779	.014
	N	20	27	30	23
Service _L	r	.439	.146	.270	.269
	Sig	.053	.468	.148	.215
	N	20	27	30	23
Cost _L	r	.345	-.040	.227	.277
	Sig	.148	.847	.245	.212
	N	19	26	28	22

JIT_P is significantly correlated with the overall lab performance score LP as well as the dimensional score Quality_L. Spearman correlation coefficients $r = 0.471$ and $r = 0.506$ uncover a positive relation of the variables and motivate further analyses. Outcomes of a linear regression model comprising at first LP and JIT_P are summarized in Table 46.

Table 46: *Linear Regression of LP Score (IV) and JIT_P Score (DV)*

	DV: JIT _P						
	Model Summary				Coefficient		
	R Square	Adjusted R Square	F-value	Durbin-Watson	Standard. Coefficient Beta	t-value	Sig
IV: LP	.222	.185	5.983	1.652	.471	2.446	.023

The Durbin-Watson test result $1.5 < d < 2.5$ indicates a non-critical level of autocorrelation. Moreover, the residual plot does not show any heteroscedastic pattern. Consequently, findings of the regression model allow for further interpretation. Figure 32 presents a scatter plot of LP and JIT_P including the regression line.

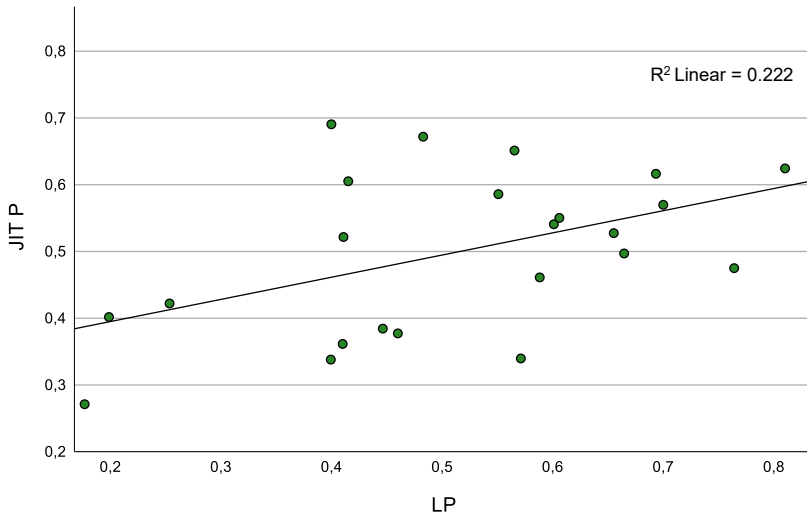


Figure 32: Regression Plot of Lab Performance Score (IV) and JIT_P Score (DV)

Based on the visualization, a positive linear relation of both variables is confirmed. The linear regression model reveals a degree of determination $r^2 = 0.222$. Hence, 22.2% of the variation in JIT manufacturing performance is determined by variation in overall lab performance.

Analogously, a second linear regression model is set-up to continue studying the significant positive correlation observed for JIT_P and $Quality_L$ as one of LP's dimensional scores. Table 47 presents the results.

Table 47: Linear Regression of $Quality_L$ Score (IV) and JIT_P Score (DV)

	DV: JIT_P						
	Model Summary				Coefficient		
	R Square	Adjusted R Square	F-value	Durbin-Watson	Standard. Coefficient Beta	t-value	Sig
IV: $Quality_L$	.256	.220	7.213	1.605	.506	2.686	.014

Based on the Durbin-Watson value observed ($1.5 < d < 2.5$) and the visual review of the residual plot, neither an unfavorable level of autocorrelation nor heteroscedasticity is noticeable. Outcomes of the regression analysis are significant at a level $p < 0.05$. Figure 33 depicts the regression plot of $Quality_L$ and JIT_P .

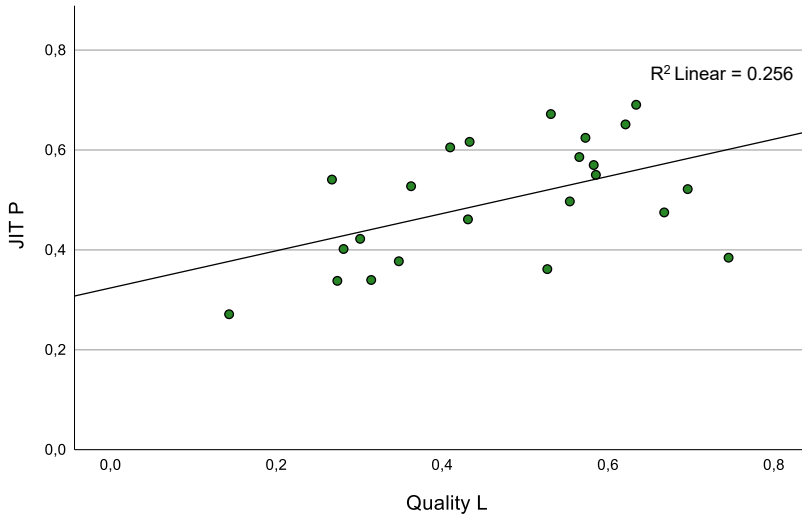


Figure 33: Regression Plot of Quality_L Score (IV) and JIT_P Score (DV)

The linear regression analysis indicates a degree of determination $r^2 = 0.256$. Accordingly, it can be assumed that 25.6% of the variance in JIT performance across pharmaceutical production sites are determined by variation in Quality_L scores summarizing the process quality of laboratory operations.

Overall, researching relations of dimensional aggregated performance scores across manufacturing and quality control has led to two significant results: JIT_P is associated with both LP and Quality_L. The degrees of determination quantified through linear regression analyses underline and proof the importance of effective QC operations for the overall delivery and supply performance of pharmaceutical production sites (cf. chapter 1.1). Neither a relation of aggregated TQM_P and Quality_L nor any further significant correlations of performance dimensions across departments have been observed.

In a next step of analyses, all underlying KPIs are evaluated for cross-departmental associations. This comprises indicators in the three performance dimensions represented by the OPEX score in manufacturing and the four dimensions aggregated to LP in quality control. In total, all combinations of 22 individual plant KPIs and 17 lab indicators contributing to the dimensional score first and finally summing-up to the OPEX and LP scores (cf. chapter 3.2.3), are evaluated in the following.

A series of Shapiro-Wilk tests revealed non-normal distributions of multiple variables across the combined benchmarking sample. That is why non-parametric Spearman correlations are chosen as appropriate method to research the cross-departmental relation of metrics. The SPSS output of all Spearman correlation analyses is given

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in Figure 34. Combinations of metrics showing significant positive or negative correlations are highlighted in yellow. Similar to the Spearman correlation analyses already presented for performance dimensions, all cross-departmental combinations of individual KPIs indicating a significant correlation are assessed for further consideration. Discussing cross-departmental associations of enabler dimensions and enabler categories in H3 will follow the same approach. Thereby, relations of the encircled metric pairs are deemed interpretable and relevant for the research at hand.

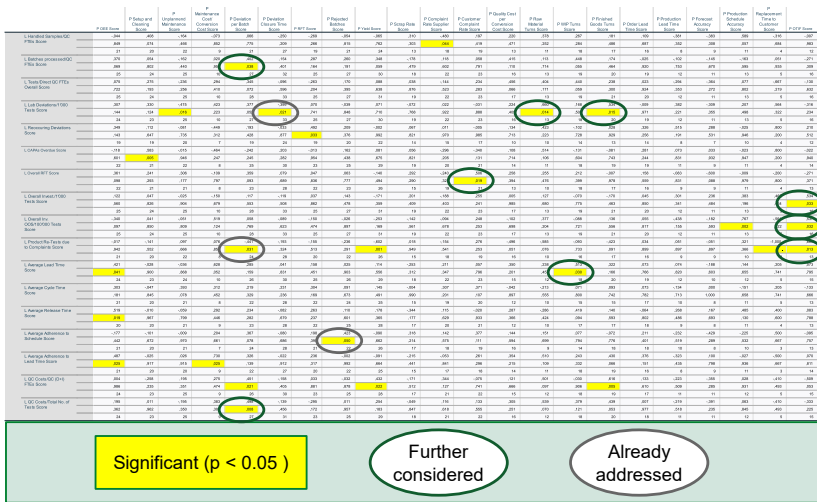


Table 48: Significant Correlations LP KPIs and TPM_P KPIs

Further considered				
Deviations/ 1000 Tests _L	ρ			-.475
	Sig			.016
	N			25
Share of CAPAs Overdue _L	ρ		.583	-.384
	Sig		.005	.023
	N		21	35
Lead Time _L	ρ	.421		
	Sig	.041		
	N	24		
Release Time _L	ρ	.519		
	Sig	.019		
	N	20		
Adherence to Lead Time _L	ρ	.487		.730
	Sig	.025		.025
	N	21		9

Each TPM_P KPI demonstrates at least one significant relation with quality control indicators. However, since the primarily focus of measurements lies on maintenance operations, relevance of associations with laboratory KPIs is hard to argue and cannot be stated. Instead, results are descriptively displayed to ensure completeness of the result presentation. Correlations observed are highlighted without assuming any determination or causation. That is why none of the presented TPM_P correlations is considered for further discussion.

Analogously, Table 49 depicts all significant ($p < 0.05$) correlations of TQM_P and LP KPIs. The set of Spearman analyses revealed eleven cross-departmental associations in total.

Table 49: Significant Correlations LP KPIs and TQM_P KPIs

Further considered		Deviations/ Batch _P	Deviation Closure Time _P	Right First Time _P	Share of Rejected Batches _P	Yield _P	Supplier Complaint Rate _P	Customer Complaint Rate _P
Handled Samples / QC FTE _L	ρ						-.480	
	Sig						.044	
	N						18	
Batches processed/ QC FTE _L	ρ	.402						
	Sig	.038						
	N	27						
Deviations / 1000 Tests _L	ρ		-.399					
	Sig		.021					
	N		33					
Share of Reoccurring Deviations _L	ρ			.492				
	Sig			.033				
	N			19				
Analytical Right First Time _L	ρ							.506
	Sig							.019
	N							21
Product Re- Tests due to Complaints _L	ρ	-.441				-.602		
	Sig	.031				.001		
	N	24				26		
Adherence to Schedule _L	ρ				.423			
	Sig				.050			
	N				22			
QC Cost/FTE _L	ρ	.451				.432		
	Sig	.021				.022		
	N	26				28		
QC Cost/Test _L	ρ	.498						
	Sig	.008						
	N	27						

The six encircled interdepartmental pairs of significantly correlated metrics are initially found to be relevant and considered for further discussion. These include the

three relations previously observed when analyzing all LR and OS components, highlighted in grey.

Completing the detailed overview of the Spearman correlation analyses results and the SPSS outcome plot, Table 50 reflects all significant ($p < 0.05$) correlations of JIT_P and LP metrics. This section of metrics is especially interesting as aggregated JIT_P performance is the only dimensional performance score that has been found to be correlated with LP and $Quality_L$ scores of laboratories.

Table 50: Significant Correlations LP KPIs and JIT_P KPIs

Further considered		Raw Material Turns _P	WIP Turns _P	Finished Good Turns _P	Production Schedule Accuracy _P	On-time Delivery in Full _P
Deviations / 1000 Tests _L	ρ	.660		.534		
	Sig	.014		.015		
	N	13		20		
Analytical Right First Time _L	ρ					
	Sig					
	N					
Investigations / 1000 Tests _L	ρ					.534
	Sig					.033
	N					16
Inval. Out of Specification/ 100000 Tests _L	ρ				.767	.537
	Sig				.002	.032
	N				13	16
Product Re-Tests due to Complaints _L	ρ					.665
	Sig					.013
	N					13
Lead Time _L	ρ		.513			
	Sig		.030			
	N		18			
QC Cost/FTE _L	ρ			.616		
	Sig			.005		
	N			19		

In total, eight significantly ($p < 0.05$) positive correlated metric combinations can be observed across all underlying components of LP and JIT_P . Two pairs of correlated

indicators are excluded from further discussion. No determining relation between the KPIs can be expected based on an initial review of the metric's content.

Overall, comprehensive correlation analyses according to Spearman across all underlying KPIs of the scores LR, LP, OS and OPEX revealed 25 significant correlations between manufacturing and quality control. Twelve out of the 25 indicator pairs are deemed relevant for the research at hand based on a supplementary evaluation of the subject fields measured by the individual indicators. The selection comprises KPIs assigned to all departmental plant performance dimensions except TPM_P. Subsequently, the identified twelve relations are presented and discussed in detail in an ascending sequence according to the lab benchmarking set-up.

Figure 35 visualizes the distributions of Batches processed/QC FTE_L and Deviations/Batch_P across the combined benchmarking database. The Spearman analysis indicated a significant positive correlation $\rho = 0.402$.

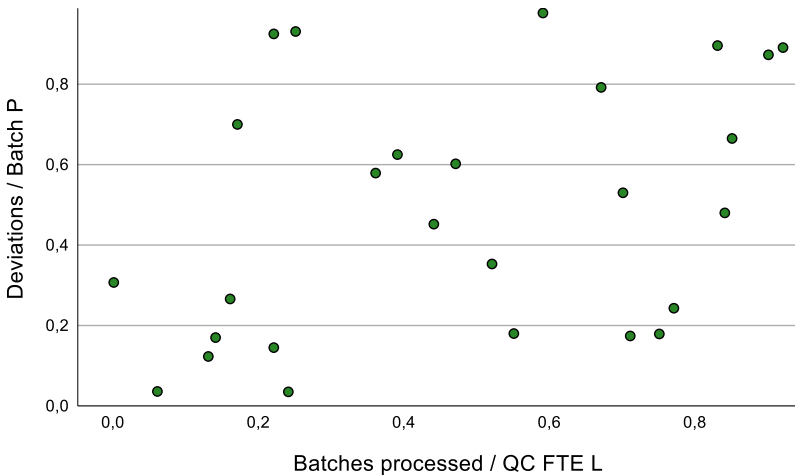


Figure 35: Scatter Plot of Batches processed/QC FTE_L and Deviations/Batch_P

The scatter plot uncovers high variations in both variables across the production sites. Even if a tendency for positive association indicated by the correlation coefficient is also visually recognizable, this trend seems to be less explicit than expected when solely interpreting the degree of correlation. However, since the correlation is significant at a level $p < 0.05$, an association of Batches processed/QC FTE in quality control and deviation rates in manufacturing can be attested.

According to the harmonized score definitions and consistent approach to determine performance in all KPIs (cf. chapter 3.2.3), the scales always indicate relative performance in the particular indicator compared to the peer group rather than the absolute measurements. Thus, higher scores always represent better performance,

regardless if lower or higher absolute values are considered favorable in the context of an indicator. Consequently, ascending performance in Deviations/Batch_P (plotted on the Y-Axis) represents lower deviation rates in manufacturing and is found to be associated with higher productivity in quality control operationalized by Batches processed/QC FTE_L.

One way to explain the relation observed is additional, unpredictable workload in QC caused by deviation handling activities. Deviations summarize all discrepancies from the routine process and must be formally documented and investigated to maintain compliance with regulatory standards. Among other discrepancies, deviations comprise out of specification and out of trend test results. These results require investigation according to a defined event handling process. Depending on the event occurred, investigations comprise re-testing or conduction of further in-depth studies tying up analytical resources in quality control. Different to everyday release testing or stability testing, it is hard to foresee or forecast such additional workload due to its unpredictability of occurrence. This can negatively impact productivity in quality control.

The next identified correlation of Deviations/1000 Test_L and Deviation Closure Time_P is plotted in Figure 36. A significant negative correlation $\rho = -0.399$ was indicated by the analysis according to Spearman.

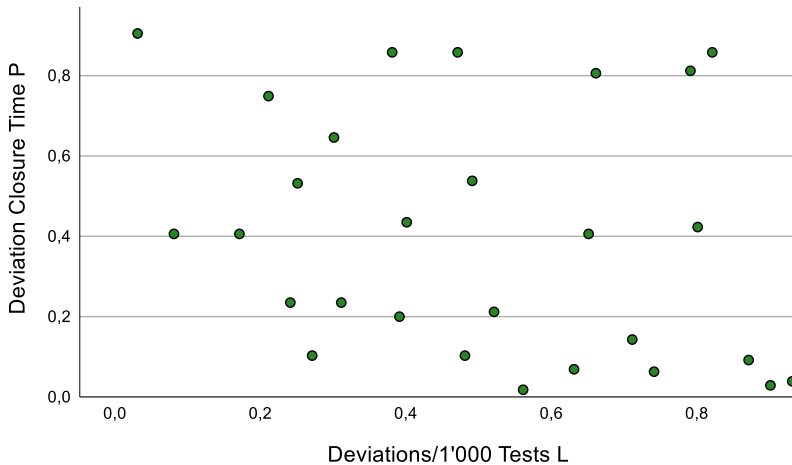


Figure 36: Scatter Plot of Deviations/1000 Tests_L and Deviation Closure Time_P

Despite a comparably high variation within distributions of both variables, the negative association indicated by the correlation coefficient is visually recognizable. Higher performance in Deviations/1000 Test_L corresponds with lower performance in Deviation Closure Time_P. Summarized in other words, fewer deviations in laboratory operations jointly occur with longer deviation closure times in the plant. Like

elaborated above, the involvement of quality control in the deviation handling and closure process can explain the association observed: Closing all open deviations is a prerequisite for final batch release. This motivates to shorten deviation closure times as much as possible and can cause pressure on the deviation handling and investigation procedures. Increasing expectations to close deviations faster and shorten investigation times require earlier completion of related analytics in quality control. This can cause higher deviation rates in testing operations.

Studying the next combination of metrics, Figure 37 provides a scatter plot of Deviations/1000 Test_L and Raw Material Turns_P. According to the Spearman correlation analysis initially conducted, the variables are significantly positive correlated with a degree of correlation $\rho = 0.660$.

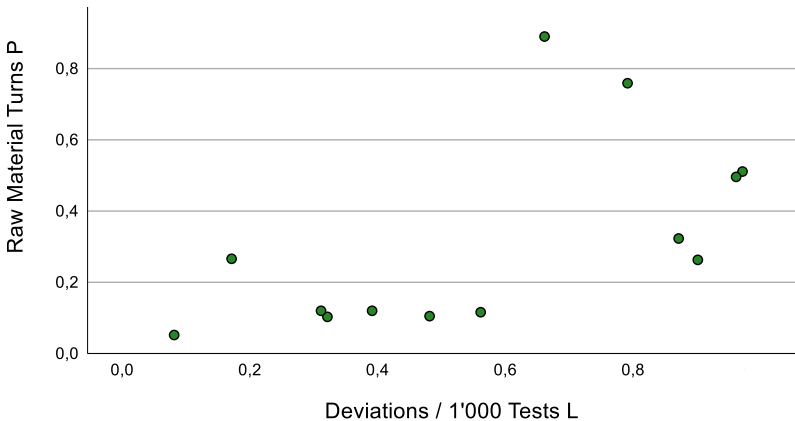


Figure 37: Scatter Plot of Deviations/1000 Tests_L and Raw Material Turns_P

The scatter plot visually reveals a positive relation of the distributions across the combined benchmarking sample. Even if the number of observations is comparably low, the identified significance allows to assume an association of both variables: Higher performance in Deviations/1000 Test_L is related to higher performance in Raw Material Turns_P. Thus, less deviations in quality control occur alongside with faster processing of raw material inventories in production. As release of every raw material batch requires inspection by quality control, the association of both variables is not a surprise. More stable testing operations in the laboratories drive reliable release routines and therefore allow for increasing the number of raw material batches processed in a period. Hence, effectiveness in quality control is the basis for reliability in release processes. This finally increases efficiency in raw material processing and enables to lowering raw material batch sizes or inventory levels according to the JIT philosophy.

Moreover, a scatter plot of Deviations/1000 Test_L and Finished Goods Turns_P is given in Figure 38. Previously performed analysis indicated a Spearman correlation coefficient $\rho = 0.534$. The correlation between both variables is significant at a level $p < 0.05$ and directional positive.

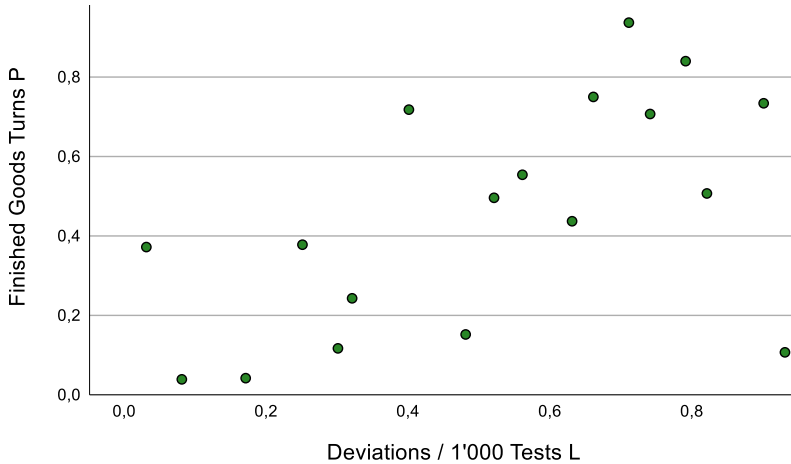


Figure 38: Scatter Plot of Deviations/1000 Tests_L and Finished Good Turns_P

The positive relation of the indicators is clearly visible in the visualization of both variables. Like previously discussed for Raw Material Turns_P, a higher performance in Deviations/1000 Tests_L is associated with a higher frequency of Finished Good Turns_P. Analogous to raw materials, processing and shipping of finished goods requires the final release of these batches including completion and review of all quality control steps. Consequently, a higher robustness in quality control indicated by fewer deviations can provide the basis for higher efficiency in finished good inventory processing.

Subsequently, the distributions of Analytical Right First Time_L, a further measurement for process quality within quality control, and Customer Complaint Rate_P are jointly evaluated. Customer Complaint Rate_P is assessed as part of the manufacturing benchmarking program and therefore marked as plant indicator. However, it quantifies the frequency of complaints received from internal or external customers on orders delivered. Thus, occurrence of justified complaints related to product quality does not solely uncover issues of manufacturing quality but also indicates that quality control did not properly fulfill its departmental role as safeguard prior to delivery. Otherwise, the quality issue would have been detected during release testing and led to rejection or rework of the batch prior to shipment.

Figure 39 provides a scatter plot of Analytical Right First Time_L and Customer Complaint Rate_P. The comprehensive set of cross-departmental KPI analyses revealed a significant positive Spearman correlation coefficient $\rho = 0.506$.

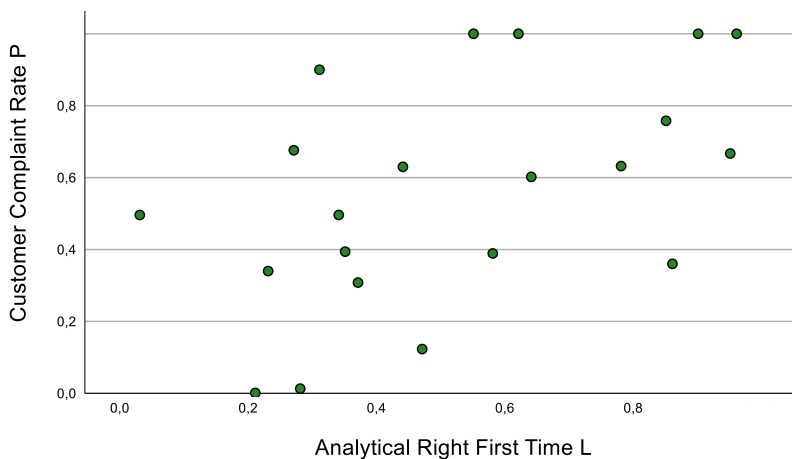


Figure 39: Scatter Plot of Analytical Right First Time_L and Customer Complaint Rate_P

A general positive relation of both variables can be visually observed across the benchmarking sample and confirms the perception indicated by the positive Spearman correlation. Due to comparably high variation in distributions of both variables, the pattern seems not to be as clear as for the previously discussed relations.

However, as the correlation is significant ($p < 0.05$) an association of both measurements is assumed: Higher analytical right first time rates in quality control correspond with fewer product-related customer complaints. Consequently, the importance of accurate quality control to ensure compliance with all specifications is demonstrated based on the combined benchmarking data sample. Effective laboratories ensure to identify quality issues early and prevent complaints from the market after delivery.

Discussed next, the metric OTIF (Abbreviation On-time Delivery in Full) is broadly applied in industry to quantify supply performance. The KPI jointly assesses adherence to delivery schedules (*on-time*) and quality of the delivered order (*in full*). Like Customer Complaint Rates, the dataset used to analyze OTIF originates from the OPEX manufacturing benchmarking and the KPI is assigned to the plant accordingly even if performance of quality control is reflected as well. Delivery of products also requires successful completion of all QC routines. Moreover, the importance of OTIF as an indicator summarizing outcome performance was highlighted in the legacy St.Gallen FDA quality metrics research, which proofed OTIF's ability to surrogate effectiveness of the pharmaceutical quality system (cf. Friedli et al., 2017, p. 29 ff.).

Similar to the previously discussed cross-departmental combinations of indicators, Overall Investigations/1000 Tests_L and On-time Delivery in Full_P have been found to be significantly ($p < 0.05$) positive correlated. The initial analysis indicated a Spearman correlation coefficient $\rho = 0.534$. Figure 40 depicts a scatter plot of Overall Investigations/1000 Tests_L and On-time Delivery in Full_P.

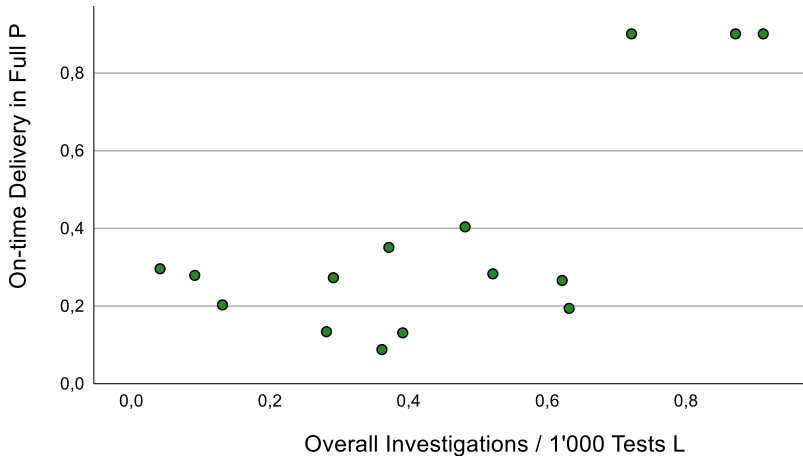


Figure 40: Scatter Plot of Investigations/1000 Tests_L and OTIF_P

Consequently, the data shows that fewer investigations in quality control correspond with a higher OTIF delivery performance. This finding is in line with observations in practice: On-going, open investigations in quality control and beyond hinder final batch release. Hence, temporary or permanent loss of batches caused by pending investigations can negatively impact delivery on-time performance depending on the production schedule, inventory levels, and forecast accuracy. Moreover, a higher proportion of laboratory investigations indicates more frequent occurrence of events to be investigated, what might be reflected in the product quality also represented by OTIF performance.

Like Overall Investigations/1000 Tests_L, the lab process quality indicator Invalidated Out of Specification/100000Tests_L also showed a positive significant ($p < 0.05$) correlation with On-time Delivery in Full_P. IOOS indicate OOS test results that have been invalidated after investigation of the root cause. Consequently, the proportion of iOOS quantifies the level of inaccuracy of analytics conducted by the laboratory. In other words, higher shares of iOOS represent more false negative test results. The scatter plot provided in Figure 41 shows the distributions of Invalidated Out of Specification/100000Tests_L and On-time Delivery in Full_P across the combined benchmarking sample. Initial Spearman correlation analysis revealed a degree of correlation $\rho = 0.537$ and indicated a significant ($p < 0.05$) relation of both variables.

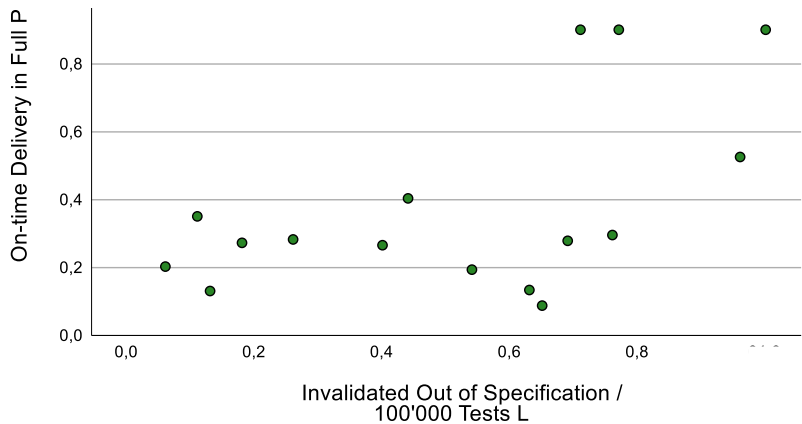


Figure 41: Scatter Plot of $iOOS/100000\ Tests_L$ and $OTIF_P$

The visualization confirms the positive association of Invalidated Out of Specification/100000Tests_L and On-time Delivery in Full_P. Similar to the investigation rates, iOOS proportions are telling about effectiveness of lab operations and can therefore impact the ability to ensure accurate product quality delivered.

Visualizing the next cross-departmental combination of indicators, Figure 42 depicts performance in Product Re-Test due to Complaints_L and Deviations/Batch_P. Both variables are significantly ($p < 0.05$) negative correlated, analyses indicated a degree of correlation $\rho = -0.441$.

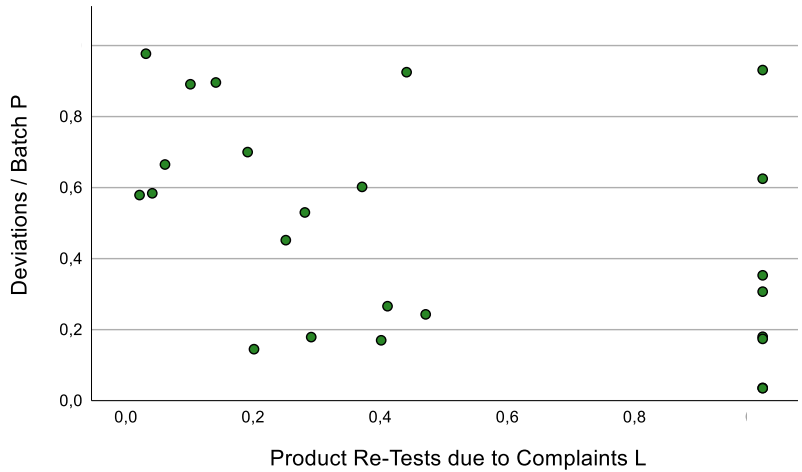


Figure 42: Scatter Plot of Re-Tests due to Complaints_L and Deviations/Batch_P

The scatter plot shows a unique pattern of multiple production sites jointly scoring best in Re-Tests due to Complaints_L on the X-Axis. This distribution also explains why the initially performed Shapiro-Wilk test suggested to reject the assumption of a normal distribution of the variable. That is why calculation of Pearson correlation coefficients was not applicable. Reviewed in the context of the quality control benchmarking program, the performance plot is not surprising at all: This group of production sites did not receive any complaints requiring re-testing in quality control. The approach to assessing performance relative to the QC lab benchmarking sample using percentile ranks (cf. chapter 3.2.3) also explains the absence of medium-level scores in case of multiple sites jointly scoring best in a small sample.

Being mindful in interpretation due to the small sample size and the non-normal distribution, analysis still revealed a significant ($p < 0.05$) Spearman correlation between both variables. Hence, an association of Product Re-Test due to Complaints_L and Deviations/Batch_P can be assumed. Higher numbers of deviations in manufacturing are considered unfavorable in general. However, higher deviation rates also indicate that product quality issues are identified within the plants. This allows to react prior to shipment and consequently positively impacts the amount of re-tests due to complaints.

Besides Deviations/Batch_P, On-time Delivery in Full_P was initially found to be significantly ($p < 0.05$) correlated ($\rho = 0.665$) with Product Re-Test due to Complaints_L as well. Figure 43 visualizes the distribution of both variables across the combined benchmarking sample.

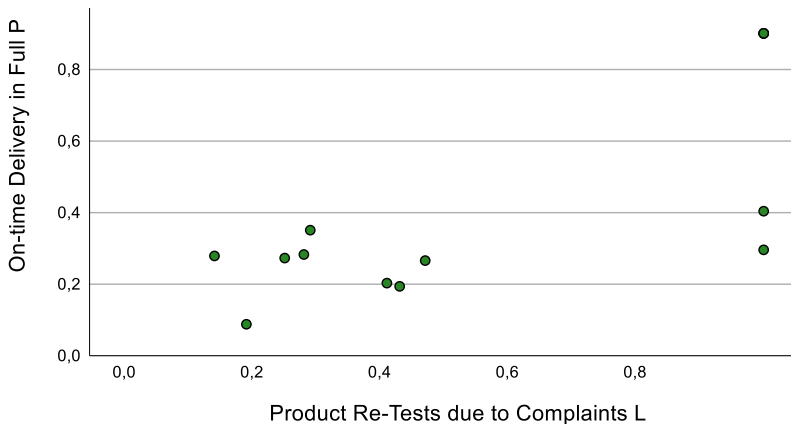


Figure 43: Scatter Plot of Re-Tests due to Complaints_L and OTIF_P

Referring to the explanation for the uniqueness of the pattern in Re-Test performance, interpretation of the association requires caution even if Spearman analyses indicated a significant correlation. As previously outlined, OTIF performance

comprises product quality in addition to adherence to delivery schedule. Consequently, a higher OTIF performance of production sites can lead to better laboratory scores in Re-Tests required. Higher OTIF rates correspond with less events of inadequate quality subsequently leading to less workload due to complaints occurring.

Still investigating the cross-departmental combinations of KPIs, Figure 44 provides a scatter plot of Lead Time_L and WIP (Abbreviation Work-in-Progress) Turns_P. According to the Spearman correlation analysis performed, this pair of indicators shows a degree of correlation $\rho = 0.513$. The correlation is directional positive and significant at a level $p < 0.05$.

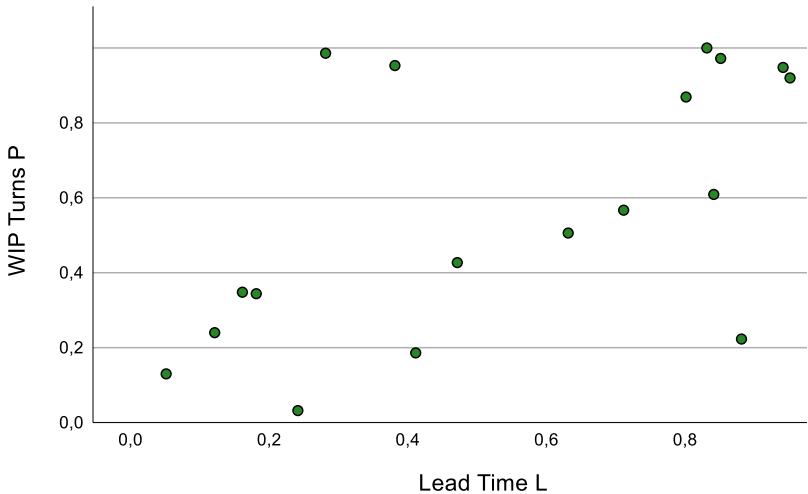


Figure 44: Scatter Plot of Lead Time_L and WIP Turns_P

The graph allows to observe a tendency of positive relation and confirms the perception indicated by the Spearman correlation analyses. Due to the present significance level $p < 0.05$, it can be assumed that higher performance in QC lead times is associated with higher performance in WIP inventory turns. Summarized in other words, shorter lead times in the laboratories can allow to process WIP inventory more often in the reference time period. Like previously presented cross-departmental associations involving turns of raw materials and finished goods, the observation underlines the importance of effective, fast-working laboratories for overall production site's efficiency and JIT performance.

The next combination of significantly correlated indicators comprises Adherence to Schedule_L and the Share of Rejected Batches_P. Analyses revealed a Spearman correlation coefficient $\rho = 0.423$. The correlation is directional positive and significant

at a level $p = 0.05$. Figure 45 depicts the distribution of performance in both scores across the combined benchmarking sample of production sites.

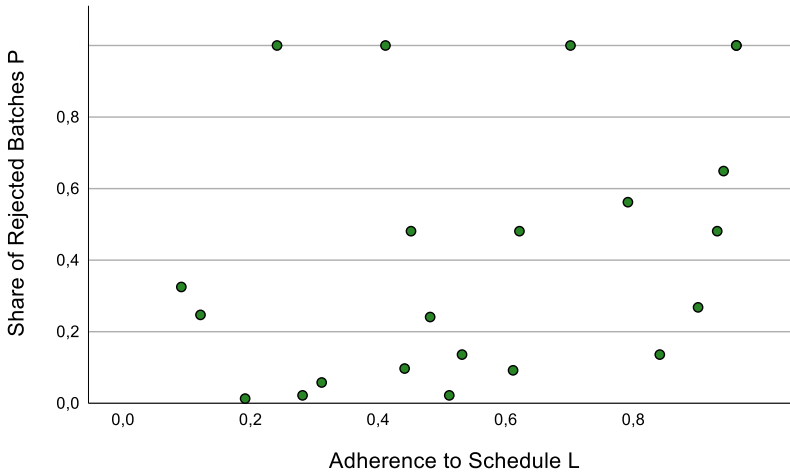


Figure 45: Scatter Plot of Adherence to Schedule_L and Share of Rejected Batches_P

Reviewing the visualization, the positive relation of both variables can be recognized, even if the distribution of performance in Share of Rejected Batches_P shows a uniliteral pattern. Considering the significant ($p = 0.05$) Spearman correlation, it can be stated that higher Adherence to Schedule in quality control is associated with a lower share of rejected batches manufactured.

Since the decision to reject batches manufactured is an outcome of procedures involving quality control, it can be assumed that rejections usually cause unpredictable extra workload for laboratories compared to processing batches, which are released without any issues. This QC workload can comprise either additional testing or documentation. Laboratories are not solely challenged by the extra amount of workload: Point of time and frequency of needs for such additional in-depth analytics on candidates for rejections cannot be foreseen and therefore hardly considered in the QC schedule.

Lastly, the Spearman correlation analysis indicated a relation of QC Cost/Test_L and Deviations/Batch_P. The correlation coefficient reaches $\rho = 0.498$, the correlation is directional positive and significant ($p < 0.05$). Distributions of both variables across the combined benchmarking sample are visualized in the scatter plot presented in Figure 46.

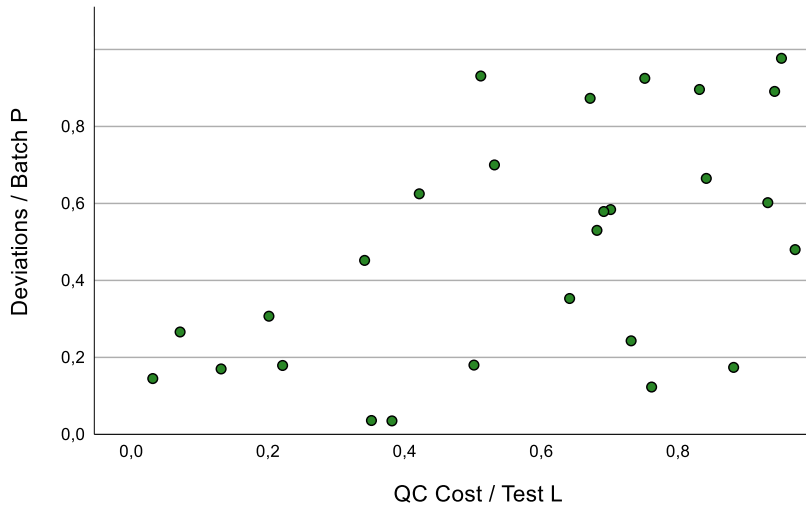


Figure 46: Scatter Plot of $QC\ Cost / Test_L$ and $Deviations / Batch_P$

The visual graph confirms the positive relation of performance scores $QC\ Cost / Test_L$ and $Deviations / Batch_P$. Referring to the significance of correlation ($p < 0.05$), it can be assumed that fewer deviations in manufacturing correspond with lower cost per test in quality control. Like previously discussed for the association of Batches processed/ $QC\ FTE_L$ and $Deviations / Batch_P$, involvement of quality control in handling and investigating manufacturing deviations can explain this relation: Additional analytical efforts caused by deviations are also reflected in the number of tests used as denominator of the measurement. However, it is expected that cost for investigation related analyses exceeds the level of efforts for routine testing and consequently impact the ratio $QC\ Cost / Test_L$.

Key Observations Cluster H1 – KPIs across Manufacturing and Quality Control

Summarizing the analyses performed within hypotheses cluster H1, several insightful cross-departmental relations between KPIs have been observed. At first, Lab Robustness and Operational Stability have shown no association with each other again. This observation confirms results of legacy research (cf. chapter 1.1.1) based on the recent available combined benchmarking sample of pharmaceutical production sites.

The aggregated benchmarking scores OPEX and LP have been analyzed in detail in a next step to incorporate an efficiency perspective and broadly investigate the relation of overall performance across manufacturing and quality control. Different to LR and OS, both aggregated benchmarking scores revealed a positive

association at a significance level $p < 0.1$. Linear regression quantified that 16.4% of the variation in OPEX scores is determined by the variation in LP scores. Cross comparing the underlying dimensional scores, JIT_P was identified to be significantly positive correlated with LP and $Quality_L$. Degrees of determination $r^2 = 0.222$ ($LP - JIT_P$) and $r^2 = 0.256$ ($Quality_L - JIT_P$) allow to state that effectiveness in quality control contributes to Just-in-Time performance of pharmaceutical production sites. This underlines the crucial role of laboratories in the value chain.

Analyzing all cross-departmental combinations of underlying manufacturing and QC KPIs afterwards, 25 significantly ($p < 0.05$) correlated indicator pairs have been identified based on a comprehensive set of Spearman correlation analyses. Based on a content-driven review, 12 combinations have been deemed relevant and discussed in detail.

Higher laboratory performance in

- Batches processed/QC FTE_L
- Deviations/1000 Tests_L
- Analytical Right-First Time_L
- Investigations/1000 Tests_L
- Invalidated Out of Specification/100000 Tests_L
- Product Re-Test due to Complaints_L
- Lead Time_L
- Adherence to Schedule_L
- QC Cost/Test_L

is associated with higher plant performance in

- Deviations/Batch_P⁸
- Deviation Closure Time_P⁸
- Share of Rejected Batches_P
- Customer Complaint Rate_P
- Raw Material Turns_P
- WIP Turns_P
- Finished Good Turns_P
- On-time Delivery in Full_P.

Identified correlations do not allow any conclusion on causation or even the direction of cause-effect relations between variables. However, a detailed review and

⁸ Different to the other positively correlated combinations, the indicator Deviation Closure Time revealed a significant negative correlation. Deviations/Batch_P demonstrated a negative correlation with Product Re-Test due to Complaints_L in addition to two positive correlations with QC indicators. However, negatively correlated does not necessarily equate with unfavorable. See detailed explanations in the corresponding passages.

discussions of the significantly correlated cross-departmental indicator pairs provided context on all KPIs and conceivable explanations for the associations observed.

Cluster H2 – Enabler Implementation across Manufacturing and QC

The second cluster of hypotheses investigates the cross-departmental relation of OPEX maturity levels in detail. According to the testing framework (cf. chapter 3.2.2) and the score calculation (cf. chapter 3.2.3), maturity is operationalized by aggregated enabler implementation levels measured in the benchmarking programs for OPEX manufacturing and quality control (cf. chapter 3.2.1). Furthermore, the interplay of different enabler dimensions and categories is investigated in addition to evaluating the association of overall aggregated departmental enabler implementation levels.

At first, the relation of overall enabler implementation plant and overall enabler implementation lab is analyzed. Both scores represent the highest levels of departmental aggregation (cf. chapter 3.2.2). Figure 47 reveals the results in the form of a scatter plot.

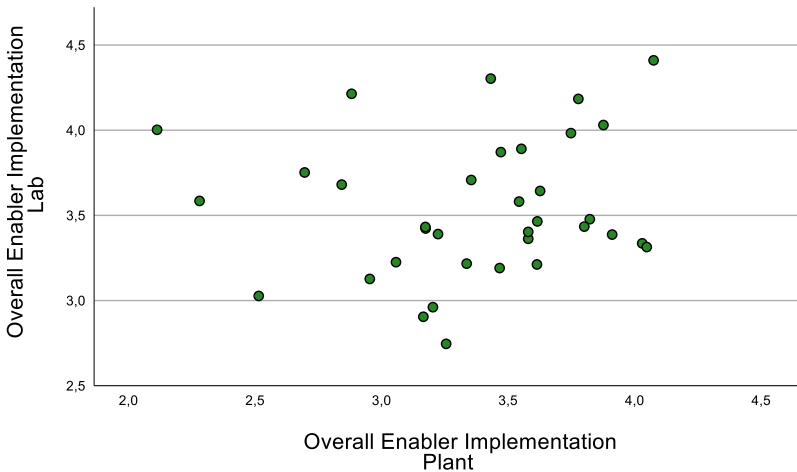


Figure 47: Scatter Plot of Overall Enabler Implementation Plant and Lab

Based on the visualization, there is no clear pattern across overall enabler implementation plant and overall enabler implementation lab. Individual production sites show very different combinations of departmental implementation levels. A tendency of a slight positive linear relation between both variables is noticeable in the scatter plot and motivates a subsequent correlation analysis. In order to confirm the preconditions for calculating Pearson correlation coefficients, both variables are tested for normal distribution using the Shapiro-Wilk test. Table 51 summarizes the results.

Table 51: Test for Normal Distribution of Overall Enabler Implementation Plant and Lab

	Shapiro-Wilk Test		
	Statistic	df	Sig
Overall Enabler Implementation Plant	.949	35	.102
Overall Enabler Implementation Lab	.974	35	.570

Test results $p > 0.05$ are confirmed by the graphical Q-Q plots and suggest not to reject the null hypothesis of the Shapiro-Wilk Test presuming normal distributions. Consequently, normal distribution is confirmed for both departmental overall enabler implementation levels. Since continuous metric scales are used to calculate the aggregated implementation levels and the scatter plot did not reveal any non-linear pattern, all preconditions are met and the correlation coefficient according to Pearson is calculated to formalize the relation of both variables. The result is given in Table 52.

Table 52: Pearson Correlation Analysis of Overall Enabler Implementation Plant and Lab

	Overall Enabler Implementation Lab	
	r	.112
	Sig (2-tailed)	.520
	N	35

A Pearson correlation coefficient $r = 0.112$ confirms the very slight positive relation between both variables. However, no significance can be attested. Whereas the analyses above did not uncover any noticeable association of the departmental overall enabler implementation levels, the underlying departmental maturity dimensions are checked for cross-departmental relation in the following. This comprises TPM, TQM, JIT, EMS and Basic Elements enabler implementation levels in manufacturing and the dimensions Maintenance & Quality, Planning & Steering and Management System in quality control. Multiple Shapiro-Wilk tests shown in Table 53 are performed to investigate the variable distributions of all enabler dimensions.

Table 53: *Test for Normal Distribution of Enabler Implementation Dimensions Plant and Lab*

	Shapiro-Wilk Test		
	Statistic	df	Sig
TPM Enabler Implementation _p	.956	35	.177
TQM Enabler Implementation _p	.940	35	.057
JIT Enabler Implementation _p	.953	35	.137
EMS Enabler Implementation _p	.920	35	.015
Basic Elements Enabler Implementation _p	.973	35	.519
Maintenance & Quality Implementation _L	.978	35	.707
Planning & Steering Implementation _L	.973	35	.540
Management System Implementation _L	.972	35	.495

The Shapiro-Wilk test of EMS Enabler Implementation_p indicates a significant test result ($p < 0.05$). A review of the Q-Q plot confirms the test results and leads to a rejection of the null hypothesis. Consequently, EMS Enabler Implementation levels in manufacturing are not normally distributed and prohibit the application of Pearson correlation analyses.

That is why subsequent analyses are performed according to the non-parametric approach of Spearman to ensure consistency of analyses across all enabler dimension comparisons. Table 54 presents the Spearman correlation coefficients ρ for all cross-departmental combinations of enabler dimensions.

Table 54: *Spearman Correlation Analyses of Enabler Implementation Dimensions Plant and Lab*

		Overall Enabler Implementation Lab	Maintenance & Quality Implementation _L	Planning & Steering Implementation _L	Management System Implementation _L
Overall Implementation Plant	ρ	.155	.284	-.018	.200
	Sig	.375	.098	.919	.250
	N	35	35	35	35
TPM Implementation _P	ρ	.102	.256	-.063	.132
	Sig	.560	.138	.720	.449
	N	35	35	35	35
TQM Implementation _P	ρ	.242	.320	.056	.363
	Sig	.162	.061	.748	.032
	N	35	35	35	35
JIT Implementation _P	ρ	.063	.236	-.024	.035
	Sig	.721	.173	.890	.843
	N	35	35	35	35
EMS Implementation _P	ρ	.081	.140	-.047	.195
	Sig	.642	.421	.790	.263
	N	35	35	35	35
Basic Elements Implementation _P	ρ	.089	.171	-.009	.072
	Sig	.611	.327	.961	.683
	N	35	35	35	35

Correlation analyses do not demonstrate significant positive or negative associations of dimensional enabler implementation levels across departments for almost all tested variables. Only the TQM Enabler Implementation level in manufacturing is significantly ($p < 0.05$) positive correlated with the implementation of Management System enabler in quality control. However, the correlation coefficient $\rho = 0.363$ does not indicate a strong relation that is also not deemed relevant for further consideration and detailed discussion. The majority of TQM enabler categories discuss various aspects of process quality, while the Management System enabler focus on the totally different field of managerial practices in quality control. Nevertheless, the correlation shows an association of maturity levels in the quality departments. TQM in manufacturing might benefit from the cultural mindset at sites operating a robust

3 Performance across Manufacturing and QC Labs

Management System in their quality organizations (including quality control) and vice versa.

Subsequently, implementation levels of underlying categories within all dimensions (cf. chapter 3.2.3) are checked for associations across departments. Shapiro-Wilk tests indicated non-normal distributions for a set of enabler categories. That is why all correlation analyses are performed according to the non-parametric Spearman approach instead of calculation Pearson's r. Figure 48 shows the high-level SPSS output of all correlation analyses. Coherent to H1, all significant correlations are highlighted in yellow. Encircled category pairs are deemed insightful for further interpretation.

		L Preventive Maintenance Implementation	L Technology Assessment and Change Implementation	L Housekeeping Implementation	L Process Management Implementation	L Standardization and Simplification Implementation	L Setup Reduction Implementation	L Pull Production Implementation	L Layout Optimization Implementation	L Planning Adherence Implementation	L Visual Management Implementation	L Management Commitment and Company Culture Implementation	L Employee Involvement and Continuous Improvement Implementation	L Functional Integration and Qualification Implementation
P Preventive Maintenance Implementation	Correlation Coefficient	.146	.189	.138	.204	.153	.090	.046	.281	.132	.009	.078	.233	.045
	Sig. (2-tailed)	.287	.277	.430	.126	.279	.608	.768	.130	.450	.856	.664	.179	.799
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Technology assessment and usage Implementation	Correlation Coefficient	.144	.309	.341	.181	.138	.009	.246	.130	.106	.002	-.009	.283	.003
	Sig. (2-tailed)	.246	.004	.005	.205	.208	.429	.055	.122	.441	.546	.981	.069	.127
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Housekeeping Implementation	Correlation Coefficient	.177	.406	.155	.141	.173	.208	.244	.210	.028	-.158	.245	.071	.262
	Sig. (2-tailed)	.269	.035	.558	.419	.219	.095	.063	.049	.870	.372	.041	.684	.262
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Process Management Implementation	Correlation Coefficient	.136	.216	.071	.207	.270	-.054	-.057	.211	.109	.209	.107	.437	.246
	Sig. (2-tailed)	.437	.214	.724	.232	.117	.768	.740	.231	.682	.239	.585	.001	.154
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Cross functional product development Implementation	Correlation Coefficient	.173	.454	.156	.228	.269	.185	.062	.042	.018	-.117	.145	.416	.332
	Sig. (2-tailed)	.321	.009	.371	.168	.118	.287	.636	.810	.919	.203	.405	.007	.051
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Customer involvement Implementation	Correlation Coefficient	.150	.157	.160	.283	.106	.232	-.088	.085	-.160	-.049	.079	.176	.091
	Sig. (2-tailed)	.550	.375	.367	.105	.651	.130	.820	.633	.275	.781	.608	.313	.608
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Supplier quality management Implementation	Correlation Coefficient	.127	.008	.034	.092	-.121	.057	-.212	.018	-.201	-.235	.101	.035	.106
	Sig. (2-tailed)	.466	.872	.844	.599	.460	.747	.222	.920	.247	.174	.662	.886	.543
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Setup time reduction Implementation	Correlation Coefficient	.191	.271	.241	.447	.287	.092	.152	.072	.083	-.094	.055	.267	.247
	Sig. (2-tailed)	.271	.115	.116	.091	.702	.734	.382	.881	.761	.676	.795	.232	.269
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Pull Production Implementation	Correlation Coefficient	.323	.258	.071	.093	.277	.184	.043	.264	-.201	.138	-.207	.079	.254
	Sig. (2-tailed)	.004	.225	.606	.295	.069	.299	.650	.138	.249	.430	.004	.652	.141
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Layout optimization Implementation	Correlation Coefficient	.376	.202	.169	.268	.307	.146	.078	.147	-.112	.128	.163	.087	.091
	Sig. (2-tailed)	.007	.244	.362	.116	.073	.403	.607	.490	.521	.462	.081	.279	.603
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Planning adherence Implementation	Correlation Coefficient	.189	.045	.044	.099	.042	-.069	.003	.070	-.270	-.163	-.046	.024	.076
	Sig. (2-tailed)	.276	.797	.713	.271	.810	.693	.985	.688	.117	.250	.795	.861	.663
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Decision making Implementation	Correlation Coefficient	.117	.169	.262	.185	.162	.080	-.240	.316	.004	-.022	.129	.365	.223
	Sig. (2-tailed)	.603	.363	.139	.288	.265	.647	.132	.045	.760	.861	.414	.023	.179
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Management commitment and company culture Implementation	Correlation Coefficient	.130	.012	.003	.003	-.040	.017	.150	.255	-.100	-.084	-.014	.012	.199
	Sig. (2-tailed)	.456	.948	.987	.984	.818	.822	.555	.175	.566	.716	.908	.144	.275
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Employee involvement and continuous improvement Implementation	Correlation Coefficient	.241	.074	.071	.241	.102	.024	-.121	.210	.079	-.059	.006	.241	.110
	Sig. (2-tailed)	.162	.674	.683	.162	.286	.882	.440	.227	.660	.735	.949	.162	.509
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Functional integration and qualification Implementation	Correlation Coefficient	.124	.084	.154	-.080	.045	-.208	-.212	.094	-.217	-.072	-.213	.089	.098
	Sig. (2-tailed)	.476	.629	.351	.648	.766	.231	.222	.760	.210	.680	.219	.612	.685
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Standardization Implementation	Correlation Coefficient	.336	.145	.149	.108	.210	.115	.019	.086	.062	-.018	.133	.093	.158
	Sig. (2-tailed)	.047	.406	.392	.537	.227	.211	.941	.613	.722	.916	.445	.564	.364
	N	35	35	35	35	35	35	35	35	35	35	35	35	35
P Visual Management Implementation	Correlation Coefficient	.094	-.115	.142	.117	.110	.091	.143	.330	-.291	.078	-.166	.016	.098
	Sig. (2-tailed)	.681	.514	.422	.474	.653	.695	.421	.053	.162	.659	.703	.929	.627
	N	34	34	34	34	34	34	34	34	34	34	34	34	34

Significant ($p < 0.05$)

Further considered

Figure 48: SPSS Output – Spearman Correlation Analyses of Enabler Categories Implementation Plant and Lab

Table 55 summarizes the outcomes of the comprehensive set of Spearman correlations analyses and the associated SPSS output. To present the comprehensive content in an easier digestible format, selection of enabler category pairs included in the table is limited to all significant correlations observed. Overall, the Spearman

correlation analyses revealed eleven significant ($p < 0.05$) relations between enabler categories across manufacturing and quality control.

Table 55: Significant Correlations Enabler Categories Implementation Plant and Lab

Further considered		Preventive Maintenance _L	Technology Assessment & Usage _L	House-keeping _L	Pull Approach _L	Layout Optimization _L	Employee Involvement & CI _L
Technology Assessment & Usage _P	ρ			.341			
	Sig			.045			
	N			35			
House-keeping _P	ρ			.456	-.384	.338	
	Sig			.006	.023	.047	
	N			35	35	35	
Process Management _P	ρ						.427
	Sig						.011
	N						35
Cross-func. product development _P	ρ		.454				.448
	Sig		.006				.007
	N		35				35
Layout Optimization _P	ρ	.375					
	Sig	.027					
	N	35					
Direction Setting _P	ρ					.335	.383
	Sig					.049	.023
	N					35	35
Standardization _P	ρ	.338					
	Sig	.047					
	N	35					

After an initial review of the significant ($p < 0.05$) correlations, six out of the eleven pairs are considered insightful and encircled in Figure 48 and Table 55, while the remaining five significant combinations are hard to interpret and consequently excluded. Due to the manifoldness of subject fields assessed in the maturity assessments, statistic correlation of enabler implementation levels between categories that are not related content-wise can likely occur and is not seen as an issue: Even if the data shows a significant association of Housekeeping in manufacturing and Layout

Optimization maturity in quality control, both subject fields are not related to each other in practice. That is why the occurrence of correlation cannot be transferred in actionable implications, different to the encircled six significant cross-departmental combinations of enabler categories. Subsequently, these selected six significantly positive correlations are reviewed and discussed in detail. Explanations follow the ascending order of plant enabler categories applied in Table 55.

Figure 49 presents a scatter plot of enabler implementation levels concerning Housekeeping for both departments manufacturing and quality control. The average categorial implementation levels comprise answers to three underlying questions in the OPEX manufacturing benchmarking and four questions summarizing the House-keeping enabler implementation level in quality control.

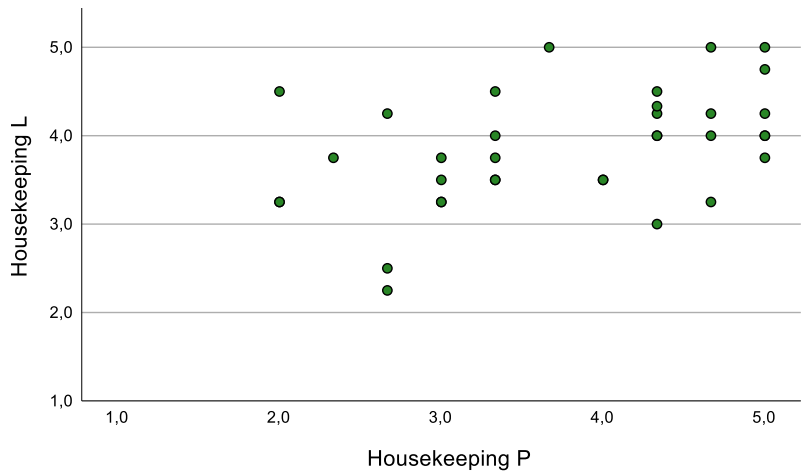


Figure 49: Scatter Plot of Housekeeping Implementation Plant and Housekeeping Implementation Lab

The scatter plot confirms the positive association of Housekeeping in manufacturing and Housekeeping in quality control indicated by the Spearman correlation coefficient $\rho = 0.456$. Housekeeping is assigned to the maintenance sections of both benchmarking models and thereby acts as fundamental enabling practice to maintain the working environment and equipment status in manufacturing and quality control. It is a key component of CI programs and Production Systems. Assuming that integrated cross-departmental OPEX management is still rather new to pharmaceutical production sites, an association of Housekeeping maturity can already be observed as it is anchored in the fundament of comprehensive improvement efforts in operations. Furthermore, Housekeeping related practices are comparably simple to transfer and train across departments.

Furthermore, the analysis revealed a significant positive Spearman correlation of $\rho = 0.427$ between Process Management enabler implementation in manufacturing and Employee Involvement enabler implementation in quality control. A scatter plot of both variables is given in Figure 50.

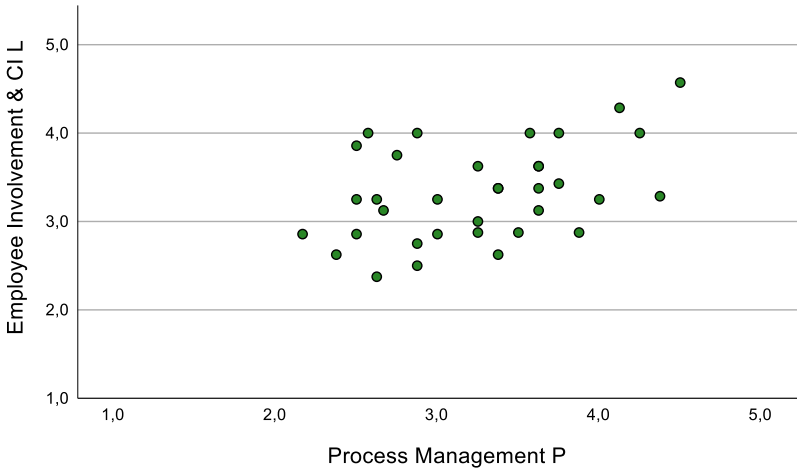


Figure 50: Scatter Plot of Process Management Implementation Plant and Employee Involvement & CI Implementation Lab

A positive correlation between both variables is confirmed by the visualization. As significance was shown in Table 55, it can be concluded that Employee Involvement & Continuous Improvement in quality control is associated with Process Management maturity in manufacturing. Since Process Management comprises awareness for minimizing variance in any kind of business processes through accurate documentation besides the technical monitoring of process parameters, implementing such practices can help to establish a culture of Continuous Improvement across departments. Moreover, closely managing processes requires delegation of responsibility for these processes to employees. Thus, involvement and ownership are fostered.

As a next combination, implementation levels of Cross-functional Product Development enabler in manufacturing and Technology Assessment & Usage enabler in quality control are visualized in Figure 51. Analysis according to Spearman indicated a significant positive correlation $\rho = 0.454$ between both variables.



Figure 51: Scatter Plot of Cross-functional Product Development Implementation Plant and Technology Assessment & Usage Implementation Lab

A linear pattern confirms the positive association of Cross-functional Product Development and Technology Assessment & Usage. As indicated by the correlation analysis, Cross-functional Product Development in manufacturing and Employee Involvement in quality control show a similar association visualized in Figure 52.

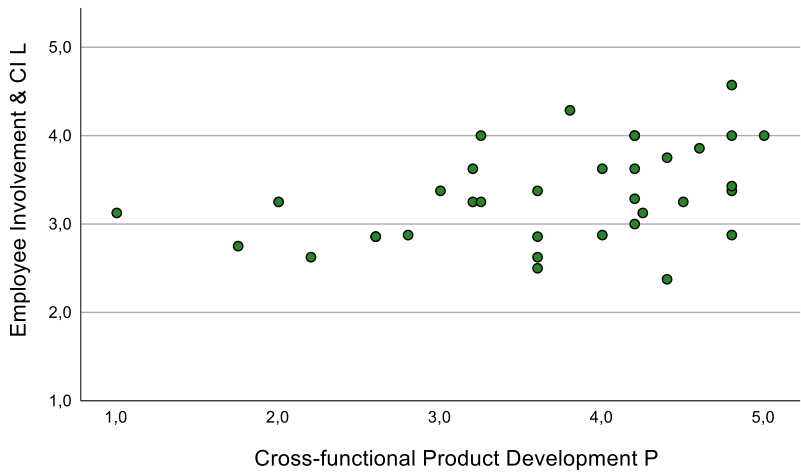


Figure 52: Scatter Plot of Cross-functional Product Development Implementation Plant and Employee Involvement & CI Implementation Lab

Even if assessed as part of the manufacturing benchmarking program, Cross-functional Product Development enabler implementation represent broader competencies of the entire organization in collaborating across departments. Following the site internal value chain, it is not surprising that a robust interface between development and operations is also associated with higher maturity levels in quality control. Capabilities in cross-functional collaboration allow to transfer practices between departments. These seem to pay off in managerial maturity indicated by Employee Involvement and technical maturity for structurally performing assessments of emerging solutions to stay at the leading edge of new technologies. Literature confirms the observation that innovativeness in R&D (Abbreviation Research and Development) and technology can act as catalyzer and motivator for cross-departmental collaboration (cf. chapter 4.4.3).

Moving on to the next pair of enabler implementation categories, Figure 53 presents a scatter plot of Direction Setting in manufacturing and Layout Optimization in quality control across the combined benchmarking sample. A Spearman correlation coefficient of $\rho = 0.355$ indicates a positive association of the variables.

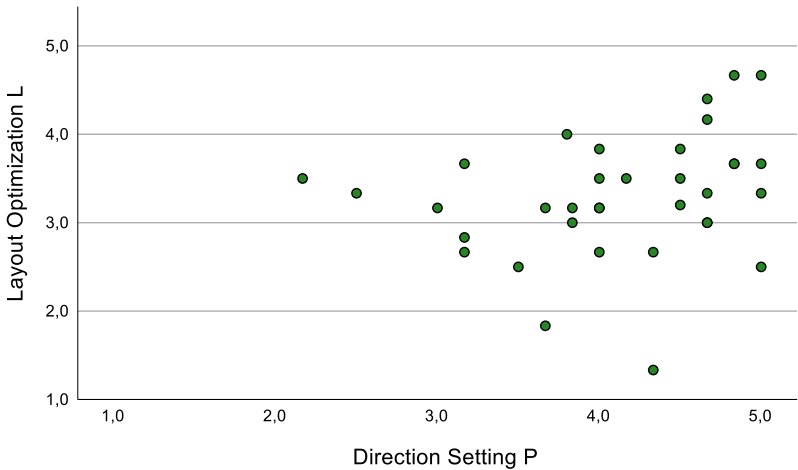


Figure 53: Scatter Plot of Direction Setting Implementation Plant and Layout Optimization Implementation Lab

The relation of Direction Setting in manufacturing and Layout Optimization in quality control is visible in the graph. Consequently, an association of enabler implementation levels across both categories can be attested.

Analogously, the relation of Direction Setting in manufacturing and Employee Involvement & Continuous Improvement in quality control is investigated based on the

Spearman correlation coefficient $\rho = 0.388$ initially identified. Figure 54 provides a scatter plot of implementation levels across the categories.

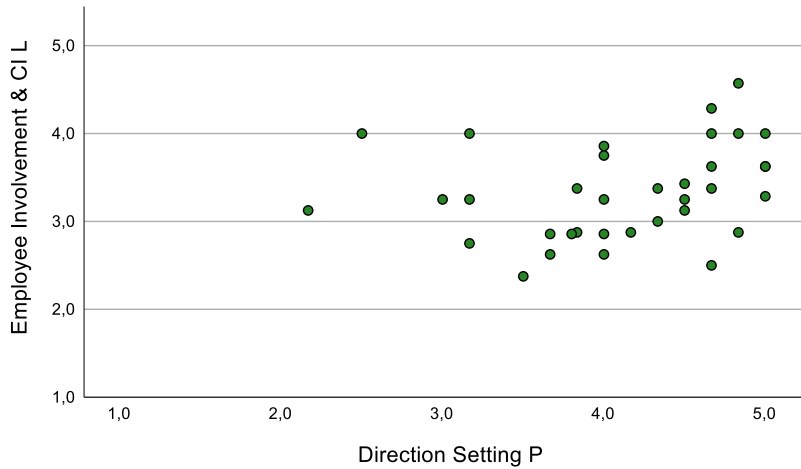


Figure 54: Scatter Plot of Direction Setting Implementation Plant and Employee Involvement & CI Implementation Lab

The visual pattern supports the observation of a positive relation between both variables across the benchmarking sample. Hence, implementing Direction Setting enablers is associated with higher maturity levels in Employee Involvement & Continuous Improvement.

Like elaborated above in the context of observations made on Cross-functional product development capabilities, Direction Setting enabler address competencies of the organization beyond the manufacturing department. Classified as EMS enabler, the assessment questions in the category Direction Setting discuss aspects of the site's future development. The category comprises alignment of the site priorities with the vision or mission of the organization in addition to its interplay with corporate interests and objectives. As the analyses results demonstrate, following a clear strategy in these subject fields and communicating the strategy to the workforce is associated with higher maturity across departments, measured independently as part of the QC lab benchmarking. Data uncovers this relation for maturity in Employee Involvement and maturity in practical application of the improvement philosophy by fostering layout optimization according to lean flow principles in quality control.

Key Observations Cluster H2 – Enabler Implementation across Manufacturing and QC

Summarizing the analyses performed within hypothesis cluster H2, no relation between aggregated overall enabler implementation levels across manufacturing and quality control has been observed. The same holds true for the underlying enabler dimensions TPM_P, TQM_P, JIT_P, EMS_P, and Basic Elements_P tested for correlations with Maintenance & Quality_L, Planning & Steering_L, and Management System_L. Solely TQM_P enabler implementation levels show a significant positive correlation with the degree of Management System_L maturity.

However, eleven cross-departmental combinations of Enabler categories revealed a significant positive correlation, while not any significant negative correlations have been observed. Six out of the eleven combinations are deemed relevant based on a content-driven review and identified as important enabler categories that can help to foster maturity alignment between manufacturing and quality control.

Increased maturity in the plant enabler categories

- Housekeeping_P
- Process Management_P
- Cross-functional Product Development_P
- Direction Setting_P

is associated with higher maturity in the lab enabler categories

- Housekeeping_L
- Technology Assessment & Usage_L
- Layout Optimization_L
- Employee Involvement & CL_L

Consequently, these enabler categories should be understood as particular levers for cross-departmental alignment and capability transfer based on the associations of maturity levels in manufacturing and quality control, which have been uncovered by the previous analyses.

Cluster H3 – Enabler Implementation & Structural Context

The third cluster of hypotheses discusses the relation of OPEX maturity and the structural context of production sites. Maturity is operationalized by multiple aggregated enabler implementation levels, the structural context pharmaceutical production sites operate in is broken down into four contextual factors: (1) The size of production sites measured by the total number of FTEs employed, (2) the geographic region the site is located in grouped by continents, (3) the production technologies present at site grouped in DS and DP production, and (4) the portfolio complexity measured by departmental as well as combined aggregated complexity indexes.

Figure 55 presents a box plot of overall enabler implementation levels measured in the manufacturing benchmarking for five different groups of production sites. The five groups are compiled based on the number of employees at the production sites and arranged in an ascending order from the left to the right of the chart.

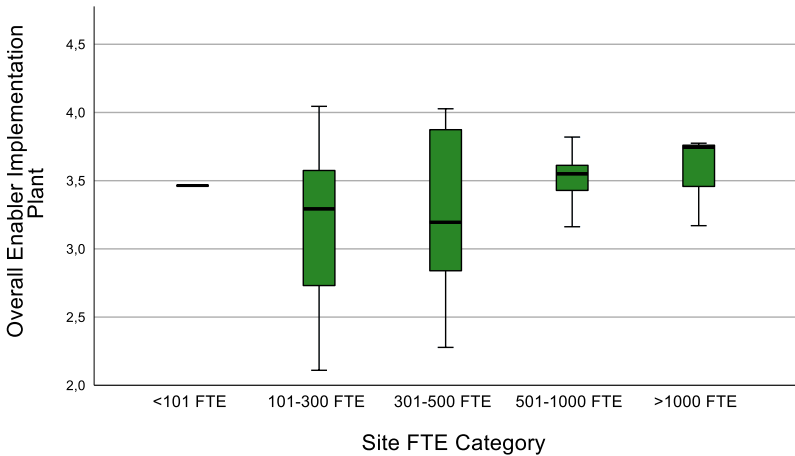


Figure 55: Box Plot of Site FTE Categories and Overall Enabler Implementation Plant

There is a tendency of larger production sites showing higher aggregated enabler implementation in manufacturing. However, enabler implementation varies within and across all five groups. The limited sample size and comparably lower number of production sites in the groups <101 FTEs and >1000 FTEs (cf. chapter 3.2.1) need to be taken into consideration when interpreting the plot. Nevertheless, the majority of sites represented in the three groups ranging from 101 to 1000 FTE support the trend observed.

Analogously, the distribution of overall enabler implementation levels in quality control is analyzed descriptively for the five groups of production sites. A box plot is given in Figure 56. Again, the five groups are compiled based on the number of employees at the production sites and arranged in an ascending order from the left to the right of the chart.

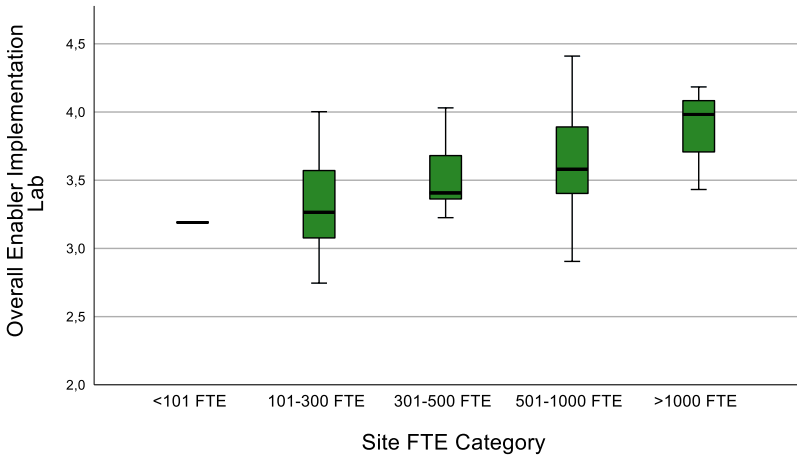


Figure 56: Box Plot of Site FTE Categories and Overall Enabler Implementation Lab

The pattern of larger production sites showing higher levels of overall enabler implementation is confirmed for quality control and seems to be clearer than in manufacturing. Both median and percentile boxes indicate higher aggregated enabler implementation in QC in an ascending order of the five groups. Sites employing between 501 and 1000 FTE show the highest variance of enabler implementation in quality control compared to other sites, while comparably low differences in enabler implementation within this group was observed in manufacturing.

In order to also consider cross-departmental enabler implementation levels, the combined enabler implementation is set into relation with the size of production sites in Figure 57. The above introduced categorization of sites distinguishing five categories applies. Striving to confirm the previous observed tendency while minimizing the risk of misinterpretation caused by the different group sizes, the type of visualization is changed from a box plot to a scatter plot. Every dot indicates the aggregated overall enabler implementation level combining manufacturing and quality control for one production site of the sample.

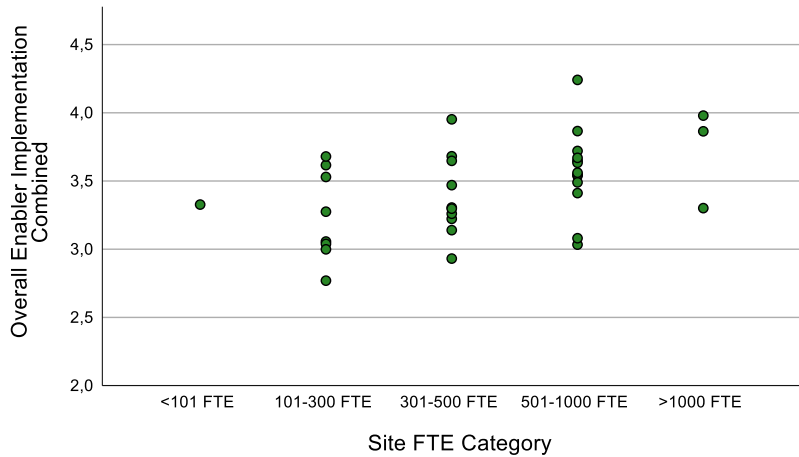


Figure 57: Scatter Plot of Site FTE Categories and Overall Enabler Implementation Combined

The observation of larger production sites showing higher enabler implementation levels still holds true and is also valid for combined maturity across manufacturing and quality control. In the following, this occurrence in the descriptive evaluation is further investigated and tested for significance by a correlation analysis. Since the five groups of production sites form a categorial non-continuous scale, correlation analyses according to Pearson is not applicable. However, as the groups are formed in an ascending order, these can be seen as ordinal scale and allow to formalize the relation by calculating Spearman’s correlation coefficient ρ . Table 56 provides the outcome of the calculation.

Table 56: Spearman Correlation Analysis of Site FTE Categories and Overall Enabler Implementation Level Combined

Site FTE Category	Overall Enabler Implementation Combined	
	ρ	.437
	Sig (2-tailed)	.009
	N	35

The correlation coefficient $\rho = 0.437$ indicates a positive correlation of the site FTE category and the overall enabler implementation level across manufacturing and quality control. For the overall sample of combined benchmarking datasets (N=35) the correlation is significant ($p < 0.01$) and confirms the observation made based on the descriptive box and scatter plots: Higher enabler implementation levels across

manufacturing and quality control are associated with a higher number of FTEs employed at site.

Based on this outcome, the relation of enabler implementation alignment between manufacturing and quality control and the size of pharmaceutical production sites is questioned in addition to the enabler implementation levels. A descriptive dual axis chart allows to integratedly visualize both the combined enabler implementation level and the degree of cross-departmental alignment (cf. chapter 3.2.3). Reacting on the additional complexity of a dual axis visualization, the number of groups is simplified to two in the following: All sites are distinguished by employing a number of FTEs either below the median or above the median of the sample. The chart is given in Figure 58: Bars correspond to the left Y-Axis and visualize the level of overall enabler implementation, while the line indicates the degree of cross-departmental enabler implementation alignment according to the scale on the right Y-Axis.

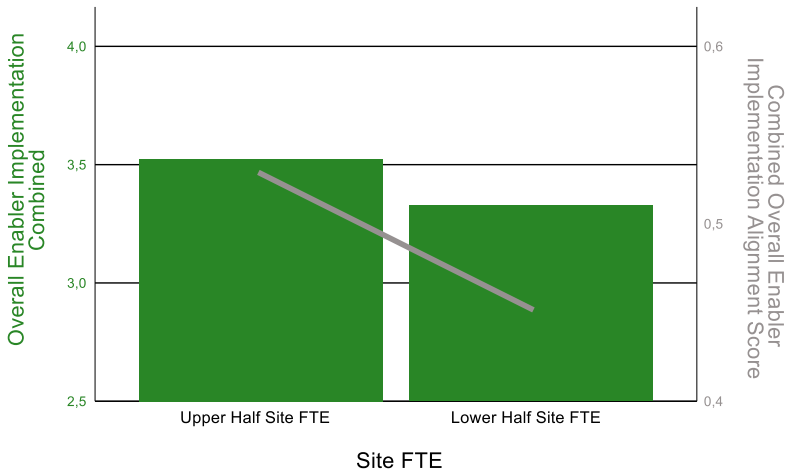


Figure 58: Dual Axis Chart of Site FTE, Overall Enabler Implementation Combined, and Overall Enabler Implementation Alignment Score

The chart indicates a similar trend for cross-departmental enabler alignment like already observed for combined enabler implementation: Larger production sites show less differences in OPEX maturity across manufacturing and quality control. Unlike the association of combined enabler implementation level and the size of production sizes, this observation cannot be tested for significance. Limitations at hand caused by the size of the available benchmarking sample and the measurement scale prohibit the use of further group statistic techniques. That is why the association of enabler alignment and sizes of production sites is an outcome of pure descriptive statistics and needs to be understood accordingly.

Subsequently, the relation of enabler implementation and the geographic region of production sites is researched for manufacturing, quality control, and across departments. Therefore, production sites are assigned to four groups according to the continent they are located at. Figure 59 visualizes the enabler implementation levels in manufacturing for sites belonging to the four geographical groups.

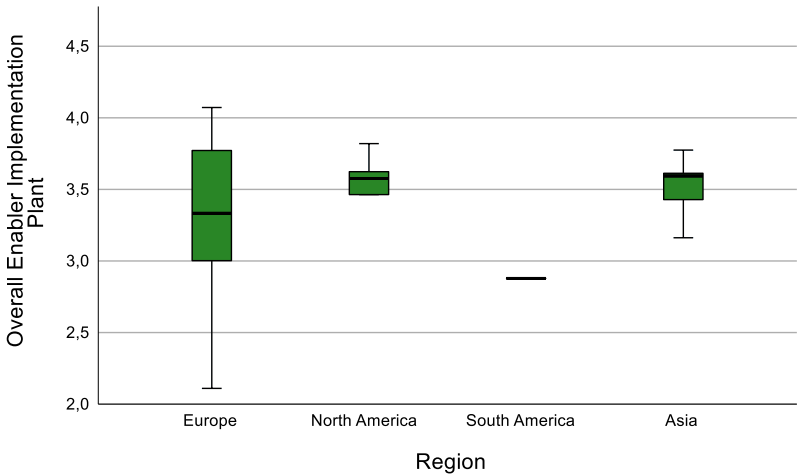


Figure 59: Box Plot of Regions and Overall Enabler Implementation Plant

The distribution of enabler implementation levels across the four regions is similarly analyzed for the quality control departments. A box plot is provided in Figure 60.

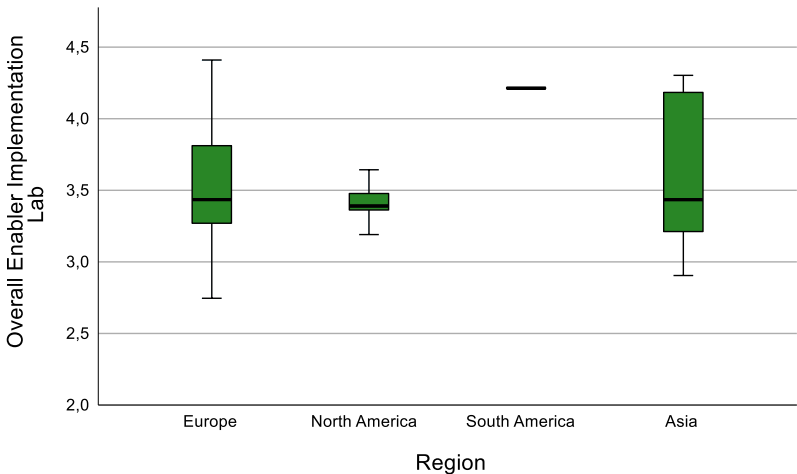


Figure 60: Box Plot of Regions and Overall Enabler Implementation Lab

There is no tendency of regions associated with comparably lower or higher enabler implementation observable. All group's medians indicate similar levels of in average plant enabler implementation. The same holds also true for quality control. Solely South America shows a comparably high level of overall enabler implementation in quality control alongside with a comparably low implementation level in manufacturing. However, since only one out of the 35 data sets is assigned to the group South America, this observation is based on a single production site and deemed as an outlier. Differences in variance within the groups can be explained by the tremendously different group sizes (cf. chapter 3.2.1) of the benchmarking population not directly visible in box plots. 65% of the production sites are located in Europe and therefore assigned to the left group, consequently higher domestic differences exist compared to other regions.

An analysis of combined enabler implementation across manufacturing and quality control is performed to confirm the absence of regional patterns. Similar to the visualization of combined enabler implementation and site sizes, a scatter plot is chosen to visualize the number of observations per group and allows consideration of different group sizes for interpretation. Figure 61 presents the outcomes.

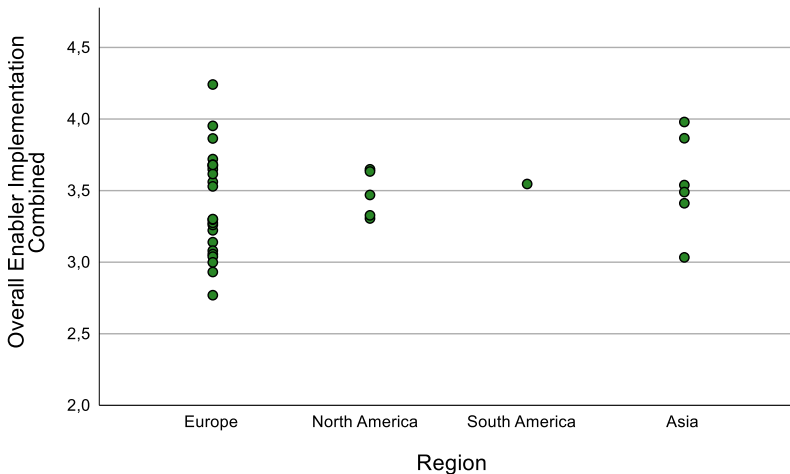


Figure 61: Scatter Plot of Regions and Overall Enabler Implementation Combined

The combined analysis underlines that no association of enabler implementation with the geographic location of production sites can be observed neither individually for manufacturing or quality control nor across departments. Grouping sites according to their regions leads to a nominal categorical scale, the four regions cannot be ranked in an ascending or descending order. That is why the grouping variable lacks ordinal characteristics and correlation or regression analyses cannot be applied to the data set to attest significance. However, since descriptive statistics did not

uncover any tendencies for associations, it can be concluded that there is no relation between enabler implementation and region of production sites in the combined benchmarking sample at hand.

Following analyses examine the relation of departmental or cross-departmental overall enabler implementation levels and the production technologies operated on site. In a first step, the benchmarking sample is assigned to three groups according to the individual operations: Drug Substance Production, Drug Product Production, or both Drug Substance and Drug Product Production. Figure 62 reveals the distributions of combined enabler implementation levels across plant and lab for all three groups.

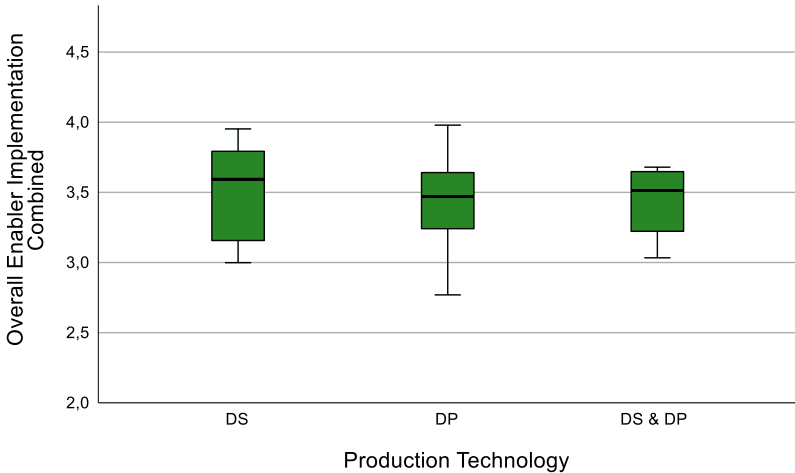


Figure 62: Box Plot of Production Technologies and Overall Enabler Implementation Combined

The three clusters corresponding to the production technology at site show very few differences in their median of combined enabler implementation levels. Furthermore, there are only minor differences in the inner group distributions. DS sites seems to show a narrower range of implementation levels, while lower minimum and higher maximum levels can be observed for DP sites. Analogously, distribution analyses were exclusively performed for the departmental overall enabler implementation. Outcomes support the results of the combined analyses presented in Figure 62: Only very minor differences in overall enabler implementation levels across the three groups are observable in manufacturing and quality control. No additional implications can be drawn, that is why departmental box plots are not presented as additional visualizations.

Since enabler implementation levels do not differ between production technologies, the sample is supplementary tested for associations of the degree of maturity alignment across departments and the three technologies. A descriptive dual axis chart allows to visualize the combined enabler implementation level and the degree of cross-departmental enabler implementation alignment (cf. chapter 3.2.3) per group. The chart is given in Figure 63: Bars correspond to the left Y-Axis and present the combined level of overall enabler implementation, while the line indicates the degree of cross-departmental enabler implementation alignment according to the scale on the right Y-Axis.

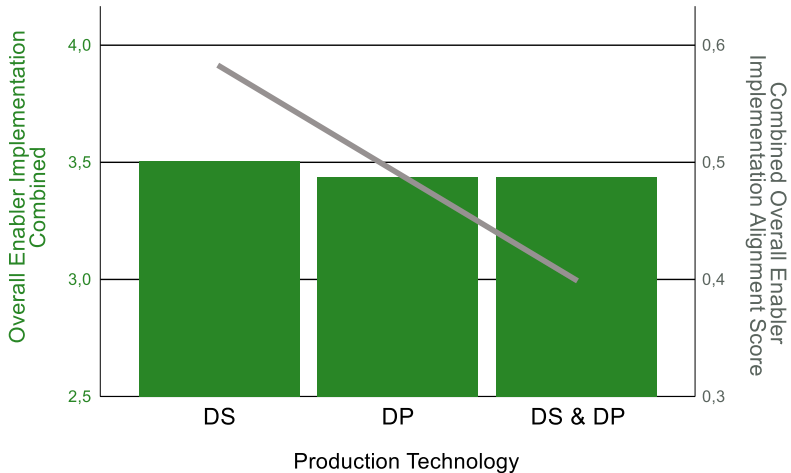


Figure 63: Dual Axis Chart of Production Technologies, Overall Enabler Implementation Combined, and Overall Enabler Implementation Alignment Score

DS sites show a higher degree of departmental alignment in enabler implementation than DP sites. Production sites running operations in both areas DS and DP score lowest in enabler alignment. Hence, aligning OPEX maturity across departments and transferring practices between manufacturing and quality control seems to be more related to the production environment of Drug Substance even if there is no difference in the aggregated combined implementation levels observable.

Like the previously discussed regions, the three different groups cannot be ranked in an ascending or descending order. Consequently, the nominal scale does not allow for correlation or regression analyses: The observed relation of production technology and cross-departmental alignment in enabler implementation is solely based on descriptive statistics.

Lastly, the fourth selected contextual factor portfolio complexity is tested for association with enabler implementation in manufacturing, quality control, and across both departments. Outcomes of the descriptive statistics are visualized as scatter plots

in the following. Due to the continuous metric scales of all variables and the absence of categories box plots are not appropriate. Figure 64 presents the scatter plot of departmental levels of complexity (cf. chapter 3.2.3) and overall enabler implementation in manufacturing for the benchmarking sample.

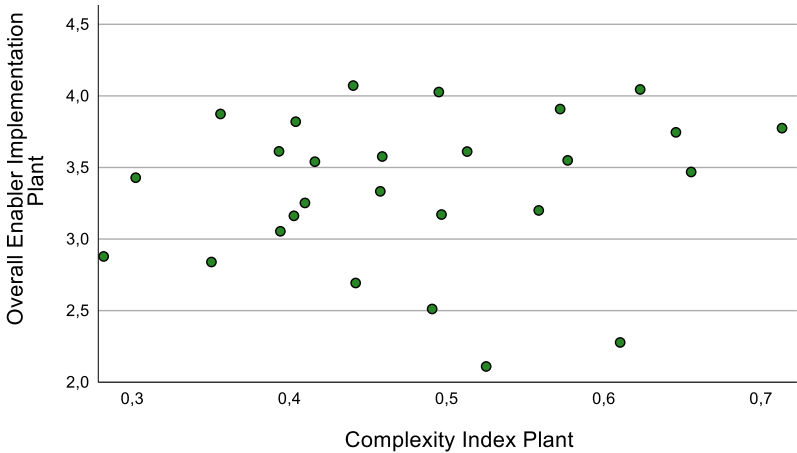


Figure 64: Scatter Plot of Complexity Index Plant and Overall Enabler Implementation Plant

Neither patterns or clusters across different production sites nor a linear relation are observable. Consequently, there seems to be no relation between the levels of complexity and enabler implementation in manufacturing. Outcomes of the identical analyses for quality control are presented in the scatter plot given in Figure 65.

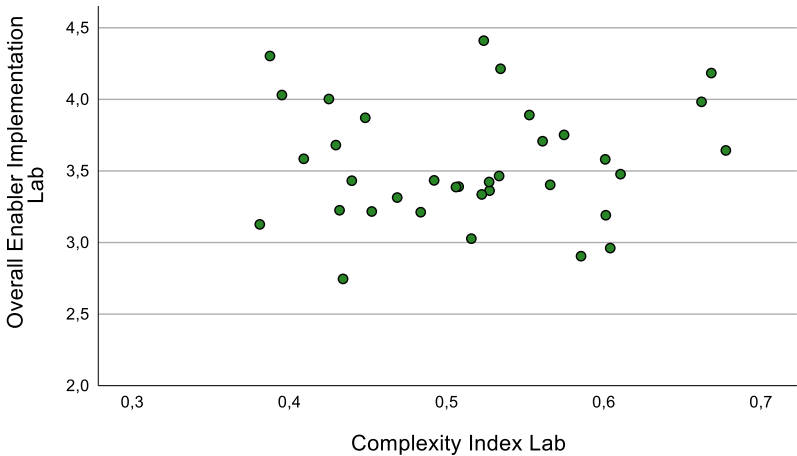


Figure 65: Scatter Plot of Complexity Index Lab and Overall Enabler Implementation Lab

Like shown for the manufacturing department, no apparent association of the overall enabler implementation with the existing level of portfolio complexity is visible in the descriptive analyses of the QC variables. Hypothesizing that the interdependency of both departments could impact the relation of portfolio complexity and enabler implementation levels, the analyses is repeated for the combined complexity index and the aggregated overall enabler implementation incorporating both departments manufacturing and quality control. Figure 66 visualizes the analyses in a scatter plot of both variables.

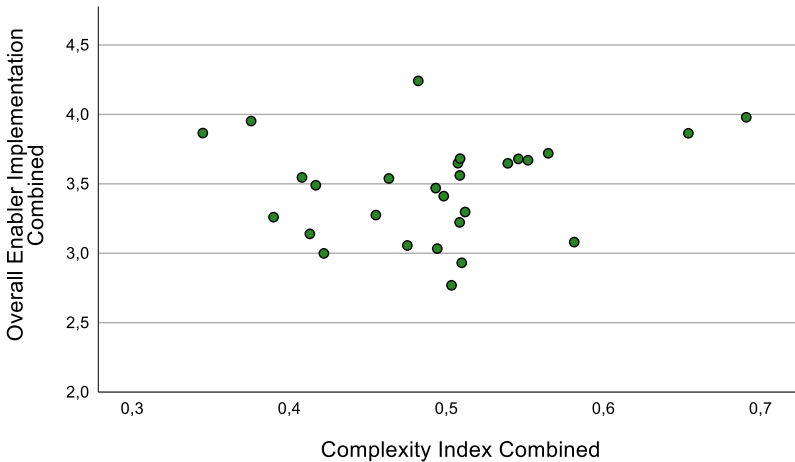


Figure 66: Scatter Plot of Complexity Index Combined and Overall Enabler Implementation Combined

Results of the previous departmental analyses are directionally confirmed by the combined analysis. Neither a clear positive or negative relation nor any other pattern can be drawn from the visualization. However, there seems to be a tendency of a slight positive correlation between the cross-departmental complexity index and the combined overall enabler implementation level.

Completing the set of analyses, the complexity index alignment score is finally evaluated for relation with the present level of cross-departmental enabler implementation. Similar to the previously discussed overall enabler implementation alignment score, the complexity index alignment score does not allow to draw any conclusions on the existing level of portfolio complexity but quantifies the difference of departmental complexity between manufacturing and quality control. Low alignment scores uncover inconsistent complexity levels at the production site. The scatter plot in Figure 67 presents the level of complexity alignment alongside with the combined overall enabler implementation level for each site.

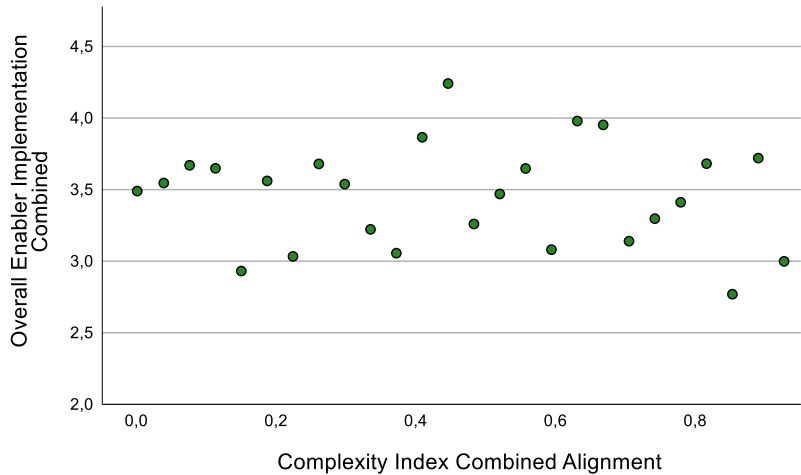


Figure 67: Scatter Plot of Complexity Alignment Index and Overall Enabler Implementation Combined

No observation of any relation between the variance in complexity across departments and the combined overall enabler implementation level can be made. Consequently, neither the level of portfolio complexity across departments nor the degree of complexity alignment between manufacturing and quality control seems to be associated with the level of OPEX maturity within and across departments.

Striving to confirm this outcome of the descriptive analyses, additional correlation tests are performed. All variables contain values on a metric scale and therefore allow for the determination of Pearson correlation coefficients. Shapiro-Wilk tests are performed to confirm the normal distribution of all variables as an additional precondition for correlation analyses according to Pearson. Table 57 lists the results of the test for all three measurements.

Table 57: Test for Normal Distribution of Overall Enabler Implementation Combined, Complexity Index Combined, and Complexity Index Alignment

Shapiro-Wilk Test: Complexity and Overall Enabler Implementation			
	Statistic	df	Sig
Overall Enabler Implementation Combined	.985	35	.904
Complexity Index Combined	.959	30	.322
Complexity Index Combined Alignment	.958	30	.312

Shapiro-Wilk tests revealed significance levels $p > 0.05$ for all indicators. Complemented by the graphical review of the Q-Q plots, normal distribution is confirmed (cf. appendix A.2). Furthermore, linearity can be assumed since no non-linear patterns were observed in the descriptive analyses of the scatter plots. All requirements for conducting Pearson correlation analyses are fulfilled, outcomes of the correlation tests are summarized in Table 58.

Table 58: Pearson Correlation Analyses of Combined Complexity, Complexity Alignment, and Overall Enabler Implementation Combined

		Overall Enabler Implementation Combined
Complexity Index Combined	r	.166
	Sig (2-tailed)	.397
	N	28
Complexity Index Combined Alignment	r	-.056
	Sig (2-tailed)	.776
	N	28

Outcomes of the descriptive statistics indicating the absence of any relation or association between existing portfolio complexity, the degree of complexity alignment and the combined enabler implementation level are confirmed. Even if the Pearson correlation coefficients $r > 0$ indicate a very slight positive correlation between Complexity Index Combined and Overall Enabler Implementation Combined, this correlation is not significant at all.

Key Observations Cluster H3 – Enabler Implementation & Structural Context

Summarizing the analyses performed within hypothesis cluster H3, an association of cross-departmental enabler implementation level and the size of production sites has been observed. The correlation was found to be significant at a level $p < 0.01$. Further analyses did not uncover any clear association of enabler implementation levels and the other structural factors geographic region, production technology, and portfolio complexity.

Cluster H4 – Aggregated KPI Scores & Enabler Implementation Levels across Manufacturing and Quality Control

Previous passages discussed associations of performance scores (cf. H1) across departments and cross-departmental enabler implementation levels (cf. H2) individually. In the following, the interplay of maturity and performance across manufacturing and quality control is discussed in detail to address the hypotheses of cluster H4. Therefore, the combined site scores (cf. chapter 3.2.3) are used for analyses to jointly study enabler implementation levels and performance scores of plant and lab.

At first, the relation of Overall Enabler Implementation Combined and OPEX & LP Combined is tested. Prior to conducting the correlation analyses, required preconditions for credible Pearson correlation coefficients are evaluated. Table 59 presents the outcomes of a Shapiro-Wilk test for normal distribution of both combined scores.

Table 59: Test for Normal Distribution of Combined Performance and Maturity Scores

	Shapiro-Wilk Test: Combined Scores		
	Statistic	df	Sig
Overall Enabler Implementation combined	.985	35	.904
OPEX & LP combined	.954	20	.428

Reviewing the associated Q-Q plots supports the outcome of the Shapiro-Wilk tests. Since the tests did not reveal significance ($p > 0.05$), normal distribution of both scores can be assumed. Furthermore, variables' scales are metric and no indication of any non-linear relations exists. Consequently, Pearson correlation analysis is applicable and conducted. The result of the correlation test is given in Table 60.

Table 60: Pearson Correlation Analysis Overall Enabler Implementation Combined and OPEX & LP Combined

	OPEX & LP combined	
	r	-.090
	Sig (2-tailed)	.705
	N	20

No correlation between the scores Overall Enabler Implementation Combined and OPEX & LP Combined can be observed. Hence, there seems to be no association of KPI scoring comprising manufacturing and quality control with the average maturity levels in both departments.

In addition to the level of combined enabler implementation and combined performance scoring, the degrees of alignment in maturity & KPIs are evaluated for correlation considering manufacturing and quality control in a combined manner. Both alignment scores serve as inverted measures to operationalize differences in enabler implementation and aggregated KPI scores between departments (cf. chapter 3.2.3). In order to determine the appropriate statistical method for analysis, both scores are tested for normal distribution first. Table 61 summarizes the results of the Shapiro-Wilk tests.

Table 61: Test for Normal Distribution of Performance and Enabler Alignment Scores

	Shapiro-Wilk Test: Alignment Scores		
	Statistic	df	Sig
Overall Enabler Implementation Alignment	.957	35	.182
OPEX & LP Alignment	.960	20	.551

Supplemented by a review of the Q-Q plots, the non-significant test results ($p > 0.05$) suggest not to reject the null hypothesis of normally distributed variables. As both aggregated measurements use metric scales and linear relation is assumed, all criteria for assessing correlation using Pearson's coefficient r are fulfilled. Outcomes of the Pearson correlation analysis are presented in Table 62.

Table 62: Pearson Correlation Analysis of Overall Enabler Implementation Alignment and OPEX & LP Alignment

	OPEX & LP Alignment	
	r	.205
	Sig (2-tailed)	.387
	N	20

The Pearson correlation $r = 0.205$ indicates a positively directed but very slight relation of both alignment scores. However, since this correlation is neither significant at levels $p < 0.05$ nor $p < 0.1$, no association of the degree of cross-departmental alignment in enabler implementation and the degree of cross-departmental alignment in KPI scoring can be stated.

Analyzing the relation of cross-departmental Overall Enabler Implementation Combined and OPEX & LP Combined as well as investigating the relation of both alignment scores did not reveal any association. That is why both perspectives – combined enabler implementation & KPI levels alongside with the degrees of alignment – are integrated in the following. The association of LP & OPEX scores (representing cross-departmental consistency in KPI scores across departments) is evaluated depending on the present level of combined cross-departmental maturity.

For this purpose, two groups of pharmaceutical production sites are distinguished: LH (Abbreviation Lower Half) sites showing a cross-departmental overall enabler implementation level below the median of the benchmarking sample and TH (Abbreviation Top Half) sites showing a cross-departmental overall enabler implementation level above the median of the benchmarking sample. Subsequently, the relation of LP & OPEX scores is determined individually for both groups of production

sites. Table 63 depicts the results, applicability of Pearson correlation analyses was previously demonstrated for all variables.

Table 63: Pearson Correlation Analysis of LP and OPEX Score - Grouped by Overall Enabler Implementation Combined

		OPEX <i>LH - Below median overall Enabler implementation combined</i>	OPEX <i>TH - Above median overall Enabler implementation combined</i>
LP <i>LH - Below median overall Enabler implementation combined</i>	r	.330	
	Sig	.322	
	N	11	
LP <i>TH - Above median overall Enabler implementation combined</i>	r		.687
	Sig		.041
	N		9

There is a slight positive correlation between LP and OPEX score observable for production sites showing a below median combined overall enabler implementation level. Differently, for production sites with a top half combined overall enabler implementation level a significant ($p < 0.05$) and clear positive correlation $r = 0.687$ of LP and OPEX scores is revealed.

Following-up on this observation, a linear regression of both scores LP (IV) and OPEX (DV) is exclusively performed for the group of production sites showing a top half cross-departmental overall enabler implementation level. Table 64 presents the regression model.

Table 64: Linear Regression of LP Score (IV) and OPEX Score (DV) – Above Median Overall Enabler Implementation Combined Exclusive

DV: OPEX TH Enabler combined							
Model Summary					Coefficient		
	R Square	Adjusted R Square	F-value	Durbin-Watson	Standard. Coefficient Beta	t-value	Sig
IV: LP <i>TH Enabler comb.</i>	.471	.396	6.241	2.125	.687	2.498	.041

A positive association of both scores is indicated by the linear regression. The Durbin-Watson test result $1.5 < d < 2.5$ indicates a non-critical level of autocorrelation. Moreover, the residual plot does not show any heteroscedastic pattern. A degree of determination $r^2 = 0.471$ indicates that 47.1% of the variation in OPEX scores are determined by the variation in LP scores but only for production sites showing an

above median cross-departmental maturity level. A scatter plot of OPEX & LP scores highlighting the two groups distinguished by cross-departmental enabler implementation levels is given in Figure 68. The regression line for the group of TH enabler sites is included.

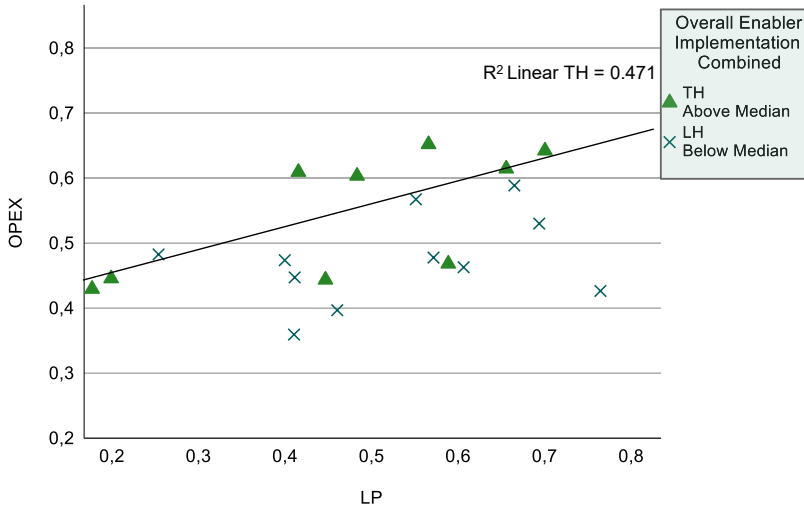


Figure 68: Regression Plot of LP and OPEX Score – Above Median Enabler Implementation Sites

Consequently, it can be stated that the degree of association between overall performance in manufacturing and quality control corresponds with the level of cross-departmental maturity at site. More mature production sites seem to perform more consistently in KPIs across departments.

Key Observations Cluster H4 – Aggregated KPI Scores & Enabler Implementation Levels across Manufacturing and Quality Control

Summarizing the analyses performed within hypotheses cluster H4, the benchmarking data has not indicated any relation of combined enabler implementation and the level of combined KPI scoring. Moreover, no association of cross-departmental alignment levels in enabler implementation and cross-departmental alignment levels in KPI scores has been identified. However, the group of top half production sites selected by combined enabler implementation demonstrate a significant ($p < 0.05$) association of LP and OPEX performance with a high degree of determination ($r^2 = 0.471$), while the lower half does not. Hence, establishing combined cross-departmental OPEX maturity can be one lever to leverage performance differences between manufacturing and quality control.

Cluster H5 – Compliance Status, Enabler Implementation & Performance Levels across Manufacturing and Quality Control

The fifth cluster of hypotheses strives to research the interplay of cross-departmental maturity, combined performance scores, and the compliance status of pharmaceutical production sites. Consistent to cluster H4, the previously introduced aggregated overall enabler implementation level combined serves as operationalization of cross-departmental maturity, while the combined LP & OPEX score quantifies effectiveness and efficiency of operations in manufacturing and quality control during the analyses.

Like in previous studies (cf. Friedli et al., 2018, p. 21 ff.; 2019, p. 61 ff.) compliance status of pharmaceutical production sites is classified based on the final outcomes of U.S. FDA inspections. Based on all observations made during inspections, the agency communicates its final decision whether follow-up actions are suggested to the production sites. This decision can serve as aggregated summary of the inspection performance at the same time. Three categories are distinguished: NAI (Abbreviation No Action Indicated), VAI (Abbreviation Voluntary Action Indicated) and OAI (Abbreviation Official Action Indicated).

For the purpose of subsequent analyses, the final inspection outcome of the inspection closest to the time of benchmarking participation is used as a compliance indicator for all production sites of the combined benchmarking sample. Production sites that are either not FDA regulated or have not been inspected in the time period of one year prior or after providing the benchmarking data are classified as not FDA inspected. Moreover, sites having received an VAI or OAI inspection result form one category in the subsequent analyses due to the limited size of the sample.

In a first step, descriptive analyses evaluate differences in cross-departmental maturity and combined KPI scores depending on the compliance status. Therefore, box plots are compiled to analyze distributions of the three compliance categories based on the combined benchmarking database. Figure 69 provides an overview of the distribution of Overall Enabler Implementation Combined within and across compliance categories. The left box shows enabler implementation within not FDA inspected production sites, distribution of enabler implementation across NAI sites is visualized in the middle of the chart, and the right box summarizes maturity observed for the group of OAI/VAI production sites.

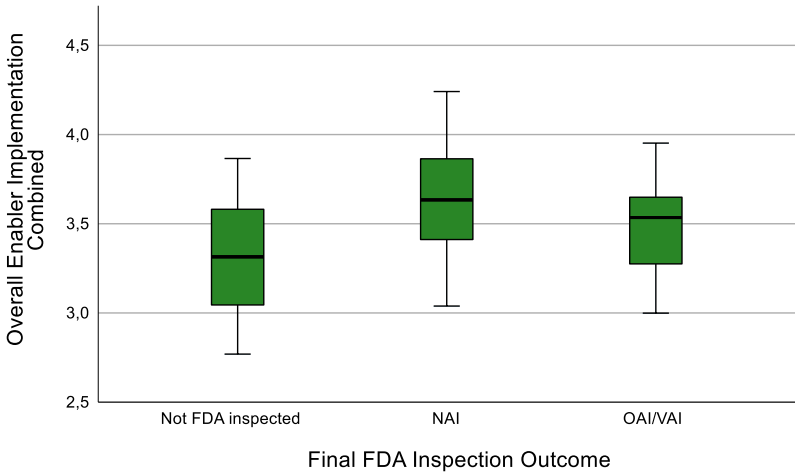


Figure 69: Box Plot of FDA Inspection Outcomes and Overall Enabler Implementation Combined

Production sites, which received the most favorable inspection outcome NAI, score higher in Overall Enabler Implementation Combined compared to sites receiving an VAI or OAI inspection outcome. In the context of not FDA inspected production sites, Overall Enabler Implementation Combined demonstrates lower aggregated maturity levels compared to all FDA inspected sites, regardless of the inspection outcome. This observation holds true for the median of the three compliance categories as well as the inner group minimum and maximum values.

Analogously, a descriptive analysis of combined LP & OPEX scores by compliance status is conducted to evaluate the relation of cross-departmental benchmarking performance scores and inspection outcomes. The box plot is presented in Figure 70. Starting from the left and moving on to the right of the chart, distributions of LP & OPEX Combined scores are visualized for production sites that have not been FDA inspected, sites received NAI as final inspection decision, and sites that have been voluntarily or officially asked to conducted an action based on the inspection.

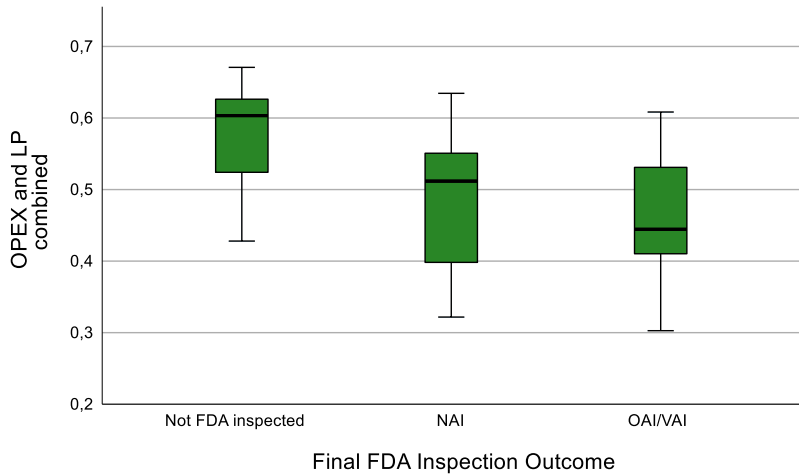


Figure 70: Box Plot of FDA Inspection Outcomes and OPEX LP Score combined

The boxplot of compliance status and cross-departmental KPI scores leads to rather similar observations across the two groups of FDA regulated production sites. NAI sites show slightly higher aggregated LP & OPEX combined scores than OAI/VAI production sites. However, variance within the group of NAI sites seems to be higher as well. The lower percentile of NAI sites scores below the lower percentile of OAI/VAI sites. Consequently, no clear implication can be drawn. Unlike the pattern observed on Overall Enabler Implementation Combined and compliance status, not FDA inspected production sites demonstrate the highest aggregated performance scores.

Since distinguishing sites by their approval and compliance status leads to a categorical scale, the variables do not allow testing for statistically significance of relations to confirm the tendencies noticed. Consequently, observations are limited to the outcomes of descriptive statistics. This needs to be taken into account during interpretation alongside with the limitations caused by the small sample size.

In the following, differences in the cross-departmental association of maturity and aggregated KPI scores across the different groups of production sites by compliance status are investigated. In that way, the above-mentioned barrier of categorical scales is overcome since all variables use metric scales and allow within group analyses first before comparing the outcomes across the different categories. A scatter plot of Overall Enabler Implementation Lab and Overall Enabler Implementation Plant is shown in Figure 71. The three groups of production sites distinguished by compliance status are individually labeled to allow for a descriptive evaluation of differences in maturity patterns.

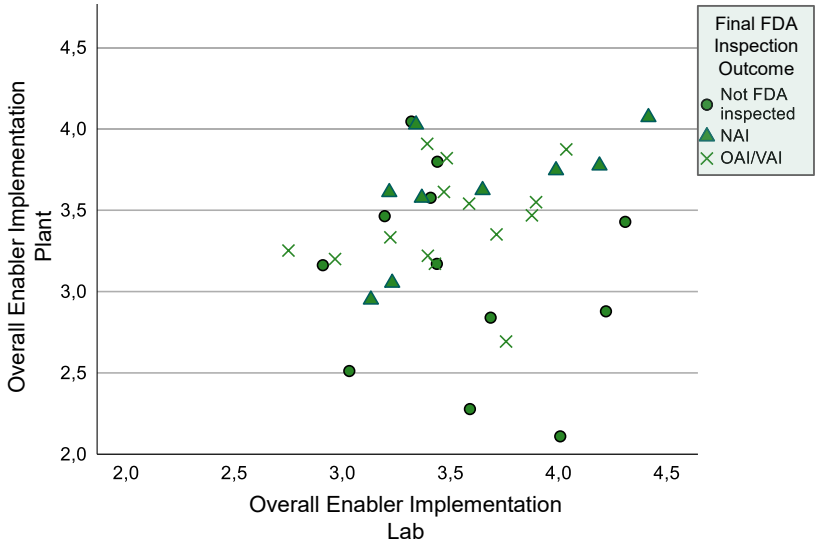


Figure 71: Scatter Plot of Overall Enabler Implementation Lab and Plant – Grouped by FDA Inspection Outcomes

Similar to the outcomes of analyses performed on departmental enabler implementation levels in cluster H2, the scatter plot does not uncover any clear pattern for the entire combined benchmarking population. However, individually evaluating the different compliance categories leads to additional observations: Previous box plot analysis revealed a tendency of sites receiving more favorable FDA inspections outcomes showing a higher level of maturity indicated by higher overall enabler implementation combined. This finding is also visible in the scatter plot of the two underlying departmental enabler implementation levels assessed for laboratories and manufacturing plants. Moreover, NAI production sites seem to show less variance in the cross-departmental distribution of enabler implementation levels compared to the other two groups.

Further investigating the descriptive observations, correlation analyses testing the relation of Overall Enabler Implementation Level Plant and Overall Enabler Implementation Lab are individually performed for all three groups of sites distinguished by compliance status. Eligibility of variables for Pearson correlation analyses was already demonstrated (cf. H2) by confirming normal distributions, appropriate scale levels, and linear relations. Table 65 summarizes the results of the three correlation analyses.

Table 65: *Pearson Correlation Analyses of Overall Enabler Implementation Lab and Plant – Grouped by FDA Inspection Outcome*

		Overall Enabler Implementation Plant <i>Not FDA inspected</i>	Overall Enabler Implementation Plant <i>NAI</i>	Overall Enabler Implementation Plant <i>OAI/VAI</i>
Overall Enabler Implementation Lab <i>Not FDA inspected</i>	r	-.224		
	Sig	.484		
	N	12		
Overall Enabler Implementation Lab <i>NAI</i>	r		.649	
	Sig		.059	
	N		9	
Overall Enabler Implementation Lab <i>OAI/VAI</i>	r			.239
	Sig			.411
	N			14

Identified Pearson correlation coefficients confirm observations drawn from the scatter plot. While not FDA inspected production sites show a negative correlation of Overall Enabler Implementation Lab and Overall Enabler Implementation Plant, a positive correlation is indicated for both groups of FDA inspected sites. Furthermore, NAI sites show a much higher degree of correlation $r = 0.649$ compared to the other two compliance categories. Hence, production sites receiving favorable inspection outcomes show a higher association of maturity levels in manufacturing and quality control than sites receiving actions indicated or sites, which are not FDA inspected at all. Even if significance ($p < 0.05$) of correlation cannot be stated for all compliance categories, the association observed for NAI sites ($p = 0.059$) is much closer to the 5% significance level than associations indicated for the further two compliance categories.

Analogously, the association of aggregated KPI scores across manufacturing and quality control is researched while incorporating the compliance status measured by FDA inspection outcomes. In a first step of descriptive analysis, the distributions of LP and OPEX score based on the combined benchmarking sample are plotted in Figure 72. Different labels highlight again the compliance status of each production site: Not FDA inspected, No Action Indicated or Voluntary Action Indicated / Official Action Indicated.

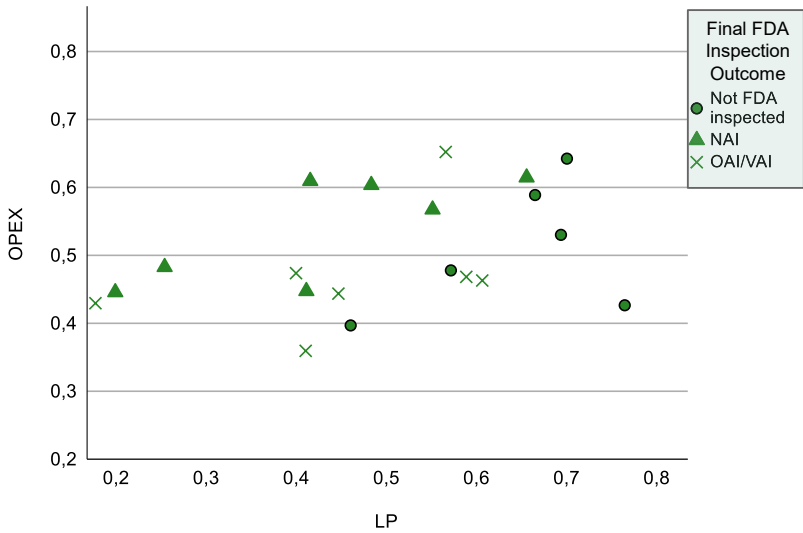


Figure 72: Scatter Plot of LP and OPEX Score – Grouped by FDA Inspection Outcomes

The scatter plot confirms the observations initially made based on the box plot. NAI sites show higher aggregated departmental performance scores compared to OAI/VAI sites. Overall combined performance of not FDA regulated production sites seems to be more driven by comparably high LP performance scores, than by their OPEX scores. The entire sample indicates a tendency of positive relation between LP and OPEX scores that can be observed across all production sites (cf. H1). There is no visually striking pattern of differences in the degree of cross-departmental association between the three compliance categories.

Striving to quantify the observations made, correlation analyses on the relation of LP and OPEX scores are individually performed for all three groups of sites distinguished by compliance status. As elaborated prior to conducting the calculations in cluster H1, both aggregated scores LP and OPEX are normally distributed, use a metric scale and there is no reason to assume any non-linear relations. Consequently, all preconditions are met and Pearson's approach to determine the degree of correlation between variables is applicable. Results of the individual correlation analyses per compliance category are summarized in Table 66.

Table 66: *Pearson Correlation Analyses of LP and OPEX Scores – Grouped by FDA Inspection Outcomes*

		OPEX <i>Not FDA inspected</i>	OPEX <i>NAI</i>	OPEX <i>OAI/VAI</i>
LP <i>Not FDA inspected</i>	r	.448		
	Sig	.373		
	N	6		
LP <i>NAI</i>	r		.756	
	Sig		.049	
	N		7	
LP <i>OAI/VAI</i>	r			.436
	Sig			.328
	N			7

All three groups of production sites show a positive correlation between LP and OPEX scores. Analyses revealed the highest degree of correlation ($r = 0.756$) for NAI sites, while lower levels of positive correlation are recognizable for the two other compliance categories. Moreover, the positive correlation of LP and OPEX scores is solely significant ($p < 0.05$) for sites having received NAI as final inspection outcome. Consequently, it can be assumed that higher aggregated performance in quality control is associated with higher aggregated performance in manufacturing for sites performing well in FDA inspections.

Further detailing the observed significant correlation for NAI production sites, a linear regression of LP scores (IV) and OPEX scores (DV) is performed within the compliance category. Table 67 presents the regression model.

Table 67: *Linear Regression of NAI Exclusive LP Score (IV) and OPEX Score (DV)*

DV: OPEX NAI							
Model Summary					Coefficient		
	R Square	Adjusted R Square	F-value	Durbin-Watson	Standard. Coefficient Beta	t-value	Sig
IV: LP NAI	.572	.486	6.681	1.959	.756	2.585	.049

Based on the Durbin-Watson value observed ($1.5 < d < 2.5$) and the visual review of the residual plot, almost no autocorrelation and no critical level of heteroscedasticity is noticeable. Outcomes of the regression analysis are significant at a level

$p < 0.05$ and visualized in Figure 73, highlighting the compliance category NAI in scope of the linear regression at hand.

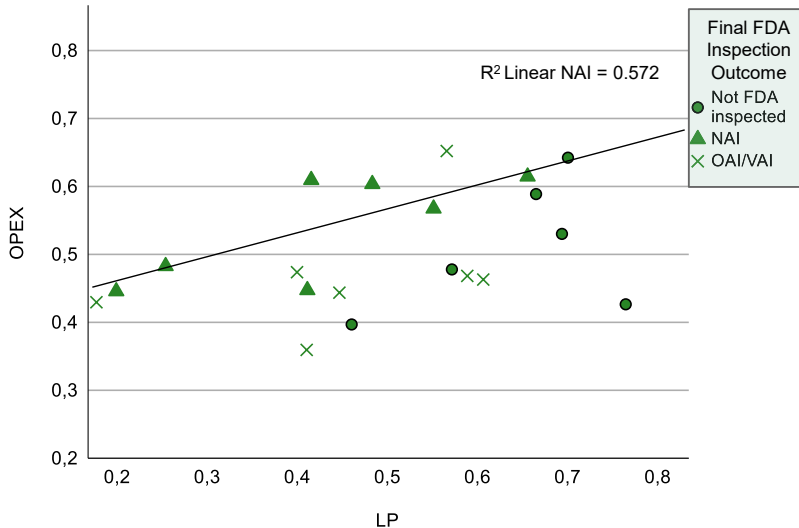


Figure 73: Regression Plot of LP and OPEX Scores – Grouped by FDA Inspection Outcomes

The linear regression analysis indicates a degree of determination $r^2 = 0.572$. Accordingly, it can be assumed that 57.2% of the variance in OPEX scores across pharmaceutical production sites performing best in FDA inspections can be explained by variance in aggregated LP scores reflecting overall performance of laboratory operations.

Key Observations Cluster H5 – Compliance Status, Enabler Implementation & Performance Levels across Manufacturing and Quality Control

Summarizing the analyses performed within hypothesis cluster H5, descriptive analyses have indicated higher combined maturity levels across manufacturing and quality control for sites scoring NAI in FDA inspections compared to production sites receiving unfavorable inspection outcomes or not inspected sites. Moreover, NAI sites have shown a much higher level of consistency in departmental enabler implementation levels. Analyzing the interplay of KPI scores and compliance, no clear pattern of higher combined performance and the inspection outcomes has been observed, even if NAI sites score slightly higher than the compliance category OAI/VAI. However, the group of sites received NAI as final inspection outcome shows a significant ($p < 0.05$) association of LP and OPEX performance with a high degree of determination ($r^2 = 0.572$), while positive but not significant correlations have been

uncovered for the other compliance categories. Thus, higher combined maturity across manufacturing and quality control and consistent performance across department can contribute to receiving favorable inspection results from authorities.

3.2.5 Outcomes

The combined St.Gallen benchmarking database allowed comprehensive quantitative research along the formulated testing framework and hypotheses clusters (cf. chapter 3.2.2). Results of the individual analyses have been previously presented and discussed in detail within chapter 3.2.4. In the following, outcomes and conclusions for all hypotheses are summarized.

Within hypotheses cluster H1, cross-departmental interdependencies of performance scores were researched based on the combined benchmarking sample. Table 68 summarizes the outcomes of all analyses, three of the four initially derived hypotheses are rejected.

Table 68: Result Summary – Hypotheses Cluster H1

H1	The effectiveness and efficiency in quality control is not related to the effectiveness and efficiency in manufacturing	Analyses Outcome
H1a	Lab Robustness in quality control is not related to Operational Stability in manufacturing	Accepted
H1b	Underlying metrics of Lab Robustness in quality control are not related to underlying metrics of Operational Stability in manufacturing	Rejected
H1c	Lab Performance in quality control is not related to OPEX Scores in manufacturing	Rejected
H1d	Underlying metrics of Lab Performance in quality control are not related to underlying metrics of OPEX Scores in manufacturing	Rejected

Confirming results of legacy research (cf. chapter 1.1.1), no association of Lab Robustness and Operational Stability has been found. In contrast to that, the aggregated benchmarking scores OPEX and LP have revealed a positive correlation at a significance level $p < 0.1$ and a degree of determination $r^2 = 16.4\%$. Furthermore, a significant association of process quality performance in laboratories with Just-in-Time performance of the plant has been observed and proves the importance of quality control for overall delivery and supply performance. Deep-diving in the underlying departmental metrics, analyses have led to twelve relevant combinations of cross-departmental measurements that are related across manufacturing and quality control.

Following the testing framework, hypotheses cluster H2 investigated dependencies of enabler implementation levels across manufacturing and quality control in detail. One of the three hypotheses stated prior to analyses is rejected. Aggregated outcomes are depicted in Table 69.

Table 69: Result Summary – Hypotheses Cluster H2

H2	The enabler implementation level in quality control is not related to the enabler implementation level in manufacturing	Analyses Outcome
H2a	The overall enabler implementation level in quality control is not related to the overall enabler implementation level in manufacturing	Accepted
H2b	The implementation level of individual enabler dimensions in quality control is not related to the implementation level of individual enabler dimensions in manufacturing	Accepted
H2c	The implementation level of underlying enabler categories in quality control is not related to the implementation level of underlying enabler categories in manufacturing	Rejected

No relation between aggregated overall enabler implementation levels across manufacturing and quality control has been observed. Furthermore, analyses of dimensional enabler implementations did not uncover any significant cross-departmental associations deemed insightful. Different to the departmental and dimensional levels, six relevant interdepartmental combinations of enabler categories have been identified and discussed in detail. Due to their association, these enabler categories can act as particular levers for cross-departmental alignment and capability transfer.

Hypotheses cluster H3 discussed the relation of cross-departmental maturity levels and the structural context of production sites. Table 70 presents the aggregated outcomes of analyses, one of the four hypotheses formulated is rejected.

Table 70: Result Summary – Hypotheses Cluster H3

H3	The enabler implementation level across quality control and manufacturing is not related to the structural context of pharmaceutical production sites	Analyses Outcome
H3a	The enabler implementation level across quality control and manufacturing is not related to the size of pharmaceutical production sites	Rejected
H3b	The enabler implementation level across quality control and manufacturing is not related to the geographical region of pharmaceutical production sites	Accepted
H3c	The enabler implementation level across quality control and manufacturing is not related to the production technology of pharmaceutical production sites	Accepted
H3d	The enabler implementation level across quality control and manufacturing is not related to the portfolio complexity of pharmaceutical production sites	Accepted

The size of pharmaceutical production sites has been found to be significantly associated with cross-departmental enabler implementation levels: Larger production sites show a higher maturity across manufacturing and quality control. Further analyses did not uncover any associations between enabler implementation

levels and the other structural factors geographical region, production technology, and portfolio complexity.

In a next step, hypotheses cluster H4 focused on the interplay of maturity and performance across manufacturing and quality control. According to the analyses' outcomes, one of the two formulated hypotheses is rejected. See Table 71 for a summary.

Table 71: Result Summary – Hypotheses Cluster H4

H4	The effectiveness and efficiency across quality control and manufacturing is not related to the enabler implementation level across quality control and manufacturing	Analyses Outcome
H4a	Combined OPEX performance in quality control and manufacturing is not related to the combined enabler implementation level across quality control and manufacturing	Accepted
H4b	The association of OPEX performance between quality control and manufacturing is not related to the combined enabler implementation level across quality control and manufacturing	Rejected

The benchmarking data has not indicated any relation of combined enabler implementation and combined KPI scores. However, segmenting the overall sample by maturity levels, the group of top half production sites in combined enabler implementation has shown a significant association of LP and OPEX performance with a high degree of determination. Differently, the lower half has not shown such pattern.

Lastly, hypotheses cluster H5 discussed the relations of cross-departmental maturity, performance levels, and compliance status. Table 72 summarizes the results, three of the four hypotheses are rejected based on the implications drawn from the combined benchmarking database and inspection record of the production sites.

Table 72: Result Summary – Hypotheses Cluster H5

H5	The enabler implementation and performance level across quality control and manufacturing is not related to the compliance status of pharmaceutical productions sites	Analyses Outcome
H5a	The combined enabler implementation level across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical productions sites	Rejected
H5b	The association of enabler implementation levels across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical productions sites	Rejected
H5c	The OPEX performance across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical productions sites	Accepted
H5d	The association of OPEX performance across quality control and manufacturing is not related to the regulatory surveillance status and inspection outcomes of pharmaceutical productions sites	Rejected

Descriptive analyses have uncovered higher cross-departmental maturity levels for production sites receiving favorable FDA inspection outcomes alongside with a much higher consistency in enabler implementation compared to other sites. Even if NAI sites score slightly higher in combined performance than the compliance category OAI/VAI, no clear pattern of compliance status and cross-departmental KPI scores has been observed. Unlike that, only the sites performing best in inspections show a significant association of KPI scores across manufacturing and quality control.

3.3 Analyses based on Global Quality Benchmarking Study

In addition to the St.Gallen OPEX manufacturing and QC lab benchmarking databases (cf. chapter 3.2), a third independent database is used for quantitative analyses of intra-site performance differences and alignment across manufacturing and quality control. This database has been established as an outcome of the project *Global Benchmarking: Baselineing Pharmaceutical Quality Management* performed in parallel to this dissertation striving to inform the research with industry data. Study aims and mode of operation have previously been summarized as part of the introductory data gathering strategy (cf. chapter 1.2.5). During the project, a short version *Quality Benchmarking Study* of the full title and a corresponding acronym QBS (Abbreviation Quality Benchmarking Study) have been established to avoid regular usage of the comprehensive project title and simplify everyday communication. Hence, the acronym QBS is also used to refer to the study in the following sections.

The database comprises recent performance metrics, maturity attributes, and contextual factors from 208 pharmaceutical production sites gathered during the year 2020. All data sets contain a selection of metrics from both departments manufacturing and quality control that allow to additionally research their interplay from another perspective. Due to the integrated nature of the program, the number of production site data sets across both departments exceeds the data availability from the St.Gallen benchmarking databases (cf. chapter 3.2.1). Consequently, the QBS database can supplement the analyses performed and enriches the quantitative research of this thesis. However, it needs to be noted that the scope of the study was limited to selected key metrics. Therefore, analytical options based on the QBS database are narrower and limited to the smaller subset of OPEX manufacturing and QC lab metrics collected.

In the following, quantitative investigation of intra-site performance differences and alignment between manufacturing and quality control is presented leveraging the power of the QBS database. Chapter 3.3.1 provides details of the conceptualization of the study assessment including reasoning to select the subset of metrics. Furthermore, the chapter outlines characteristics of the overall QBS sample. Hereafter, chapter 3.3.2 introduces the testing framework structuring all analyses based on the QBS database and derives hypotheses. In order to operationalize the hypotheses

tests, a set of additional indicators and newly aggregated scores is compiled and introduced in chapter 3.3.3. After that, chapter 3.3.4 outlines and discusses results of the quantitative analyses conducted. Finally, chapter 3.3.5 summarizes the outcomes and derives conclusions for all hypotheses formulated.

Parts of this chapter, especially in sections 3.3.1 and 3.3.4, have been previously published and are adapted from thesis-related articles the author wrote in parallel to this dissertation:

Ritz, M., & Friedli, T. (2020). A Global Initiative to Baseline Pharmaceutical Quality Management. St. Gallen Seeks OpEx Info from Industry. *PDA Letter*. <https://www.Pda.org/pda-letter-portal/home/full-article/st.-gallen-seeks-opex-info-from-industry>

Ritz, M., & Friedli, T. (2021). Conceptualizing a Streamlined Performance Assessment – The St.Gallen APQ Benchmarking Tool. *Pharmaceutical Engineering, ISPE iSpeak*. <https://ispe.org/pharmaceutical-engineering/ispeak/conceptualizing-streamlined-performance-assessment-stgallen-apq>

Seiss, M., Ritz, M., Russel, S., Bernasconi, M., & Friedli, T. (2021). *2020 Quality Benchmarking Study – A Global Initiative to Baseline Pharmaceutical Quality Management* (Unpublished FDA-internal research report). Dun&Bradstreet and University of St.Gallen.

3.3.1 Data Gathering & Sample Overview

QBS strived to gather operational data from hundreds of pharmaceutical production sites across the globe. That is why the University of St.Gallen partnered with D&B (Abbreviation Dun & Bradstreet) to jointly execute this project and bring together competencies of each partner: While the St.Gallen research team was responsible for conceptualizing a streamlined OPEX assessment model for the study, D&B with its global reach and local organizations in numerous countries was leading the execution and data gathering. QBS was made possible by funding of the U.S. FDA aiming to inform the further development of the Quality Metrics Initiative (cf. chapter 1.1.1) with insights from the collected benchmarking data. The project team intensified industry to participate in the study by offering a site-individual benchmarking report to all participants free of charge.

This project set-up fundamentally differed from the earlier explained St.Gallen OPEX manufacturing and QC lab benchmarking studies. Other than in the two programs, potential participants were approached proactively to participate in the study and fill the QBS questionnaire. Additionally, the team followed an ambitious overall project timeline requiring to limit the data gathering period to 5 month and faced the challenge to initially train D&B's country stewards, who were not familiar with researching OPEX in pharmaceutical production.

In consequence, there was a strong need to tremendously narrow down the scope, scale, and size of the QBS study compared to the full St.Gallen OPEX manufacturing & QC lab benchmarking programs. However, the St.Gallen team prioritized to ensure the assessment module is still able to measure overall OPEX performance in a balanced way and in accordance with the philosophy of system thinking (cf. chapter 2.1.1). These objectives led to a trade-off between conceptualizing an assessment that is (1) as shortened, streamlined, and user-friendly as possible and (2) still comprehensive enough to measure performance in a balanced way allowing reliable and insightful conclusions for both participating industry and researchers. In the following, the development of the QBS assessment is outlined.

Considering the theory of constraints as foundation of balanced performance management (cf. chapter 1.2.1) and recognizing trade-offs in manufacturing (cf. Skinner, 1969, p. 138 ff.) the four metric dimensions Maintenance, Quality, Delivery and People were defined to structure the QBS assessment in a first conceptual step. This selection is also in line with the established St.Gallen Operational Excellence Model (cf. chapter 2.1.1) and partly represents four key elements of the model: TPM, TQM, JIT, and EMS. Figure 74 visualizes the dimensional structure as well as the subsequent challenge to select and allocate specific metrics per dimension from the broad range of content available through the full benchmarking programs (cf. chapter 3.2.1).

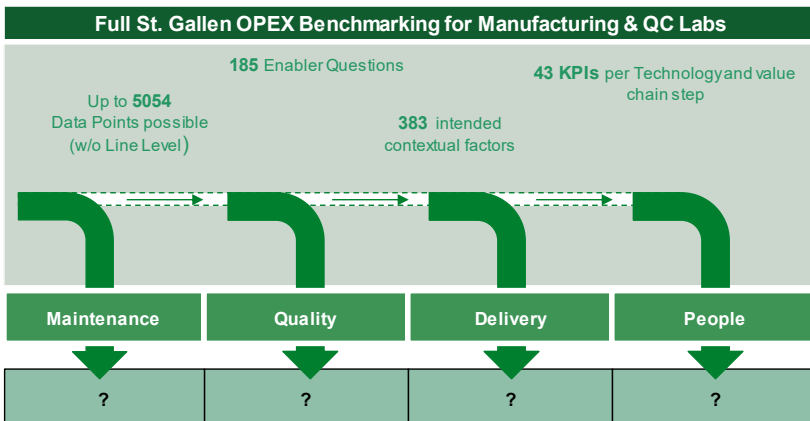


Figure 74: QBS Metrics Selection

In a next conceptual step, a pre-selection of potential metric candidates was derived based on the legacy research in the field of quality metrics published in the three comprehensive St.Gallen FDA Quality Metrics Research reports, cf. Friedli et al. (2017, 2019) and Friedli, Köhler, et al. (2018). Furthermore, experience from

supporting pharmaceutical companies⁹ in developing and enhancing their internal metrics systems over the last years was taken into account when selecting the candidates based on theoretical reasoning and academic expertise. Table 73 depicts the pre-selection of performance indicators derived.

Table 73: Qualitative Pre-Selection of QBS Metrics Candidates

Maintenance	Quality	Delivery	People
1. Unplanned Maintenance	1. Rejected Batches	1. Service Level – Delivery (OTIF)	1. Safety level
2. Maintenance Costs per Conversion Costs	2. Right First Time	2. Deviation Closure Time	2. Sick leave
3. Overall Equipment Effectiveness (OEE)	3. Recurring Deviation	3. Days on Hand (DOH)	3. Employee Fluctuation
4. Setup and Cleaning	4. Quality Costs per Conversion Costs	4. Priority orders	4. CAPA closed on-time
	5. QA Release Time	5. Number of Stockouts	5. Improvement suggestions
	6. IOOS rate (Lab)	6. Complaint Rate (Customer)	6. Qualification level
	7. Deviations per Batch	7. Adherence to standard lead time (Lab)	7. Functional integration
	8. Yield	8. Release time	8. Group work
	9. Scrap Rate	9. Complaint Rate (Supplier)	
		10. Service Level – Supplier	

All pre-selected metrics are well-known parts of the full St.Gallen benchmarking programs (cf. chapter 3.2.1). Hence, the already available data sets of pharmaceutical production sites gathered in the full St.Gallen benchmarking programs were further used to analyze the contribution of all pre-selected metrics to overall performance and determined the final metrics selection. With this in mind statistical exploration - especially correlation, regression analyses and t-tests – was applied to identify the subset of metrics surrogating overall performance best: Each metric candidate introduced in Table 73 was evaluated for its relation with and its contribution to the OPEX score as well as the strength of correlation and determination. Ensuring sufficient coverage of the four defined performance dimensions and considering co-correlation in between metrics candidates, a set of 13 metrics was selected to comprise the performance assessment of the QBS.

In a final step, comparison of an abbreviated overall performance score combining the chosen 13 measures only, and the comprehensive OPEX performance score used in the full benchmarking programs provided confidence for the selection. The newly derived QBS performance score aggregating the 13 identified metrics to be

⁹ The author consulted an Indian biopharmaceutical company, a German pharmaceutical CMO and a US pharmaceutical company in developing and enhancing their company-specific metric systems during his time as a Research Associate at the University of St.Gallen.

used in the QBS positively correlates with the OPEX benchmarking score calculated based on the St.Gallen benchmarking databases. Additionally, two different ways of aggregating the QBS score and corresponding calculations were evaluated during the validation procedure: Either calculating dimensional scores aggregating the individual metrics within Maintenance, Quality, Delivery and People first and then calculating the QBS performance score as average of the four dimensional scores or calculating the QBS performance score as equally weighted average of all 13 individual metrics disregarding their assignment to the four defined performance dimensions. The latter option led to higher correlation and determination of overall performance and was therefore specified as aggregation logic of the QBS performance score. A degree of determination $r^2 = 38.5\%$ provides confidence that the selected set of metrics is capable to meaningfully surrogate overall performance in pharmaceutical production as measured by the OPEX performance score in the full benchmarking programs.

The questionnaire used in the *Global Quality Benchmarking study* was completed with 18 enabler questions. Those have been derived in semi-structured remote workshops together with the U.S. Food and Drug Administration and are reflecting the three maturity categories Organization, Social/Employee, and Technical/Tools. All individual questions were informed by previous quality metrics research and the full St.Gallen benchmarking programs. However, following the objective to conceptualize an as streamlined assessment as possible, the operationalization of individual answer options was revisited and updated compared to the legacy questions. Special attention was paid on incorporating constructs to assess Quality Management Maturity in line with FDA's current priorities (FDA, 2020, p. 1 f.). Thus, in addition to measuring the current outcome performance, the QBS provides insights about the implementation level of practices associated with striving for continuously improving performance. Analogous to the full St.Gallen benchmarking programs, this powerful combination of assessment modules allows both industry and researchers to not solely quantify strength & weaknesses in outcome performance metrics but also to recognize patterns in relation to enabler implementation levels. Consequently, corresponding levers to increase OPEX maturity can be identified.

Lastly, a set of contextual factors completed the QBS questionnaire. Business nature, production type and production technology were questioned in the study alongside with information such as the production site size or geographical location. The purpose for adding this information was twofold: Contextual factors allow to set up well-suited peer groups of comparable productions sites to perform the benchmarking and to consider production site's specific characteristics when interpreting benchmarking results. Hence, incorporating the context ensures to meaningfully derive implications being mindful of the operating environment. Furthermore, there was a strong interest of research and the FDA as funding institution to utilize the QBS database to investigate and better understand differences in outcome metrics

performance, maturity and the individual relation across different production technologies and regions. That is why additional questions about specific dosage forms produced, detailed manufacturing activities performed and marketing/approval of products for the U.S. market were added to the contextual section of the assessment.

Figure 75 provides a summary of the QBS assessment content across the three major pillars outcome metrics, enabler, and contextual factors. Appendix A.5 includes a copy of the full QBS assessment questionnaire in the format used for data gathering. This comprises definitions of all metrics and maturity scale elements.

QBS Performance Score			
Maintenance	Quality	Delivery	People
1. Share of Unplanned Maintenance 2. Maintenance FTE / Total FTE	3. Rejected Batches 4. Recurring Deviations 5. Quality FTE / Total FTE 6. IOOS rate (Lab) 7. Deviation Closure Time	8. Service Level – Delivery (OTIF) 9. Service Level – Supplier (OTIF) 10. Customer Complaint Rate 11. Adherence to standard lead time (Lab)	12. Safety level 13. Sick leave
Enabler		Contextual factors	
Dedicated questions allow to access basic capabilities: - Organization Enablers - Social & Employee Enablers - Technical & Tool Enablers		Supplementing context addressing the profile: - Site Type [CMOs, Generics producer, Patented drugs producer] - Site Size [FTEs] - Production Technology Platforms [Chemical DS, Biological DS, Sterile DP, Non-sterile DP] - Production Technology Size [FTEs] - Inventory Days on Hand	

Figure 75: Overview Streamlined OPEX Assessment for QBS (Seiss et al., 2021, p. 12 ff.)

After having completed the study, the QBS database contains benchmarking data from 208 pharmaceutical production sites around the globe. These datasets are available for the research at hand. Apart from Africa, all continents are represented in the study with most production sites located in USA (North America), India & South Korea (Asia) and Germany (Europe). Figure 76 shows the proportion of production sites across the main regions of the world.

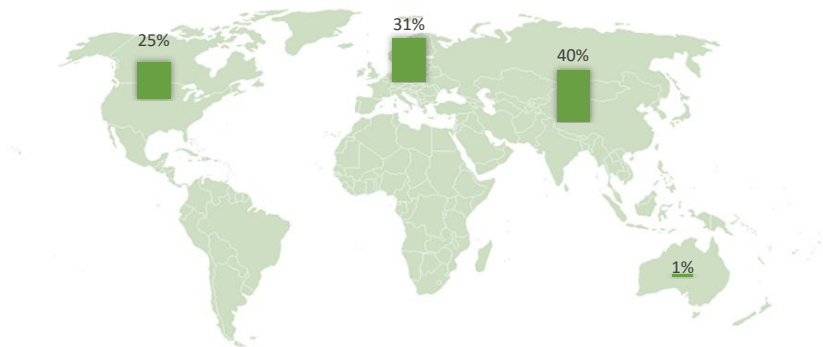


Figure 76: QBS – Sites per Region

All three major business natures of pharmaceutical production are represented in the QBS population: Branded-pharma production, manufacturing of generic products and CMOs (Abbreviation Contract Manufacturing Organization). Additionally, four main peer groups based on the type of pharmaceutical products processed on site are distinguished to ensure apple-to-apple comparisons: (1) Chemical Drug Substance / Small Molecules, (2) Biological Drug Substance / Large Molecules, (3) Sterile Drug Products and (4) Non-Sterile Drug Products. Multi-technology sites include operational data for more than one production technology. Similar to the broad geographical split discussed above, different sizes of production sites are covered in the database. Figure 77 provides the detailed sample set-up.

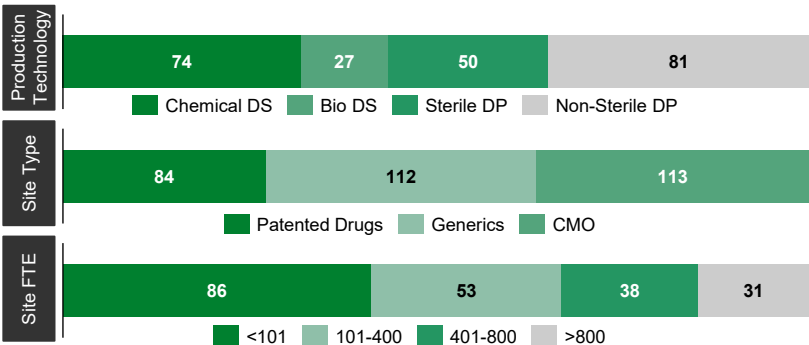


Figure 77: QBS - Sample Set-Up

3.3.2 Testing Framework & Hypotheses

Still striving to address SRQ 1 (cf. chapter 1.2.2) and uncover causes for cross-departmental performance differences alongside with drivers for alignment, a set of additional hypotheses tailored to analyze the QBS database is formulated. They serve as supplement to the five hypotheses clusters previously discussed based on the combined St.Gallen benchmarking database (cf. chapter 3.2) not aiming to replicate the studies. In that way, performance across manufacturing and quality control is researched once more based on a larger and independent sample of pharmaceutical production sites.

Due to the nature of the Global Benchmarking Study, subsequent analyses are limited to KPI scorings. Even if a maturity assessment was also build in the QBS concept (cf. chapter 3.2.1), enabler implementation levels are assessed in a combined manner including manufacturing and quality control for the entire production site. Thus, department specific maturity indicators that would allow for drawing conclusions on departmental and cross-departmental relations are not available.

Overall, three hypotheses are formulated and form the additional cluster H6. Figure 78 presents the positioning of the hypotheses in the QBS architecture and outlines the testing framework.

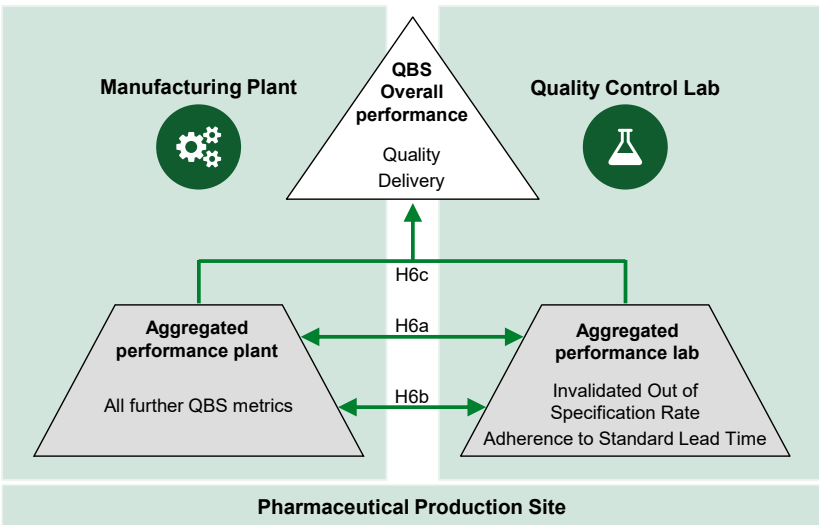


Figure 78: Additional Hypotheses QBS

Subsequently, the hypotheses H6a – H6c are depicted in Table 74. The cluster comprises testing the relation of aggregated departmental performance and evaluating underlying metrics for cross-departmental associations.

Table 74: Cluster H6 – QBS Laboratory & Plant Performance

H6	The performance in quality control laboratories is not related to the performance in manufacturing plants of pharmaceutical production sites
H6a	Aggregated lab performance is not related to aggregated plant performance
H6b	Underlying metrics of aggregated lab performance are not related to underlying metrics of aggregated plant performance
H6c	Coupled quality effectiveness across quality control and manufacturing is not related to overall cross-departmental performance

These hypotheses are tailored to be tested based on the QBS database. Following the iterative research approach (cf. chapter 1.2.4), content has been informed by findings of legacy research (cf. chapter 1.1.1) and the outcomes of the comprehensive analyses based on the combined St.Gallen benchmarking database (cf. chapter 3.2). That is why aggregated performance is approached as comprehensively as possible and comprises both effectiveness and efficiency. It reflects the entire set of QBS metrics per departments. Further explanations on how hypotheses are operationalized are included in the score definitions outlined in the subsequent chapter 3.3.3.

3.3.3 Score Development & Calculation

Similar to the approach outlined in the context of the combined St.Gallen benchmarking database (cf. chapter 3.2.3), absolute values in performance indicators of the QBS are transferred in relative performance scores. Percentile ranks calculated within the individual metric samples and peer groups determine the position of a site compared to other participants. The directional positive optimization direction of all metrics is considered during the normalization. Thus, higher values shown in the following have always to be understood as better performance in the respective metric or score. This general approach allows to compare across all natures of data points and different units.

Consequently, all indicators analyzed and displayed in chapter 3.3.4 refer to the percentile ranked, relative performance scores instead of the absolute measurements provided. A standardized scale from 0 (indicating lowest performance in the very indicator compared to the peer group) to 1 (indicating highest performance in the very indicator compared to the peer group) applies consistently across all data points and analyses. On this basis, a set of aggregated scores tailored to the research at hand is newly calculated to address the three hypotheses outlined in chapter 3.3.2. These scores complement and enrich the individual indicators and dimensional benchmarking scores directly available from the Global Quality Benchmarking (cf. chapter 3.3.1).

Subsequent passages introduce the newly aggregated QBS scores, their components, and underlying calculations. Each table details one aggregated score in a standardized manner: The first column names the score, all underlying components are listed in the second column, the third column provides the original measurement unit and the fourth column indicates whether higher or lower values on the original measurement scale are considered as higher performance in the aggregated score calculation. Definitions of all underlying QBS indicators are presented in appendix A.5. Names of some indicators are synonymously used in the St.Gallen benchmarking programs. In order to maintain transparency and simplify identifying the origin of data attributes across the entire thesis, all indicators of the QBS sample are marked with the index *QBS* in the analyses presented in the following.

All aggregated scores are calculated as equally weighted average of the percentile-ranked performance levels in the underlying metrics. Hence, scales range from 0 (indicating lowest aggregated performance across all underlying QBS metrics compared to the peer group) to 1 (indicating highest aggregated performance across all underlying QBS metrics compared to the peer group).

At first, aggregated departmental performance scores are calculated for manufacturing operations and quality control. Two of the thirteen QBS metrics explicitly address laboratories and therefore jointly form the QBS Lab Score according to Table 75. Consequently, the QBS Lab Score addresses both quality and service effectiveness. Ensuring to maintain this balance, a threshold is applied for calculation. QBS Lab scores are only compiled for production sites having provided both indicators.

Table 75: QBS Lab Score

Score	Indicator	Unit of measurement	Directional positive
QBS Lab	Invalidated Out Of Specification Rate _{QBS}	%	Down
	Adherence to Standard Lead Time Lab _{QBS}	%	Up

Similarly, the QBS plant score is calculated out of the remaining metrics with a clear focus on manufacturing operations. However, the separation of the overall indicator landscape in either manufacturing or quality control is not fully distinguishing. Lab performance might impact the performance in overarching metrics assigned to performance in manufacturing. That is why “QBS Plant” is a more precise label to classify the summarized indicators and will be used instead of “Manufacturing Performance Score” in the following analyses.

QBS Plant is an adaption of the total QBS score used in the benchmarking study reports for industry participants. It comprises the eleven metrics besides the two QC-exclusive measured stated above. Thus, the score represents all four performance dimensions Maintenance, Quality, Delivery, and People. Table 76 depicts all indicators. A 50% threshold is applied for the calculation of all QBS Plant scores:

Aggregated performance is only calculated for production site data sets containing at least six of the eleven indicators.

Table 76: QBS Plant Score

Score	Indicator	Unit of measurement	Directional positive
QBS Plant	Share of Unplanned Maintenance _{QBS}	%	Down
	Maintenance FTE/Total FTE _{QBS}	%	Down
	Share of Rejected Batches _{QBS}	%	Down
	Share of Reoccurring Deviations _{QBS}	%	Down
	Quality FTE/Total FTE _{QBS}	%	Down
	Deviation Closure Time _{QBS}	Days	Down
	Service Level - Delivery (OTIF) _{QBS}	%	Up
	Service Level - Supplier (OTIF) _{QBS}	%	Up
	Customer Complaint Rate _{QBS}	%	Down
	Safety Level _{QBS}	No	Down
	Sick Leave _{QBS}	%	Down

Following the operationalization of the hypotheses framework and targeting to allow for testing of cross-departmental interplay, the score QBS Coupled Quality Effectiveness is defined. It aggregates combined performance in Share of Rejected Batches_{QBS} and Invalidated out of Specification Rate_{QBS}. Hence, the score quantifies the QBS perspective on robustness in both manufacturing and quality control operations. The score is calculated according to Table 77 requiring availability of both metrics as a precondition.

Table 77: QBS Coupled Quality Effectiveness Score

Score	Indicator	Unit of measurement	Directional positive
QBS Coupled Quality Effectiveness	Share of Rejected Batches _{QBS}	%	Down
	Invalidated Out Of Specification Rate _{QBS}	%	Down

Furthermore, the score QBS Quality exclusive is newly derived. It is needed as counterpart to allow testing the just introduced Coupled Effectiveness score for association with broader performance scorings. Striving to avoid self-induced effects within the analyses, QBS Quality exclusive comprises all indicators of the dimension Quality, that are not reflected in QBS Coupled Effectiveness. As outlined in Table

78, three indicators quantifying both effectiveness and efficiency are considered. Due to the manifoldness of these indicators, a 100% threshold is applied and availability of all three indicators required. In that way, it is ensured not to bias aggregated scores by overemphasizing single underlying perspectives.

Table 78: QBS Quality Exclusive Score

Score	Indicator	Unit of measurement	Directional positive
QBS Quality exclusive	Share of Reoccurring Deviations _{QBS}	%	Down
	Quality FTE/Total FTE _{QBS}	%	Down
	Deviation Closure Time _{QBS}	Days	Down

Finally, the QBS Delivery Score summarizes scoring in the performance dimension Delivery according to the QBS set-up. It comprises four indicators as outlined in Table 79 and represents both manufacturing and QC lab operations. At least three of the four indicators need to be available per site to meet the threshold for score calculation.

Table 79: QBS Delivery Score

Score	Indicator	Unit of measurement	Directional positive
QBS Delivery	Service Level - Delivery (OTIF) _{QBS}	%	Up
	Service Level - Supplier (OTIF) _{QBS}	%	Up
	Customer Complaint Rate _{QBS}	%	Down
	Adherence to Standard Lead Time Lab _{QBS}	%	Up

All introduced scores are subsequently used to test the hypotheses according to the framework outlined in chapter 3.3.2: QBS Lab and QBS Plant operationalize the assumptions of hypothesis H6a. QBS Coupled Effectiveness, QBS Quality Exclusive, and QBS Delivery provide the basis to test hypothesis H6c. Researching hypothesis H6b does not require further aggregated scores, since it addresses the interplay of the underlying QBS indicators and can be tested with the study metrics.

3.3.4 Results & Discussion

Analyses of the QBS database are presented and discussed in the following. Results are outlined according to the testing framework defined and the three hypotheses stated in hypotheses cluster 6 in chapter 3.3.2. Definitions of all indicators are available in the Global Quality Benchmarking Study questionnaire, cf. appendix A.5. All aggregated scores used in the following, underlying components, and the calculation rules have been previously introduced in chapters 3.3.1 and 3.3.3.

According to the criteria explained in chapter 3.1 and appendix A.2, eligibility of all subsequently used indicators and aggregated scores for Pearson correlation analyses and linear regression has been tested beforehand. Shapiro-Wilk tests revealed significant results ($p < 0.05$) suggesting to reject the null hypothesis presuming normal distributions for a set of indicators as well as aggregated scores. Consequently, credibility of Pearson correlation coefficients cannot be ensured. That is why solely descriptive statistics to visualize distributions of variables and Spearman correlation analyses to test relations are applied in the following passages.

At first, the relation of aggregated departmental KPI scores is researched. For this purpose, a scatter plot of QBS Lab (comprising the two QC exclusive indicators) and QBS Plant (comprising all other QBS metrics) is generated. Figure 79 visualizes the distribution of both scores across establishments.

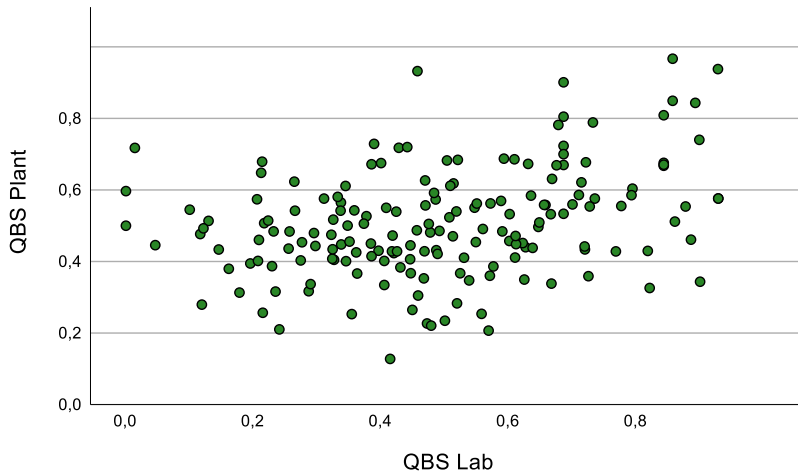


Figure 79: Scatter Plot of QBS Lab and QBS Plant

A slight positive relationship between both scores can be observed, but the visualization does not show a very clear pattern. That is why a Spearman correlation analysis is performed in addition to quantify the relation. Outcomes of the correlation analysis are summarized in Table 80.

Table 80: Spearman Correlation Analysis of QBS Lab and QBS Plant

		QBS Plant
QBS Lab	p	.314
	Sig	.000
	N	175

The correlation analysis reveals a degree of correlation $p = 0.314$ indicating a directional positive relation of both scores. Significance can be stated at a level $p < 0.01$ and allows to assume a positive association of aggregated performance in quality control and aggregated performance in the manufacturing plant based on the QBS sample. This observation triggers and motivates deeper analyses of the underlying metrics within both scores. For this purpose, follow-up analyses are conducted individually for both metrics that jointly comprise lab performance: Invalidated out of Specification Rate_{QBS} and Adherence to Standard Lead Time_{QBS} are separately evaluated for relation with further QBS metrics. Results are presented in the subsequent sections.

In the following, the relation of Invalidated out of Specification Rate_{QBS} and all QBS plant indicators in the dimensions Quality and Delivery is analyzed across the sample. Spearman correlation coefficients are depicted in Table 81.

Table 81: Spearman Correlation Analyses of iOOS Rate_{QBS} and further QBS Quality or Delivery Metrics

		Share of Rejected Batches QBS	Share of Recurring Deviations QBS	Quality FTE/ Total FTE QBS	Deviation Closure Time QBS	Service Level – Delivery (OTIF) _{QBS}	Service Level – Supplier (OTIF) _{QBS}	Customer Complaint Rate QBS
iOOS Rate QBS	p	-.117	-.012	.033	.091	.034	-.084	-.013
	Sig	.148	.886	.681	.260	.690	.333	.882
	N	155	153	157	156	144	135	128

Even the strongest positive correlation observed with Deviation Closure Time_{QBS} is not significant ($p > 0.1$) and not considered relevant. Overall, Invalidated out of Specification Rates_{QBS} do not show any significant correlations with further Quality or Delivery indicators. Hence, Invalidated out of Specification Rate_{QBS} is confirmed as crucial, direct value-adding indicator. Assessing iOOS rates as lab robustness indicator needs to be incorporated when evaluating overall effectiveness of a production site. It cannot be surrogated by any of the other effectiveness metrics selected for the QBS questionnaire.

Recognizing the importance of evaluating Invalidated out of Specification Rate_{QBS}, the metric is supplemented for a detailed analysis by Share of Rejected Batches_{QBS}, its counterpart from manufacturing. Aggregated in the QBS Coupled Quality Effectiveness Score, the combination of both metrics shall provide transparency about failure rates along the entire value chain and could therefore act as appropriate surrogate for the overall Quality and Delivery performances. To test this assumption, relations of the QBS Coupled Quality Effectiveness Score and dimensional Quality as well as Delivery performance are researched. For this purpose, both indicators Invalidated out of Specification Rate_{QBS} and Share of Rejected Batches_{QBS} are

excluded from the original Quality Dimension Performance Score and an adapted score QBS Quality exclusive is derived (cf. chapter 3.3.3). Thus, any self-induced effects leading back to metrics present in both aggregated scores are avoided. Table 82 provides the results of both Spearman correlation analyses.

Table 82: Spearman Correlation Analyses of QBS Coupled Quality Effectiveness, QBS Quality Exclusive, and QBS Delivery

		QBS Quality exclusive	QBS Delivery
QBS Coupled Quality Effectiveness	ρ	.205	.205
	Sig	.013	.012
	N	147	148

Based on the analyses, the QBS Coupled Quality Effectiveness Score is positively correlated with both scores QBS Quality exclusive and QBS Delivery. Correlations are significant at a level $p < 0.05$. Supplementing these findings, the individual distributions within both analyses are visualized to digest the relations. Figure 80 depicts a scatter plot of QBS Coupled Quality Effectiveness and QBS Quality exclusive first.

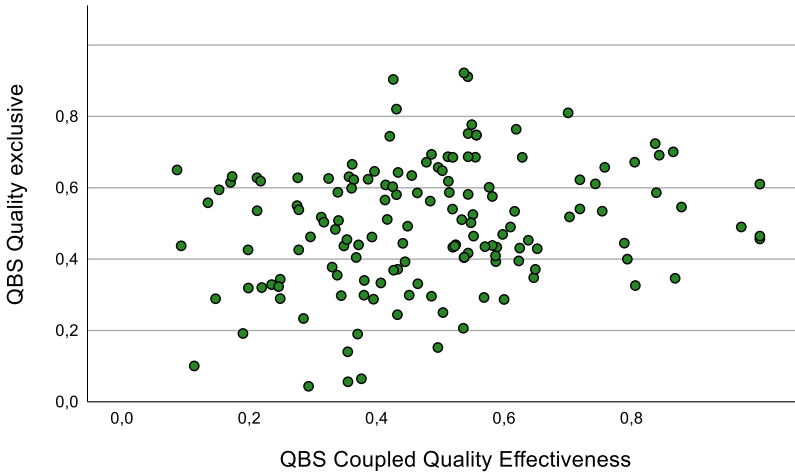


Figure 80: Scatter Plot of QBS Coupled Quality Effectiveness and QBS Quality Exclusive

The visualization confirms the tendency indicated by the correlation coefficient $\rho = 0.205$. Interpreting the graph and taking into consideration the significance level of correlation ($p < 0.05$), it can be stated that higher performance in QBS Quality

exclusive is associated with higher performance in QBS Coupled Quality Effectiveness.

Analogously, the distributions of QBS Coupled Quality Effectiveness and QBS Delivery are visualized. Figure 81 presents the corresponding scatter plot.

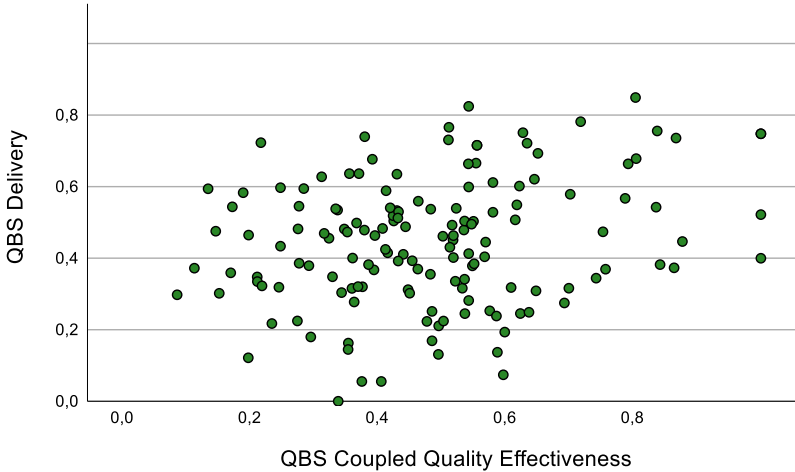


Figure 81: Scatter Plot of QBS Coupled Quality Effectiveness and QBS Delivery

The significant ($p < 0.05$) positive relation of QBS Coupled Quality Effectiveness and QBS Delivery outlined by the Spearman correlation coefficient $\rho = 0.205$ is visible in the scatter plot. Consequently, it can be assumed that higher performance in QBS Delivery is associated with higher performance in QBS Coupled Quality Effectiveness. Both analyses indicate that the coupled combination of Invalidated out of Specification Rate_{QBS} and Share of Rejected Batches_{QBS} aggregated in QBS Coupled Quality Effectiveness can be capable to surrogate additional parts of Overall Quality & Delivery Performance. Therefore, the combination is spotlighted as powerful and credible simplified score for overall effectiveness across manufacturing and quality control.

Whereas Invalidated out of Specification Rate_{QBS} does not solely correlate with any further Quality and Delivery Performance indicator, Adherence to Standard Lead Time Lab_{QBS} is identified to drive the directional positive relation between performance in QBS Lab and QBS plant scores, which has been uncovered at the beginning of the section. Consequently, Adherence to Standard Lead Time Lab_{QBS} is additionally evaluated for associations with all other QBS metrics in the dimensions Quality and Delivery. Results are summarized in Table 83 and significant correlations highlighted in bold.

Table 83: Spearman Correlation Analysis of ATL Lab_{QBS} and QBS Quality / Delivery Metrics

		Share of Rejected Batches _{QBS}	Share of Reoccurring Deviations _{QBS}	Quality FTE/ Total FTE _{QBS}	Deviation Closure Time _{QBS}	Service Level – Delivery (OTIF) _{QBS}	Service Level – Supplier (OTIF) _{QBS}	Customer Complaint Rate _{QBS}
ATL Lab _{QBS}	p	.218	.231	.168	.260	.342	.379	.134
	Sig	.005	.004	.031	.001	.000	.000	.127
	N	162	156	165	166	157	148	132

Share of Rejected Batches_{QBS}, Recurring Deviations_{QBS}, Deviation Closure Time_{QBS} and both Service Level scores show significant (levels $p < 0.05$ and $p < 0.01$) correlations with Adherence to Standard Lead Time Lab_{QBS}. All Spearman coefficients indicate directional positive relations.

Compared to the other indicators, a comparably strong relation of Adherence to Standard Lead Time Lab_{QBS} and the Service Level – Delivery (OTIF) scores is observed. Figure 82 depicts a scatter plot of Adherence to Standard Lead Time Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS} across the entire QBS sample, including all peer groups and regions.

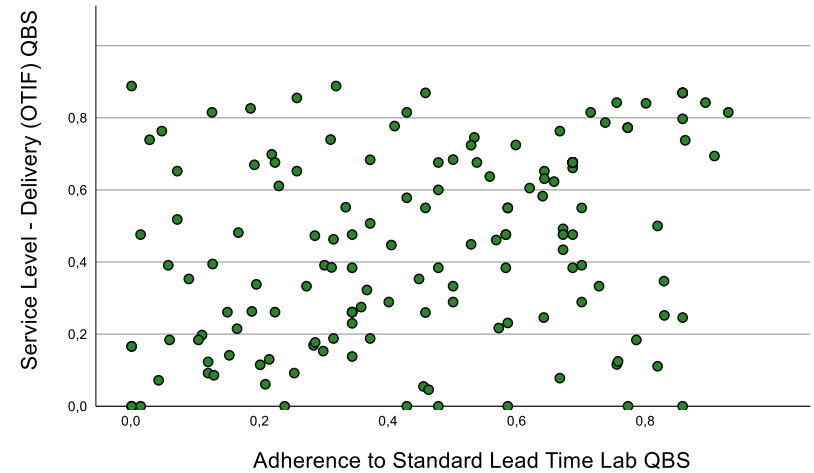


Figure 82: Scatter Plot of ATL Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS}

A positive relation of both variables can be observed in the chart. Highlighting again the significance of correlation ($p < 0.01$) and the comparable high degree of correlation $\rho = 0.324$, it can be assumed that higher performance in Adherence to

Standard Lead Time Lab_{QBS} is associated with higher performance in Service Level – Delivery (OTIF)_{QBS}.

Subsequently, the scope of the analysis is extended to breaking down different peer groups of the Global Quality Benchmarking compiled based on production technologies. Unlike the combined St.Gallen benchmarking databases (cf. chapter 3.2.1), the QBS sample is large enough to allow exclusive analyses of single indicators related to the individual production technologies. Table 84 summarizes the results of Spearman correlation analyses comprising Adherence to Standard Lead Time Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS} within all four peer groups: Small Molecules/Chemical DS, Large Molecules/Bio DS, Sterile DP, and Non-Sterile DP.

Table 84: Spearman Correlation Analyses of ATL Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS} – Grouped by Production Technology

		Service Level – Delivery (OTIF) QBS <i>All</i>	Service Level – Delivery (OTIF) QBS <i>Chemical DS</i>	Service Level – Delivery (OTIF) QBS <i>Bio DS</i>	Service Level – Delivery (OTIF) QBS <i>Sterile DP</i>	Service Level – Delivery (OTIF) QBS <i>Non-Sterile DP</i>
ATL Lab QBS <i>All</i>	ρ	.342				
	Sig	.000				
	N	157				
ATL Lab QBS <i>Chemical DS</i>	ρ		.646			
	Sig		.000			
	N		65			
ATL Lab QBS <i>BIO DS</i>	ρ			-.068		
	Sig			.788		
	N			18		
ATL Lab QBS <i>Sterile DP</i>	ρ				.354	
	Sig				.032	
	N				37	
ATL Lab QBS <i>Non-Sterile DP</i>	ρ					.353
	Sig					.003
	N					67

The previously identified overall association of Adherence to Standard Lead Time Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS} is not equally strong across all technologies and peer groups. While Small Molecules/Chemical DS, Sterile DP and Non-Sterile DP production sites show a significant ($p < 0.05$) positive relation, there is no correlation observable for Bio DS sites. However, it must be stated that the

sample size of Large Molecules/Bio DS production sites is rather small ($N=18$) compared to the other three peer groups. Hence, adhering to defined lead times in the lab seems to interdepend strongest with plant's delivery performance in the production environment of Small Molecules API sites.

Considering findings of legacy research and the outcomes of the analyses based on the combined St.Gallen benchmarking databases (cf. chapter 3.2.4), the observed association is deemed highly insightful. At first, On-time Delivery in Full can be seen as surrogate for PQS Effectiveness (cf. Friedli et al., 2017, p. 29). Additionally, the analysis revealed Adherence to Standard Lead Time Lab_{QBS} to contribute to Overall Delivery Performance of production sites. Hence, the association of quality control's performance and plant's Just-in-Time performance (cf. chapter 3.2.4) is confirmed again based on an independent benchmarking sample. Both implications can support industry in understanding laboratories as value-adding contributors to overall performance and efficiency in the value chain in addition to their traditional positioning as quality safeguards.

Key Observations Cluster H6 – QBS Laboratory & Plant Performance

Summarizing the research performed within hypotheses cluster H6 based on the QBS sample, a relation of performance scores in quality control laboratories and manufacturing plants has been uncovered. As previously indicated, the QBS data does not allow for Pearson correlation and regression analyses since normal distribution cannot be assumed for a set of variables. That is why observations are limited to correlations only and no statements on determination can be made. Aggregated QBS lab performance has been found to be positively correlated with aggregated plant performance at a significance level $p < 0.01$. The underlying two lab metrics revealed a diverse picture when analyzed in-depth.

Invalidated out of Specification Rate_{QBS} has not indicated any direct relation with all further QBS metrics assigned to the dimensions Quality and Delivery. This underlines its importance as much needed indicator for laboratories' robustness in the streamlined set of QBS metrics. Furthermore, a coupled analysis with Share of Rejected Batches_{QBS} uncovered the joint power of this cross-departmental combination to comprehensively assess Quality and Delivery performance of the entire site.

Differently, Adherence to Standard Lead Time Lab_{QBS} revealed a set of significant ($p < 0.05$) correlations with further QBS Quality and Delivery metrics. All associations are directional positive, while the strengths quantified by the degree of correlation varies across the different combinations of KPIs. In particular, the association of Adherence to Standard Lead Time Lab_{QBS} and Service Level – Delivery (OTIF)_{QBS} confirms that laboratories should be recognized and optimized as contributor to the value chain leveraging efficiency potentials in addition to ensure product quality. Based on the QBS data, this relation holds especially true for Small Molecules API production sites.

3.3.5 Outcomes

Complementing the outcomes of the analyses performed based on the combined St.Gallen benchmarking databases (cf. chapter 3.2), the QBS database was used to enrich the quantitative research in this thesis exploiting a much larger independent sample. However, since only two of the QBS metrics address performance in quality control, options for cross-departmental investigation of dependencies were limited to these metrics and the aggregated scores they are contributing to (cf. chapter 3.3.3). Detailed results of the QBS analyses have been presented and discussed in chapter 3.3.4. In the following, outcomes are summarized and conclusions for the hypotheses drawn based on the Spearman correlations observed in the analyses.

Different to the previously researched clusters (cf. chapters 3.2.2 and 3.2.5), hypotheses cluster H6 has been tailored to the available QBS database. It strived to broadly analyze the relation of manufacturing plants and quality control labs in the study. Consequences for the hypotheses are summarized and depicted in Table 85. Results lead to rejection of all three hypotheses.

Table 85: Result Summary – Hypotheses Cluster H6

H6	The performance in quality control laboratories is not related to the performance in manufacturing plants of pharmaceutical production sites	Analyses Outcome
H6a	Aggregated lab performance is not related to aggregated plant performance	Rejected
H6b	Underlying metrics of aggregated lab performance are not related to underlying metrics of aggregated plant performance	Rejected
H6c	Coupled quality effectiveness across quality control and manufacturing is not related to overall cross-departmental performance	Rejected

A significant ($p < 0.01$) positive correlation of QBS Lab and QBS Plant scores has indicated a relation of aggregated performance in quality control labs and aggregated performance in manufacturing plants. Analyzing the underlying metrics for cross-departmental associations, a set of significant ($p < 0.05$) correlations has demonstrated associations of the individual metrics. In particular, a higher adherence to standard lead times in laboratories corresponds with higher performance in Quality and Delivery metrics assigned to the manufacturing plant. Uncovering the power of combined analyses, aggregating Invalidated out of Specification Rate_{QBS} and Share of Rejected Batches_{QBS} in the score QBS Coupled Effectiveness has revealed a simplified indicator associated with overall cross-departmental Quality and Delivery performance.

3.4 Implications for OPEX Management

Chapter 3 targeted to quantitatively analyze the interplay of manufacturing and quality control in pharmaceutical production. Following-up on initial observations that motivated the overall research at hand (cf. chapter 1.1.1), testing frameworks were developed and six clusters of hypotheses derived. Afterwards, the combined St.Gallen benchmarking database (cf. chapter 3.2) and the sample available from the Global Quality Benchmarking Study (cf. chapter 3.3) allowed for comprehensive analyses that resulted in data-backed conclusions on the hypotheses.

Consolidated outcomes of the quantitative research contribute to the MRQ of the thesis and answer in particular SRQ 1 – *What are causes for performance differences and drivers for alignment across manufacturing and quality control?* Comprehensive analyses, a detailed review, and discussion of all patterns observed lead to below summarized implications for OPEX management across manufacturing and quality control. All implications are derived based on the intermediate summaries given after analyzing each hypothesis cluster (cf. chapters 3.2.4 and 3.3.4) and the consolidated outcomes (cf. chapters 3.2.5 and 3.3.5). See the corresponding chapters for details.

Patterns in KPIs across manufacturing and quality control have been examined. Besides addressing both effectiveness and efficiency, a comprehensive evaluation of all underlying benchmarking indicators revealed insights for performance management and KPI strategies. OPEX management should:

- ✓ Consider efficiency to evaluate cross-departmental performance of production sites comprehensively since only evaluating robustness and stability does not uncover all performance determinators and their associations along the value chain.
- ✓ Understand process quality in laboratories as a crucial contributor to Delivery and Just-in-Time performance of the entire production site.
- ✓ Pay special attention to the plant's Customer Complaint Rate, Raw Material Turns, WIP Turns, Finished Good Turns, and OTIF as anomalies in these metrics can also uncover issues in quality control quantifiable through Lab Deviations, Analytical RFT, iOOS Rates, Investigation Rates, Lead Times, Adherence to Lead Time, and Adherence to Schedule.
- ✓ Be mindful that Deviations/Batch, Deviation Closure Time, Share of Rejected Batches, and OTIF in manufacturing might also impact quality control's performance due to increased workload for Product Re-Test Due to Complaints or Investigations and therefore diminish lab efficiency in Batches processed/FTE or Cost/Test.
- ✓ Use Invalidated out of Specification Rate and the Share of Rejected Batches as simplified cross-departmental metric combination to measure effectiveness.

Furthermore, associations of maturity levels across manufacturing and quality control have been analyzed in an aggregated manner for the entire departments, separately for all maturity dimensions and individually for enabler categories. OPEX management should:

- ✓ Not solely rely on aggregated departmental results of maturity assessments but focus on evaluating maturity gaps across manufacturing and quality control in individual enabler categories to uncover the most powerful improvement levers.
- ✓ Avoid overemphasizing the importance of single enabler dimensions like Maintenance or Quality assuming these would particularly drive alignment across manufacturing and quality control to achieve higher combined maturity.
- ✓ Especially assess maturity of the plants concerning Housekeeping, Process Management, Cross-functional Product Development, and Direction Setting as leveraging improvements in these categories can pay off in higher cross-departmental maturity and additionally drive improvements in quality control.
- ✓ Prioritize the levers Housekeeping, Technology Assessment & Usage, Layout Optimization, and Employee Involvement in quality control associated with higher maturity in the manufacturing plant.

Additionally, the role of the individual structural context of pharmaceutical production sites has been investigated in relation to cross-departmental OPEX maturity across manufacturing plants and quality control laboratories. OPEX management should:

- ✓ Review present cross-departmental maturity at larger sites of the network first, hereby identify successful practices to enable excellence across departments and transfer these practices to the smaller production sites of the company.
- ✓ Select the larger production sites of the companies' network as frontrunners to pilot and roll out a comprehensive cross-departmental approach to OPEX, in case no initiative for alignment of manufacturing and quality control has been started yet.
- ✓ Prioritize DS production sites for allocating resources and spending efforts to align maturity levels in manufacturing and quality control.
- ✓ Disregard the geographical region and the portfolio complexity of production sites when setting-up cross-departmental OPEX initiatives.

Moreover, reviewing the interplay of combined cross-departmental maturity and combined cross-departmental KPI scores has indicated that both pillars are still important to drive overall excellence. OPEX management should:

- ✓ Value the equal importance of maturity and outcome performance by considering measures and targets for both fields in cross-departmental OPEX initiatives

since there is no direct association that would allow to surrogate one pillar through the other.

- ✓ Tailor and adapt the strategy for performance alignment across manufacturing and quality control depending on the cross-departmental maturity level on site.

Finally, the relation of maturity and KPI scores across manufacturing and quality control with the compliance level of production sites has been researched. Analyses showed differences in maturity and performance of sites receiving favorable inspection outcomes compared to others. OPEX management should:

- ✓ Recognize regulatory surveillance as external driver for maturity of production sites and take inspections as opportunities for improvements, which not regulated sites are lacking.
- ✓ Understand that compliance evaluations do not reward outstanding performance beyond required levels in single areas but react on all observations below the expected standard across all departments.
- ✓ Foster higher combined maturity in manufacturing and quality control to prevent non-favorable inspection outcomes and compliance issues.
- ✓ Prioritize consistency in KPI scores across manufacturing and quality control to increase the probability of mastering inspections without actions indicated by the regulator.

4 Approaches for Cross-departmental Collaboration & Optimization

Chapter 4 informs the research project with a systematic analysis of academic literature. As an initial literature research on OPEX across manufacturing and quality control (cf. chapter 2.2) did not lead to relevant inputs for the particular research problem, the following chapter extends the scope to take knowledge from broader subject fields and to apply it to the specific case researched in this thesis. Thus, concepts and approaches for cross-departmental management within production sites are studied not limited to Operational Excellence nor to the pharmaceutical industry in a first step. Afterwards, applicability is assessed and implications for integrated OPEX management across pharmaceutical manufacturing and quality control are derived.

The desk research especially addresses SRQ 2 (cf. chapter 1.2.2) and phase 2 *Recommendation* (cf. chapter 1.2.4) of the research approach. It informs both subsequent phases 3 and 4 in an iterative manner and directly contributes to answering the main research question of this thesis by bringing in an outside-industry perspective. In order to complement the practice-driven research phases 1 & 3, which both build on empiricism from industry as outlined in the data gathering strategy (cf. chapter 1.2.5), the literature review focuses on scholarly, peer-reviewed journals to incorporate an academic perspective.

In chapter 4.1 the chosen approach to systematic literature search and review is introduced in detail. Subsequently, chapter 4.2 presents the criteria chosen and outcomes of the structured literature search. Afterwards, relevant literature is reviewed and discussed in detail within chapters 4.3 and 4.4. Finally, chapter 4.5 summarizes the implications for OPEX management.

4.1 Methods

Conducting literature review is a key tool of management research (Tranfield et al., 2003, p. 208) and therefore forms a crucial component of the present thesis' research approach. It allows to obtain empirical evidence to answer a research question by using explicit methods (Snyder, 2019, p. 334 f.) and is consequently selected to contribute to SRQ 2. Following chapters introduce both approaches to systematic literature search (cf. chapter 4.1.1) and effective literature review (cf. chapter 4.1.2) applied for the present desk research.

4.1.1 Systematic Literature Search

The literature search follows a newly conceptualized systematic multi-step approach adapted from David and Han (2004, p. 42 ff.) and Newbert (2007, p. 125) to identify,

critically appraise and select literature for the subsequent in-depth review. It contains 8 main steps and is outlined in Figure 83.

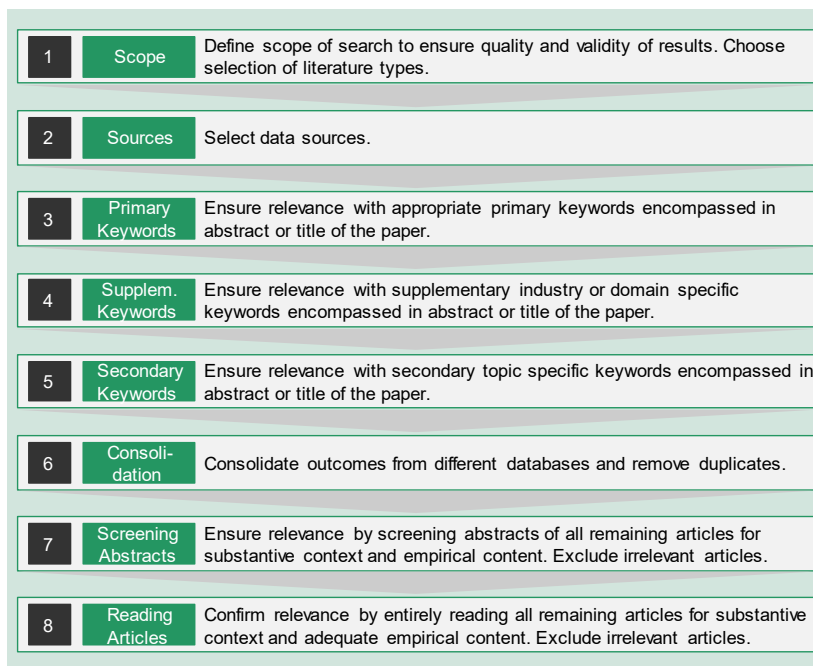


Figure 83: *Systematic Literature Search Approach – Adapted from David and Han (2004, p. 42 ff.) and Newbert (2007, p. 125)*

In accordance with Vom Brocke et al. (2009, p. 2216) as well as Webster and Watson (2002, p. 16) both backward and forward searches are performed in addition for all relevant articles revealed by the structured search process described above. Backward search describes reviewing the citations of articles and thereby identifying additional relevant papers. Complementary, forward search comprises a particular search of additional, latterly published articles citing those articles deemed relevant. Complementing the literature search with these two procedures ensures not to miss additional articles relevant for the research problem, but not meeting the criteria defined in the systematic search approach for any reason.

4.1.2 Effective Literature Review

Levy and Ellis (2006, p. 182 ff.) describe a systematic process for effective literature review. Even if especially developed for information system research, the authors underpin its general applicability to any field of social and behavioral science. Thus,

it is used in this thesis and adapted to the particular desk research conducted in the following.

The process contains three stages and six major steps within its main stage *Processing*. It is visualized in Figure 84. In the following, stage 2 *Processing* and the underlying steps are introduced in detail.

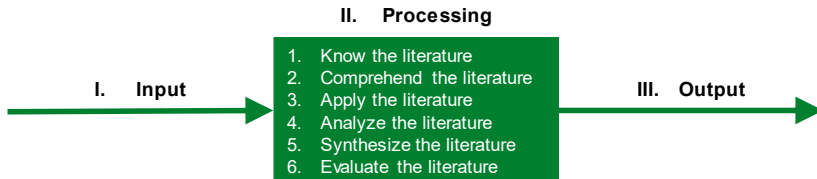


Figure 84: *Processing Literature* – Adapted from Levy and Ellis (2006, p. 182)

The first step *Know the literature* comprises listing, defining, describing, and identifying literature. Mastering the material and proving knowledge of the literature is demonstrated by extracting meaningful information from literature instead of solely reporting it. (Levy & Ellis, 2006, p. 193)

Comprehend the literature is defined as summarizing, differentiating, interpreting, and contrasting. In addition to repeating what was included in the article, this step includes to be aware of the meaning, importance and significance of the information. (Levy & Ellis, 2006, p. 193 f.)

Afterwards, *Apply the literature* identifies the major concepts of studies and assigns different articles accordingly. Thus, illustrating, relating, and classifying literature are typical activities in this step. (Levy & Ellis, 2006, p. 199)

In the fourth step *Analyze the literature* the researcher demonstrates ability to compare, connect, separate, and explain different contributions. The reader is provided with information on why recognizing patterns or relationships across articles would be valuable. (Levy & Ellis, 2006, p. 199)

Synthesize the literature means rearranging, modifying, integrating, or generalizing different literature inputs. Thus, this step targets to assemble the entire literature into a whole exceeding the sum of its parts. (Levy & Ellis, 2006, p. 200) Reinforcing the importance of this step, Levy and Ellis are perfectly aligned with the TOC as one of the theoretical lenses used for the research at hand (cf. chapter 1.2.1).

Finally, *Evaluate the literature* entails to support, select, judge, and conclude the articles. It comprises to distinguish opinions, theories, and established facts. (Levy & Ellis, 2006, p. 200)

In the following, Levy and Ellis' approach to effectively process literature is applied to the present desk research. The six underlying steps are considered in an integrated manner. They provide guidance how to review and discuss the literature in

detail within chapters 4.3 and 4.4. Stage 1 *Input* is reflected by the approach to systematically search literature (cf. chapter 4.2), while implications for OPEX management derived in chapter 4.5 serve as third stage *Output*.

4.2 Search Procedure & Outcomes

The structured literature search approach outlined in chapter 4.1.1 is applied to the present research problem. Following search aims to identify relevant literature, to provide the knowledge base to answer SRQ 2 (cf. chapter 1.2.2), and to inform the research with suitable strategies, tools, or approaches for cross-departmental alignment, collaboration, and optimization.

Subsequent passages document the selected criteria and outcomes of the structured literature search¹⁰, see chapter 4.3 for an in-depth review and the content-wise discussion of relevant articles. Primary and secondary keywords are selected to broaden the research scope from narrowly investigating Operational Excellence across manufacturing and quality control within pharmaceutical production (cf. chapter 2.2) to identifying suitable strategies for cross-departmental alignment and optimization. Supplementary keywords ensure to limit the scope to the sector of producing industries.

1. Define scope of search to ensure quality and validity of results. Choose selection of literature types:

Only scholarly, peer-reviewed journals are considered. Publication year is limited to all articles published in 2000 and afterwards. The language is pre-determined to English or German.

2. Select data sources:

Due to easy access via the university's infrastructure and the broad range of represented journals the databases EBSCOhost (Business Source Ultimate) and ProQuest are selected. Only full-text accessible articles are considered.

3. Ensure relevance with appropriate primary keywords encompassed in abstract or title of the paper:

"alignment" OR "coordination" OR "collaboration" OR "linkage" OR "transfer" OR "interdependence" OR "optimization"

¹⁰ The structured literature search was initially conducted in December 2020 and repeated in March 2021 to ensure coverage of all relevant and recent literature.

4. Ensure relevance with supplementary industry or domain specific keyword encompassed in abstract or title of the paper:

“manufactur” OR “producti*”*¹¹

5. Ensure relevance with secondary topic specific keywords encompassed in abstract or title of the paper:

(“capabilit” OR “knowledge”) AND (“interdepartmental” OR “cross-departmental” OR “across departments” OR “intra-organizational”)*

6. Consolidate outcomes from different databases and remove duplicates:

The described search led to four duplicates that have been removed.

7. Ensure relevance by screening abstracts of all remaining articles for substantive context and empirical content. Exclude irrelevant articles:

Conducting the systematic literature search described above led to 89 hits in total across the two databases. After screening all abstracts, 25 articles are taken into account for the final steps.

8. Confirm relevance by entirely reading all remaining articles for substantive context and adequate empirical content. Exclude irrelevant articles:

*After reading the full text 14 articles are finally deemed relevant.*¹²

While reviewing and discussing the relevant articles, their references were inspected and additional back- and forward search conducted as appropriate. This process led to an in-depth review of 19 additional articles, out of which 2 articles are finally considered in the subsequent discussion.

4.3 Review & Discussion

In the following, the relevant literature identified through the structured search outlined in chapter 4.2 is reviewed in detail. As introduced in chapter 4.1.2, the review

¹¹ Chapter 4 aims to identify approaches for cross-departmental collaboration not limited to the overarching thesis focus on manufacturing and quality control. Thus, different to chapter 2.2, the literature search is not limited to these two departments. However, “manufactur*” OR “producti*” are chosen as supplementary keywords to ensure focus on the manufacturing sector and exclude other industries such as finance or information technology.

¹² Steps 7 and 8 are performed with a strong focus on expected contributions to the overarching research problem of this thesis. Hence, the author rigorously excludes articles presenting content and outcomes not applicable to pharmaceutical manufacturing and quality control even if these articles match the defined search criteria. The same holds true for the review of all additional articles identified in the back- and forward search.

combines knowing, comprehending, applying, analyzing, synthesizing, and evaluating the literature in accordance with Levy and Ellis (2006, p. 182 ff.). The first steps are reflected in subsequent passages of chapter 4.3 and conducted in an integrated manner per article, while chapter 4.4 presents the latter.

The entire review and discussion are carried out with the aim to enrich the research at hand with academic and theory-driven input. That is why the three research theories of this thesis (cf. chapter 1.2.1) act as overarching basis and provide the theoretical lenses during the review process. Following paradigms guide the researcher through the review process and provide areas to pay special attention on:

1. TOC: Constraints determine overall performance rather than the highest performing part of a system. Every system has at least one constraint that is an opportunity for improvement. (Goldratt, 1990; Rahman, 1998)
2. CT: Effective organizational designs fit the contingencies of an organization including the environment, size, strategy, and any further variables moderating impact of characteristic on performance. (Donaldson, 2001, 2006)
3. TDC: Organizations need to dynamically build, renew, and deploy internal capabilities to respond to challenges. Capabilities are understood as management's ability to provide and reconfigure resources, skills, and competencies. (Teece et al., 1997; Teece & Pisano, 1994)

It was initially intended to limit the scope of the review to interdepartmental collaborations within the same organization and the secondary keywords were chosen accordingly. However, the search revealed also insightful outcomes in the context of interorganizational collaboration. That is why findings on interorganizational collaboration that are relevant for and adaptable to the present research problem OPEX across manufacturing and quality control are considered in addition. Subsequent chapters are structured accordingly: Articles assigned to the field of interorganizational collaboration are reviewed and discussed in chapter 4.3.1. Afterwards, chapter 4.3.2 summarizes outcomes in the context of interdepartmental collaboration. Both chapters discuss findings article per article and provide a recap of the presented research first, before highlighting take-aways contributing to answer SRQ 2 of this thesis.

4.3.1 Interorganizational Collaboration

Buckley and Carter (2003) examined knowledge sharing processes within multinational firms. For that purpose, five propositions on specializing in knowledge activities, knowledge frontiers, knowledge architectures, configuration of new knowledge and knowledge governance were derived based on literature and researched across four case companies. Overall, the study found mechanisms for knowledge sharing to be diverse across companies and suggests combining the

application and discovery of knowledge. The application strategy intends to use and share a given portfolio of knowledge, while the discovery strategy aims at generating new combinations of knowledge. (Buckley & Carter, 2003, p. 7 ff.)

Specialization within companies is often associated with internal knowledge frontiers occurring and functional or divisional boundaries. Knowledge management between areas requires supervision and mechanism must allow senior managers to direct firm's activities. Therefore, knowledge governance structures should take into account the boundaries between knowledge holders, active coordination of knowledge across frontiers and incentivize individuals to share knowledge. The authors identify a trade-off between breadth and depth of knowledge governance by managers leading to a combined architecture of integration and separation of knowledge across areas. Furthermore, the importance of not only applying transferred knowledge but also actively discovering capabilities through combining transferred knowledge in new mixtures is highlighted. In that way, achievements and success can be sustained in the long term. Complex IT-systems for knowledge sharing and storing are not solely sufficient to address challenges of the knowledge architecture. An impactful roll-out requires integration with appropriate incentives. (Buckley & Carter, 2003, p. 12 ff.)

Fredriksson et al. (2019) discussed inter-organizational transfer capabilities in the context of aircraft production. The authors combined an extensive literature review with studying three technology transfer cases of the company Saab in detail. A conceptual framework for inter-organizational transfer capability was conceptualized based on theory and guided the case study research along following components: Sender, receiver, transferability of the process, appropriateness of the process, and performance of the transfer. Transferability and appropriateness assess how easily the process can be transferred and if it fits well with the new context, while performance of the transfer evaluates time and cost to fulfill the transfer alongside with the resulting increase in capabilities. (Fredriksson et al., 2019, p. 151 ff.)

The study suggests performing a structured gap assessment before starting the transfer process. In addition to the appropriateness and transferability of the process, the assessment includes analyzing disseminative capacity of the sender and absorptive capacity of the receiver. Successful transfers, evaluated by transfer cost and time vs. resulting capability growth, bridge gaps on three different levels: organizational, individual, and on the job training. Detailed from an organizational to an individual level, the disseminative capacity comprises framing, disentangling, transferring, and teaching, while the absorptive capacity is detailed as recognizing, absorbing, learning, and using. In contrast to other studies and the majority of literature, which both heavily focus on the absorptive capacity, a gap in disseminative capacity is recognized in the present cases. (Fredriksson et al., 2019, p. 161 ff.)

Gonzalez et al. (2014) researched knowledge flows and conceptualized a model to manage knowledge across a multinational company by introducing a dedicated central department. The research built on a single case study with a firm in the service industry, which was facing challenges to sustain improvements in its entities. The study was looking for ways to support creation, retention, and distribution of knowledge. Finally, it shall enhance the organization's processes and improve operational performance. (Gonzalez et al., 2014, p. 611 f.)

The model follows a defined network structure, which is detailed in the organizational aspects formalization, centralization, and integration of knowledge. In this context, network should be understood as an organization that is formally recognized for its expertise in the particular field. This network is introduced by ramping-up a center of excellence in between the individual entities. While the creation & acquisition of knowledge stays part of the entities' responsibilities, the center of excellence leads the storage & retention and the distribution phases of the overarching knowledge management process. Due to the manifoldness of entities, the center of excellence is subdivided into multiple segments that each serve one cluster of entities. In the individual clusters, knowledge flows are not limited to exchanges between entities and the center of excellence segment but also encourage entities to directly interact with each other. The center of excellence facilitates storage and distribution of knowledge by fulfilling following task: Document knowledge acquired by entities, maintain a knowledge database, support with technicians & experts to provide training, and implement improvement projects. In the context of the present case study, the above-described network encourages teamwork and expends knowledge flows between individual units by still offering autonomy to the entities. Thus, the entities and its individuals are systematically empowered to solve problems based on the central knowledge disseminated but provide back their learnings and feed the center of excellence at the same time. (Gonzalez et al., 2014, p. 620 ff.)

Kalling (2003) researched the firm-internal knowledge transfer program of a multinational manufacturing company with special attention on the role of motivation across the different plants. The in-depth analysis of the single case study revealed that motivation is a crucial prerequisite for successful knowledge transfer but not naturally given. Hence, not all organizational units were always interested in knowledge transfer and it should not be presumed that knowledge was always equally well received and adapted. Instead, knowledge was identified to be contextual and motivation for knowledge transfer needs to be actively managed through corporate management control routines and the organizational structure. (Kalling, 2003, p. 115)

In the context of the case, the company's success of knowledge transfer across plants is especially determined by six factors: Local perceptions, aspiration & strategic ambitions, the view on internal competition, the view on the nature of

knowledge, program management & control, and local communication. Consequently, corporate knowledge transfer initiatives need to consider these factors in addition to cognitive aspects such as causal ambiguity or absorptive and retentive capabilities. Thereby, motivation is crucial to trigger the conversion of tacit in explicit knowledge as part of the learning process. The successful plants actively manage and enforce motivation for knowledge transfer by setting targets and offering incentives. Progress is closely monitored and activity stimulated accordingly. (Kalling, 2003, p. 199 ff.)

However, the way motivation is managed needs to be adopted to the individual context and make sure there is motivation among sources and recipients of knowledge. Content and mode of presenting knowledge must suit the transfer situation. Benchmarking programs including improvement methods, output result comparison and corresponding recognition can be one way to stimulate motivation. (Kalling, 2003, p. 124 f.)

McEvily and Marcus (2005) explored the acquisition of competitive capabilities through embedding ties in interorganizational networks and alliances. In particular, the interplay of job-shop manufacturers and suppliers to acquire capabilities was researched using a survey study and a set of case studies. The authors stated trust and information sharing as already proven informant factors to transfer capabilities between organizations and embedded ties for success. Additionally, the impact of joint problem solving formed the primarily research interest of the paper. Two hypotheses directly addressed the relation of joint problem solving and acquisition of competitive capabilities between manufacturers, suppliers, and customers. Additional four hypothesis tested whether joint problem solving mediates the relation between trust, information sharing, and the acquisition of competitive capabilities. (McEvily & Marcus, 2005, p. 1033 ff.)

Structural equation modelling indicates that joint problem solving with suppliers is positively correlated with the acquisition of capabilities, while no relation can be shown for customers. Furthermore, joint problem solving positively moderates trust and information sharing. Overall, the study concludes that embedding interorganizational ties is important for acquiring and transferring knowledge. In addition to the established mechanisms trust and information sharing, joint problem solving is proven as an important driver. (McEvily & Marcus, 2005, p. 1048 ff.)

Schotter and Bontis (2009) examined knowledge transfer to build new capabilities in multinational collaborations. In particular, the interplay of parent companies with their foreign subsidiaries and vice versa was researched to identify barriers and antecedents for capability transfer. The research design included active interviews at six subsidiaries, outcomes were analyzed following a multiple case study approach. Overall, three specific hypotheses on environmental heterogeneity, subsidiary autonomy, and managerial initiative as antecedents for local capability development

were formulated. Testing of additional two hypothesis investigated whether direct organizational linkage between managers and intensive in-person communication are positively related to reverse capability transfer. (Schotter & Bontis, 2009, p. 149 ff.)

Interview results provide confidence that managerial initiative is an antecedent for capability transfer in the context of the analyzed multinational cooperation. Each subsidiary shows differences in characteristics as well as organizational and administrative structures depending on country managers' strategy and priorities. These individual set-ups impact the organization's ability to adapt and build capabilities. Additionally, the authors state that direct person-to-person communication is crucial to leverage knowledge across organizations. Even if company-wide conferences are identified as appropriate starting points to build connections and exchange ideas on a high level of abstraction, frequent direct communication and specific joint projects are required to identify concrete potentials for capability transfer. (Schotter & Bontis, 2009, p. 160 ff.)

Uzunca (2018) researched interorganizational learning processes with a special focus on the interaction of spinoff and non-spinoff suppliers. Three central interorganizational learning mechanisms to build and transfer capabilities were identified through an inductive multiple case study: IRSC (Abbreviation Informal Relationships and Social Capital), TR (Abbreviation Transfer of Routines), and SI (Abbreviation Shared Identity). All three mechanisms anticipate and mitigate coordination while facilitating governance of joint collaborative processes. (Uzunca, 2018, p. 3267 ff.)

Following factors contribute to IRSC and can help to ensure access to key resources if urgent support is required: Hiring ex-employees from the buyer firm and making interorganizational private and personal relationships. Building such social work ties can also provide privileged access to information and business opportunities. (Uzunca, 2018, p. 3268 ff.)

TR is enabled through transferring ostensive and performative aspects of routines. Ostensive aspects comprise similarities in structure, form procedures, and flowcharts. These can be transferred through providing tangible resources such as drawings, procedures, or software. Performative aspects describe how employees bring routines to life and can be transferred by providing close guidance in everyday business, e.g. performing collaborative interorganizational problem solving. Another prerequisite for successfully transferring routines leading to synchronous production planning and sales forecasting is the relatedness of technology, production processes, and production equipment between both parties. (Uzunca, 2018, p. 3273 ff.)

Establishing a Shared Identity is identified as key contributor for the interorganizational learning process. It can be achieved by introducing a shared interorganizational language and fostering collaborative dialogues. Maintaining a shared

organizational culture helps to be more receptive about partner organization's needs. However, it is important to state and understand that separate identities are still considered and valued. Hence, the overall interorganizational learning process contains capability transfer in both directions and the eagerness of the buyer organization to learn from suppliers too. (Uzunca, 2018, p. 3276 ff.)

4.3.2 Interdepartmental Collaboration

Chatterjee et al. (2018) discussed organizational knowledge creation based on a literature review and developed a framework for transferring and creating knowledge. Therefore, the authors combined the process of SECI (Abbreviation Socialization Externalization Combination Internalization) with the concepts of LTSI (Abbreviation Learning Transfer System Inventory) to structure the interplay of tacit and explicit knowledge. As a central outcome of the theoretic research, knowledge creation and transfer within organizations are brought together considering conditions and the environment. (Chatterjee et al., 2018, p. 305 ff.)

Knowledge creation is understood as a spiral process that starts at the level of individuals and moves up across the firm overcoming sectional, departmental, divisional, and organizational barriers. This process comprises four phases of knowledge conversion: Socialization, Externalization, Combination, and Internalization. Socialization is described as sharing tacit knowledge through meetings, teleconferences, or brainstorming. Externalization enables the communication of knowledge and transforms it from tacit to explicit. As a consequence, existing knowledge is crystallized and forms already the basis for new knowledge. Combination brings together different types of explicit knowledge from in- and outside the organization. It includes the editing and processing to new forms of knowledge as well as dissemination among members of the organization. Finally, Internalization converts the new explicit knowledge again to tacit knowledge by assimilating it, connect patterns and make use of it as part of everyday routines. Consequently, knowledge creation is much more than the pure sharing process across individuals, departments, or organizations. (Chatterjee et al., 2018, p. 306 f.)

The other fundamental component of the framework LTSI allows to understand the factors affecting transfer of knowledge and learning. Outcomes of a learning process can be operationalized as a sequence of learnings, individual performance, and organizational performance. Thereby, effectiveness of the learning process and its results depend on the factors ability, environment, and motivation. Ability includes existence of opportunities to make use of learnings and the personal capacity. Environment discusses conditions such as management & peer support, organizational openness or resistance to change, and institutional feedback. Motivation is detailed as interplay of efforts invested and expectations. (Chatterjee et al., 2018, p. 308)

Coradi et al. (2015) conducted a single case study on how to design workspaces for cross-functional knowledge sharing in collaboration with the multinational pharmaceutical company Novartis. The authors found that co-locating different R&D units leverages knowledge sharing across boundaries. TDC's basic assumption that dynamic capabilities and agility are essential for long-term success provided the theoretical grounding. The co-location pilot was designed in accordance with legacy management literature suggesting co-location as an organizational mechanism to ensure cross-functional knowledge sharing. (Coradi et al., 2015, p. 236 ff.)

133 employees from three teams were co-located following a multi-space concept that includes multiple working environments such as desk areas, recreation zones, flexible meeting rooms, and laboratories. Additionally, hot desks were offered to team members located elsewhere. Proximity and visibility are used as guiding principles for the room concept: Physical distance between all employees is below 30 meters and all colleagues located in one wing of the building are visible and approachable by the others. The case study research comprised semi-structured interviews prior and after co-location as well as observations on location, duration, and characteristics of cross-functional interaction. (Coradi et al., 2015, p. 242 ff.)

Prior to co-location, project team members stated that there is almost no informal communication with colleagues located at other sites. Even formal meetings could not always be organized in a way all team members would be able to attend due to different time zones and work hours. The study identifies two main consequences of co-location positively impacting cross-functional knowledge creation: Unplanned face-to-face communication leads to faster and more precise knowledge flows than planned, formalized knowledge management. Additionally, open workspace design contributes to the creation of new knowledge through implicit socialization and self-induced combination of knowledge across functions. (Coradi et al., 2015, p. 245 ff.)

Cuijpers et al. (2011) researched costs and benefits of interdepartmental collaboration in the field of product and process innovation. A sample of 433 German manufacturing companies surveyed on innovation activities, performance, and hampering factors allowed the authors to test five hypotheses. The analysis investigated the relation of interdepartmental collaboration, innovation performance and corresponding cost, while cost was operationalized as negative impact on project delay and project termination. Differences between companies that actively collaborate across departments and the rest of the sample were quantified by applying descriptive statistics and multivariate settings. (Cuijpers et al., 2011, p. 565 ff.)

Different to product innovation, interdepartmental collaboration is positively related with firm's performance in process innovation. The authors conclude that this difference can be explained by the impact of organizational structure and systems on processes: Thus, process innovation relies on information and knowledge embedded and shared through the organization. Furthermore, process innovations are

tightly coupled with further organizational processes, that require and facilitate close collaboration for implementation of improvements. Consequently, managers need to provide resources and infrastructure enabling cross-functional collaboration to boost innovation performance. This may include facilitation of successful practice sharing across departments, investments in information & communication technologies, and shared meeting spaces. Finally, the risk of delays in innovation projects due to additional efforts and increased complexity of interdepartmental collaboration is remarked. (Cuijpers et al., 2011, p. 573)

Lapre and Van Wassenhove (2001) investigated differences in organizational structures across multiple production lines of a plant, which were variously successful in achieving productivity improvements by pursuing learning projects. A comprehensive quantitative study is conducted including full operationalization of variables and regression analyses. Productivity improvements measured are not limited to the particular line but assessed across the entire plant. (Lapré & Van Wassenhove, 2001, p. 1320 ff.)

The most successful production line is characterized by tremendous management commitment expressed by dedicating ownership for improvement project definition to the line team, strong problem solving capabilities and highly experienced personnel that conducted legacy projects in different departments. Vice-versa, replicating the model line in further plants did not lead to impactful transfer of learnings. The authors assume the lack of knowledge diversity as a differentiating factor in addition to the absence of management buy-in and interdepartmental problem solving. (Lapré & Van Wassenhove, 2001, p. 1323 f.)

Marra et al. (2016) approached the role of internal and external knowledge linkages across multiple tiers and departments of an organization. A single case study with an Italian manufacturer of automotive rubber components served as basis for the research. The authors hypothesized that crucial knowledge is developed through ties and therefore functional nodes with more ties show a higher level of knowledge resulting in higher operational performance. Findings confirmed the hypothesis, functional nodes with most connections have been identified as crucial members of the organization for knowledge creation and transfer. Furthermore, knowledge ties informed strategic investment decisions for capabilities rather than equipment, what paid off in performance improvements. (Marra et al., 2016, p. 256 ff.)

Fostering knowledge creation and exchange requires to focus on most knowledgeable individuals of the organization and its departments. According to the study, these are also the same individuals acting as central nodes in the cross-functional knowledge ties both inside and outside the organization. These key personnel can act as multipliers and deliver benefits to the entire collaboration as the example of a joint strategic decision to push TQM across R&D, production, and quality assurance shows. (Marra et al., 2016, p. 260 ff.)

Pereira et al. (2018) investigated the interplay of organizational structure, corporate culture, and human resource management to leverage interdepartmental collaboration. Following a multiple case study approach, managers of different departments in twelve global manufacturing companies were interviewed. Interviewees comprise the departments customer service, human resources, engineering, sales, and marketing. All companies operate in the automotive and chemical industry, they offer both physical products and additional services. The study focused on internal elements and barriers hindering the companies to enhance the services offered by promoting the collaboration among different areas of the companies. (Pereira et al., 2018, p. 220 ff.)

Lack of well-defined interdepartmental processes & indicators, unclear requirements for service professional profiles, and isolation of the service division within manufacturing organizations are identified as major barriers. Hence, the authors suggest introducing dedicated indicators to reward contributions towards other departments along the service development cycle to actively foster interdepartmental collaboration. Furthermore, providing key personnel with training to build, increase, or combine technical and commercial competencies shall lead to more balanced prioritization of product and service improvements. (Pereira et al., 2018, p. 223 ff.)

Shamah and Elssawabi (2015) developed an instrument to measure open innovation and trust between organizations. The study focused on assembly lines in the automotive industry but the authors state general applicability to interacting parties of a supply chain. In particular, the impact of trust within organizations and trust between organizations on open innovation were investigated. In this context, open innovation was defined as driver for developing organizational core competencies leading to an increased level of performance. (Shamah & Elssawabi, 2015, p. 50 f.)

Quantitative exploration of the relation between trust and open innovation distinguishes two different categories of trust: Internal trust comprising interorganizational trust and interpersonal trust, as well as external trust comprising suppliers, customers, and competitors. Both interorganizational and correlated interpersonal trust are positively related with open innovativeness. Correlations between all variables tested are significant and range from medium to strong. The authors conclude that interorganizational relations and trust need to be especially considered by management as both seem to be levers to implement open innovation as a driver for developing organizational core competencies. That is why using the developed measurement scale can inform suitable managerial actions to maintain aspects of trust and enable capability development. (Shamah & Elssawabi, 2015, p. 54 ff.)

Suckley et al. (2013) analyzed and addressed interdepartmental barriers in a medical device company. The study followed an ethnographic case study approach and uncovered socially constructed unwritten rules across production and quality control. A team of company internal and external researches collected data and

observations through recorded interviews as well as informal communication on different organizational levels from operators to senior management. The authors identified interdepartmental barriers between production and QC mostly caused by unwritten rules, communication issues, and the organizational structure of the company. (Suckley et al., 2013, p. 173 ff.)

Cross-departmental communication and proximity was hindered by a silo mentality. Due to lack of recognition by senior management, the immediate line managers of each department were very prominent and operatives focused on immediate departmental activities rather than understanding themselves as a part of a bigger picture. Furthermore, misuse of the QMS (Abbreviation Quality Management System) lead to incompatibilities of corporate procedures and quality standards. Coping with this mismatch, the QMS was a system for managing documents instead of truly assessing the process. This generated conflicts between the different departmental teams making use of the system. (Suckley et al., 2013, p. 183 ff.)

Identified barriers are addressed by a set of actions, including adjustments in the management structure of the company. Quality previously reported to the medical director, who was a direct board member, while manufacturing management was not represented at board level. As a result, the plant manager is introduced as new role locally overseeing both production and quality with a direct reporting line to better align strategies and show equal senior leadership attention. Furthermore, various communication channels are introduced to actively facilitate communication between management and each of the departments. Interdepartmental process improvement groups meet frequently to share issues and solutions across the areas. Impact of individual work on the entire company's position in business is evaluated and joint team-building events offered. Adjusting the scope of the QMS leads to greater emphasize on process quality and inclusion of production measures such as OEE (Abbreviation Overall Equipment Effectiveness). (Suckley et al., 2013, p. 184 ff.)

Thongpapanl et al. (2018) researched whether job rotation strategies and joint rewards systems encourage cross-functional collaboration in different organizational contexts. The research model was built on survey results across 232 Canadian firms in different industries. According to the author's literature review, job rotation shall enable employees to familiarize with a broader set of mechanism and personnel. It is found to lead to better understanding challenges and capabilities of other departments, can encourage information exchange and support cross-functional trust. Job rotation increases understanding of knowledge, its sources, and approaches to access and transfer the knowledge from appropriate persons. Hence, it is helpful to overcome the barrier of different subcultures as a consequence of specialization of knowledge in departments. (Thongpapanl et al., 2018, p. 1087 ff.)

In addition to job rotation, joint reward systems were hypothesized to offer mutual motivation for cross-functional collaboration. In that way, functional managers shall be motivated to strive for firm-level improvements rather than functional or individual goals. Thus, the positive impact of job rotation on cross-functional collaboration is complemented and both mechanisms should be combined in the overall strategy. In contrast, the authors identified mutually exclusive reward schemes to be often associated with weak cross-functional collaboration. (Thongpapanl et al., 2018, p. 1089 f.)

Based on the sample of 232 Canadian firms, the positive impact of job rotation and joint reward systems on cross-functional collaboration was tested using moderated hierarchical regression analyses. Marketing and R&D served as pilot departments for respondents within the companies. Furthermore, moderating effects of firm size and age were investigated. The results confirm the hypothesized positive relation of job rotation and joint reward systems with cross-functional collaboration. Even if no direct significant effect of the firm size on cross-functional collaboration was observed, a negative moderating effect of size on the relations of job rotation and joint reward systems with cross-functional collaboration occurred. Thus, the authors conclude both mechanisms seem to be more effective in the context of smaller companies. Firm's age indicated a very slight negative moderating effect on the relation of job rotation and cross-functional collaboration, while no interaction with joint reward systems was identified. Finally, the authors point out that both factors job rotation and joint reward systems have been confirmed as important drivers for interdepartmental collaboration, which is expected to subsequently enhance company's performance. (Thongpapanl et al., 2018, p. 1093 ff.)

4.4 Findings & Applicability

According to the approach outlined in chapter 4.1.2, outcomes of the comprehensive literature review (cf. chapter 4.3) are summarized and condensed across articles in the following. Afterwards, applicability & adaptability of findings to the research at hand – OPEX across manufacturing and quality control – is assessed and discussed¹³. Therefore, subsequent content-wise clusters of outcomes have been identified: Barriers & Boundaries (cf. chapter 4.4.1), Organizational Set-Up & Structure (cf. chapter 4.4.2) and Knowledge Management & Capability Transfer (cf. chapter 4.4.3). Each article reviewed and discussed in chapter 4.3 can contribute to multiple clusters.

¹³ The author builds on the initial semi-structured interviews (cf. appendix A.1), learnings from both exchange groups (cf. chapter 1.2.5) and the insights gained through personal project collaborations with more than 20 pharmaceutical collaborations during this time as a Research Associate at the University of St.Gallen.

4.4.1 Barriers & Boundaries

Following barriers for cross-departmental collaboration & optimization have been identified through the systematic literature search and review. Table 86 condenses the outcomes and discusses the applicability to the overarching research problem OPEX across manufacturing and quality control.

Table 86: Barriers and Boundaries for Cross-departmental Collaboration & Optimization

Barrier / Boundary	Description / Limitations	Reference	Applicability to OPEX across manufacturing & quality control
Departmental Haughtiness	Understanding interorganizational learning as a one-directional process, lacking eagerness of the more mature organization to learn from the less mature organization too.	Uzunca, 2018	Often manufacturing departments started their CI journey earlier and therefore show a higher maturity in OPEX than quality control. This can lead to haughtiness and hinder collaboration on an equal footing. This barrier must be overcome to comprehensively optimize the site-internal value chain and its interdependencies. Additionally, the very recent focus on OPEX in QC labs may result in leading-edge achievements and OPEX innovations manufacturing could equally benefit from.
Departmental prioritization of project timeline & termination	Avoiding higher risk of delays in timeline and termination of departmental improvement projects due to additional efforts and increased complexity of inter-departmental collaboration.	Cuijpers et al., 2011	Depending on the site-specific target setting and project prioritization process, this barrier is applicable to manufacturing and quality control. Department heads protect resources and prioritize immediate achievements within departments rather than contributing to cross-departmental initiatives. Such decisions hold true for both manufacturing and quality control.
Differences in time zones and worktimes	Not all parties can take place in formal exchange meetings due to different working times or time zones (in case of	Coradi et al., 2015	Since the focus lies on site-internal alignment of manufacturing and quality control, differences in time zones are not applicable and do not hinder the collaboration. However, different shift models across the departments can be in

Barrier / Boundary	Description / Limitations	Reference	Applicability to OPEX across manufacturing & quality control
	employees located elsewhere).		place and might hamper the synchronization.
Gap between absorptive and disseminative capacities	Most studies focus on the absorptive capacity of the receiving organization. However, the disseminative capacity of the sending party is equally important for a successful transfer process.	Fredriksson et al., 2019	The hurdle applies to collaborations between manufacturing and quality control. Knowledge sharing requires different capabilities than absorbing and adapting knowledge department internally. Even if pharmaceutical manufacturing areas show a comparable high OPEX maturity level across the board, there is low attention for actively building disseminative capabilities to successfully pass on practices to other departments.
Isolation of departments in manufacturing sites	Departments developing and offering the product related services are not sufficiently integrated in the plant's operational sequences along development and production of the physical products.	Pereira et al., 2018	Historically, QC was often seen as a black box in pharmaceutical production from the entire site perspective. QC is different to process engineering, supply management or quality insurance, which directly interact with the production process itself. Furthermore, separated reporting lines for quality can contribute to site-internal isolation.
Lack of management buy-in, commitment and visibility	Top-down defining fields for improvement and projects across the plant instead of empowering shop floor teams to identify and conduct inter-departmental learning projects. On the other hand, non-visible senior management leads to operatives focusing on	Lapre & Van Wassenhove, 2018 Suckley et al., 2013	The discussed trade-off between enabling bottom-up optimization through management commitment and ensuring strategic alignment across departments by top-management guidance needs to be considered for manufacturing and quality control. In pharma, it is still less common for top management to spend time on the Gemba in QC than in manufacturing. Generally, both perspectives identified in literature do not necessarily contradict each other: A visible top-

Barrier / Boundary	Description / Limitations	Reference	Applicability to OPEX across manufacturing & quality control
	immediate departmental activities recognized by the individual line management rather than understanding themselves as a part of a bigger picture.		management that ensures cross-departmental steering rather than silo optimization can still empower departmental employees to actively develop, adapt and share improvements to achieve the firm-wide objectives and fulfill the corporate strategy.
Reluctance	Not all organizational units are naturally interested in knowledge transfer. It should not be presumed that knowledge is always equally well received and adapted.	Kalling, 2013	This concern holds true for OPEX across manufacturing and quality control. In particular, different backgrounds within departments need to be considered: Workforce in pharma shows a high level of qualification across the board. While operators in manufacturing are generally receptive to the lean philosophy due to their operational backgrounds, analysts in the laboratories often hold highest educational degrees and show an R&D driven mindset. Thus, OPEX is still understood as <i>something for operations</i> and cultural barriers impacting the willingness to embed continuous improvement can be observed.
Specialization & different subcultures	Within areas, individuals specialize in similar content and workers can directly interact, while transfer of knowledge across areas requires a dedicated strategy. Additionally, common specialization leads to department-specific subcultures that hinder cross-functional collaboration.	Buckley & Carter, 2003 Thongpapanl et al., 2018	The barrier is fully applicable to OPEX across manufacturing and quality control. Core business of both departments (make vs. test), working environment (production area vs. lab) and equipment (production lines vs. testing instruments) are fundamentally different. Workforce is skilled according to its tasks and specialized to its department. Departmental subcultures due to common specialization of colleagues are observable.

4.4.2 Organizational Set-Up & Structure

Following organizational factors and aspects of cross-departmental collaboration & optimization have been identified through the systematic literature search and review. Table 87 condenses the outcomes and discusses the adaptability to the overarching research problem OPEX across manufacturing and quality control.

Table 87: Organizational Factors and Aspects for Cross-departmental Collaboration & Optimization

Organizational Factor / Aspect	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
Center of Excellence	Dedicated department leading the storage & distribution of knowledge across different entities, while these stay responsible for knowledge creation.	Gonzalez et al., 2014	In some pharmaceutical companies corporate centers of excellence are already established to either facilitate OPEX within manufacturing or quality control across the different sites of a company's network (cf. chapter 5.3). Integrating the idea of focusing on cross-departmental knowledge sharing in the site OPEX organizations and expand those to centers of excellence can help to foster cross-functional collaboration and capability transfer.
Co-location of cross-functional teams & shared meeting spaces	Proximity and visibility of different co-located functions positively impact cross-functional knowledge creation: Unplanned face-to-face communication leads to faster and more precise knowledge flows than planned, formalized knowledge management. Open workspace design contributes to the creation of new knowledge through implicit socialization and self-	Coradi et al., 2015 Cuijpers et al., 2011	Obviously, working areas for production and QC both require decent floor space and a specialized area. However, recent layouts of pharmaceutical production plants strive to closely allocate production, laboratories, and warehouses in order to minimize distances along the value chain. Additionally, the vision of integrated on- and inline quality control is discussed in pharma but not systematically realized yet. Consequently, creating permanent visibility between shop floor operators and analysts is hard to realize. Departmental roles in charge of Continuous Improvement and OPEX are usually located in

Organizational Factor / Aspect	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
	inducted combination of knowledge across functions. Shared meeting spaces increase number of encounters across departments and can be a starting point for information exchange.		office areas and do not have their desks directly on the shop floor or in the laboratories. Hence, co-location of production and QC OPEX functions is doable and can help to foster exchange through unplanned face-to-face communication. Furthermore, both production and QC workforce regularly hold meetings as part of their everyday job. The concept of conducting these meetings in shared meeting room areas rather than establishing dedicated departmental meeting rooms is adaptable as long as distances between individual work areas and shared meeting areas can be minimized.
Combined knowledge architecture of integration and partition	Address the trade-off between specific depth and cross-functional breadth of knowledge through a combined architecture depending on the individual need for knowledge per topic.	Buckley & Carter, 2003	The described trade-off fully applies to manufacturing and quality control. Each department requires specific knowledge, while an integrated approach to OPEX is needed at the same time. Thus, structuring and formalizing the symbiosis of knowledge types per function can help to build tailored individual profiles for OPEX roles across manufacturing and quality control.
Integrated cross-departmental QMS	Emphasize process quality by inclusion of production measures in the QMS rather than designing the QMS as a system for managing documents.	Suckley et al., 2013	Producing pharmaceutical products encloses and requires operating a proper QMS. However, current systems focus very much on documenting compliance in both areas manufacturing and quality control. Such documentations already cover the entire site value chain and have to aim for completeness. Integrating the QMS with CI efforts and thereby emphasizing process quality

Organizational Factor / Aspect	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
			measures can be a lever to benefit from the existing cross-departmental scope of QMS and expand the purpose from showing compliance to integrated optimization.
Integrated expertise	Enroll ex-employees of organization from which capabilities shall be transferred.	Uzunca, 2018	OPEX professionals previously working with manufacturing can bring-in valuable insights in QC or vice versa. However, specific context of the roles per department needs to be addressed by tailored qualification.
Interdepartmental indicators	Introduce dedicated indicators to reward contributions towards other departments along the site internal value chain to actively foster inter-departmental collaboration.	Pereira et al., 2018	Both manufacturing and quality control work with indicators to monitor and report performance & compliance. However, as of today KPI systems are mostly defined and used departmental. Complementing or redefining these indicators paying special attention on interdepartmental contribution is applicable. Especially harmonizing and sequentially connecting service and supply indicators in both departments can not only enhance collaboration, but also help to increase transparency along the entire site value chain.
Job rotation	Organizationally enable employees to familiarize with a broader set of mechanism leading to better understanding challenges and capabilities of other departments. Job rotation increases understanding of knowledge and its sources. It	Thongpapanl et al., 2018	Applicability of regular job rotation is limited to dedicated OPEX resources in manufacturing and/or quality control. Departmental staff not dedicated to OPEX but in charge of continuous improvement as part of their everyday job in production or laboratory cannot regularly rotate and fulfill everyday tasks in the other department alongside with rotating for OPEX purpose. That is why keeping departmental dedication of job profiles – but

Organizational Factor / Aspect	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
	provides access to appropriate persons as source for knowledge transfer. Hence, it is helpful to overcome the barrier of different subcultures.		building cross-functional improvement project teams to drive forward exchange – is more doable in the context of departmental workforce.
Joint reward systems	Motivate functional managers to strive for firm-level improvements rather than functional or individual goals. In that way foster cross-functional collaboration.	Thongpapanl et al., 2018	This aspect totally applies to manufacturing and QC. Departmental management in both areas is usually incentivized with variable salary surcharges based on yearly achievements. Adjusting targets from departmental to site level can foster alignment and push interest for QC and vice versa. The same holds true for recognition: Awarding sites instead of areas helps to increase cross-functional team spirit.
Knowledge nodes establishing multiple organizational ties	Connect most knowledgeable individuals per department as cross-functional knowledge multipliers.	Marra et al., 2016	Still considering the discussed trade-off between knowledge breadth and depth within departments, selecting most knowledgeable individuals as multipliers can help to accelerate knowledge transfer and collaboration across manufacturing and quality control. However, most knowledgeable shall not be defined based on specific operating or testing expertise but reflect selection of individuals well-educated about application of OPEX principles and tools in the respective department.

Organizational Factor / Aspect	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
Local management position overseeing both departments	Introduce a site level role overseeing both production and quality with a direct reporting line to better align strategies and show equal senior leadership attention to both areas.	Suckley et al., 2013	Going back to the strict divide of operations and quality in pharmaceutical reporting lines – often constituted to address regulatory requirements – such positions are rarely established in pharmaceutical production sites. Thus, the collaboration between manufacturing and quality control can highly benefit from cross-departmental oversight on a site level. Introducing such a middle-management position with a dotted reporting line would not contradict the separation of operations and quality in senior management on an above-site level.
Organizational openness & resistance to change	Organizational conditions that allow changes determine the ability to make use of learnings & newly created knowledge.	Chatterjee et al., 2018	Operating in a heavily regulated GMP environment is often seen as hindering changes in both departments and causes reluctance to any changes even if not GMP relevant. Hence, the issue highlighted is applicable to the research problem at hand and necessitates to clearly distinguish changes that require validation and approval according to GMP from non-GMP relevant adjustments.
Production and technology relatedness	Enable synchronous production planning and sales forecasting by standardizing equipment and processes.	Uzunca, 2018	Due to the different task profiles across manufacturing and quality control, achieving technology relatedness and standardizing equipment across both departments is not applicable. However, standardizing processes in the meaning of managerial routines, e.g. aligning huddle meeting set-ups across departments, is seen as beneficial across manufacturing and quality control.

4.4.3 Knowledge Management & Capability Transfer

Following practices and mechanisms for cross-departmental knowledge management & capability transfer have been identified through the systematic literature search and review. Table 88 condenses the outcomes and discusses the adaptability to the overarching research problem OPEX across manufacturing and quality control.

Table 88: Practices and Mechanisms for Knowledge Management & Capability Dispersion

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
Enable direct person-to-person communication	Company-wide conferences are appropriate starting points to build connections and exchange ideas, but frequent direct communication and specific joint projects are required to identify concrete potentials for capability transfer.	Schotter & Bontis, 2009	Regular communication is seen as key lever for OPEX capability sharing across manufacturing and quality control. Dedicated sharing events may act as baseline but need to kick-off everyday collaboration for effective knowledge transfer. Because of separated work areas and core businesses, accidental exchange across manufacturing and QC is unlikely. Hence, actively fostering direct person-to-person interaction is important.
Ensure trust	Trust is a mechanism to embed interorganizational ties and acquire capabilities. It provides confidence that advice provided, and recommendations made by an exchange partner are of high quality. Trust ensures willingness to make extra efforts to exchange beyond the formal collaboration to help each other. Furthermore, inter-organizational and	McEvily & Marcus, 2015 Shamah & Elssawabi, 2015	Actively fostering trust can accelerate knowledge sharing and OPEX capability transfer across manufacturing and quality control. Avoiding departmental competition, especially regarding allocation of investment budgets, and underlining the value-adding contribution of both departments to the pharmaceutical value chain are prerequisites for colleagues trusting in each other across both departments. Additionally, a culture of making failures transparent by proactive communication and recognizing learnings beyond the own department can contribute to the organizational trust. Establishing joint ownership and responsibility for on-schedule

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
	interpersonal trust are positively related with open innovation as a driver for developing organizational core competencies.		release of batches, a crucial milestone of making pharmaceutical goods available to the market both departments heavily contribute to, is a further concrete measure to expand trust. This can act as cross-departmental baseline for open capability sharing.
Establish a shared organizational culture	Introduce a common interorganizational language and foster collaborative dialogues helps to be more receptive about other organizations' needs.	Uzunca, 2018	Due to the earlier discussed departmental focus and specialization of job profiles in manufacturing and quality control, introducing an interdepartmental OPEX language is seen as powerful lever for cross-departmental optimization.
Evaluate prior to knowledge & capability transfer processes	Besides disseminative capabilities of the sender and absorptive capabilities of the receiver, transferability and appropriateness of the capability should be evaluated. Transferability and appropriateness assess how easily the process and capabilities can be transferred and if they fit well with the new context. Additionally, consider time and cost to conduct the transfer.	Fredriksson et al., 2019	Highly important for capability dispersion across manufacturing and quality control. A structured evaluation of the capability and the transfer process can provide clarity on applicability and importance of the capability in the context of the other department. Furthermore, emphasizing such structured evaluations facilitates the conceptualization of a holistic capability transfer concept between manufacturing and quality control instead of individual transfers. Even if the return on investment might be hard to precisely quantify for some OPEX capabilities, incorporating cost and efforts for the transfer in the evaluation, and balancing those with applicability and importance, perfectly reflects the OPEX philosophy considering both effectiveness and efficiency.

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
Foster collaborative Problem Solving & Introduce cross-departmental process improvement groups.	Transfer performative aspects of routines on the job by performing joint problem solving in interorganizational teams. Achieve improvements by bringing in experience of having solved problems in other departments. Cross-departmental teams should meet frequently to share issues and solutions. Joint problem solving moderates the positive relation of interorganizational trust, information sharing and capability acquisition.	Uzunca, 2018 Lapre & Van Wassenhove, 2018 McEvily & Marcus, 2015 Suckley et al., 2013	Problem solving is a key capability in both fields manufacturing and quality control. Cross-departmental teams are already set-up for the investigation of deviations as part of the event handling process, often facilitated by quality assurance. Intensifying these collaborations and expanding the scope to cross-functional exchange groups beyond event handling to support problem solving in both manufacturing and quality control is seen as effective measure with twofold benefits: While problem solving itself is directly enriched by broader cross-functional expertise, such teamwork may also lead to implicit knowledge sharing and capability transfer as integral part of the collaboration. The same approach is seen as beneficial for dedicated process improvement groups operating across manufacturing and quality control. These groups should proactively screen for process improvements.
Incentivize & motivate individuals to share knowledge	Providing physic rewards such as individual bonuses for successful cross-functional teamwork. Integrate reward and recognition system with knowledge sharing objectives. Motivation determines the effectiveness of knowledge sharing & creation, summarizing the balance of efforts invested and	Buckley & Carter, 2003 Chatterjee et al., 2018 Kalling, 2003	As targets are usually set departmental in manufacturing and quality control, actively incentivize key individuals to share knowledge across both departments is important. The above discussed integration of indicators, cross-functional metrics, and reward systems is one way to motivate. Making disseminating parties benefit from achievements realized due to adaption of their shared capabilities in other departments and joint celebration of success can further motivate cross-functional sharing. Furthermore, the historical understanding of quality control as a needed

4 Approaches for Cross-departmental Collaboration & Optimization

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
	expectations. It is not naturally given but needs to be actively managed by managerial control mechanism ensuring that both sources and recipients understand the value of knowledge transfer.		cost center rather than a value-adding contributor to the overall production and release chain (cf. appendix A.1) requires particular attention for actively motivating OPEX functions to optimize across departments. Highlighting not only the value of receiving capabilities but particularly making clear the benefit of disseminating capabilities for oneself additionally motivates the employees.
Make private & personal relationships	Actively foster building of social work ties to provide privileged access to information and business opportunities. Offer joint cross-functional team events.	Uzunca, 2018 Suckley et al., 2013	Fully applicable and powerful to address the earlier mentioned risk for isolation of departments in facilities. Departmental management of manufacturing and quality control can act as role model and accelerate networking by providing team building budgets and events that are bound to the specific purpose of cross-departmental events.
Provide tangible resources such as drawings, procedures, and software	Transfer ostensive aspects of routines to achieve similarities in structure and procedures.	Uzunca, 2018	Considering the different task profiles and working environments across manufacturing and quality control, transferring and harmonizing tangible resources as a baseline for capability sharing is hardly applicable. However, standardized managerial procedures (e.g. huddle meetings) and OPEX execution routines can simplify and accelerate cross-functional collaboration.
Run benchmarking	Benchmarking programs including improvement methods, output result comparison and corresponding recognition can be one way to	Kalling, 2013	Network-internal and company-external benchmarking are broadly used in pharmaceutical production. While these programs historically focused on operations, analyzing QC labs in comparison to each other is one of industry's hot topics (cf. chapter

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
	stimulate motivation for knowledge transfer and measuring progress.		1.1). The St.Gallen experience in offering manufacturing, QC and combined benchmarking shows that cross-functional benchmarking across manufacturing and quality control creates transparency, especially in the field of OPEX maturity.
Show managerial initiative	Managerial initiative is an antecedent for capability transfer. It impacts organizational and administrative structures depending on managers' strategy and priorities. Resulting setups enable/disable the organizations ability to adapt and build capabilities. Managerial support determines the effectiveness of learning processes.	Schotter & Bontis, 2009 Chatterjee et al., 2018	Highlighting once more the power of departmental management due to the usually separated reporting lines in pharmaceutical producers, managerial initiative for cross-functional collaboration is extremely important in the present context. Besides fostering collaboration of operators and analysts between manufacturing and quality control, senior managerial initiative can also comprise investment in dedicated OPEX resources supporting across areas. Furthermore, management showing presence in key OPEX collaboration projects is an easy way to underpin the importance of cross-functional collaboration.
Understand knowledge creation beyond knowledge sharing	Knowledge conversion from tacit to explicit knowledge requires socialization, externalization, combination, and internalization. It comprises actions such as crystallizing, editing, processing, adapting, imbibing, and applying shared knowledge in addition to the sharing process itself.	Chatterjee et al., 2018	Successful OPEX capability transfer across manufacturing and quality control as an interdepartmental process requires adaption to the departmental context. Adoption is not solely sufficient. Understanding knowledge creation beyond sharing and pay attention on careful combination and internalization of shared knowledge, is important and applicable. Moreover, actively supporting the steps of socializing and externalizing knowledge across manufacturing and quality control can help to initiate regular cross-departmental collaboration.

Practice / Mechanism	Description / Benefits	Reference	Adaptability to OPEX across manufacturing & quality control
Use innovation projects as catalysts & multiplier for cross-departmental collaboration	Process innovation relies on information and knowledge embedded and shared through the organization. Thus, process innovation projects are tightly coupled with further organizational processes. Such projects require and generally facilitate close collaboration for implementation of any improvements.	Cuijpers et al., 2011	Innovation is a common field of interest across manufacturing and quality control. Therefore, it can act as catalyst for collaboration across departments. Examples of on-going digitalization initiatives in the pharmaceutical industry are already set-up accordingly: Selected departmental use cases are piloted first. In case of success, these pilots are subsequently abstracted and broadly rolled-out. However, process innovation can only facilitate cross-departmental collaboration, if the innovations can be generalized and are applicable to both manufacturing and quality control.

4.5 Implications for OPEX Management

The purpose of the present chapter was to inform the research at hand with approaches for cross-departmental collaboration from theory and other industries. Therefore, the research problem was abstracted, and the scope extended to cross-departmental management within production sites not limited to Operational Excellence nor to the pharmaceutical industry.

Consolidated outcomes of this desk research contribute to the MRQ of the thesis and answer in particular SRQ 2 – *What are suitable strategies, approaches, and tools to overcome organizational barriers and dispense OPEX capabilities across departments?* The systematic literature search (cf. chapter 4.2) & review (cf. chapter 4.3) alongside with the evaluation of applicability & adaptability (cf. chapter 4.4) leads to below summarized implications for OPEX management across pharmaceutical manufacturing and quality control. See chapter 4.4 for supplementary detailed descriptions of the individual outcomes.

A set of barriers and boundaries for cross-departmental collaboration have been identified and need to be addressed across pharmaceutical manufacturing and quality control. OPEX management should:

- ✓ Show awareness of departmental haughtiness due to different maturity levels, reluctance to change caused by the GMP mindset, and prioritization of departmental projects by individuals in charge.

- ✓ Consider departmental specialization & individual subcultures of departments.
- ✓ Avoid isolation of departments within manufacturing sites and exclusion from cross-departmental exchange because of missing direct process interfaces.
- ✓ Prevent impression of lacking management buy-in, actively demonstrate commitment to cross-departmental collaboration by sponsoring initiatives and ensuring personnel visibility in interdepartmental projects.
- ✓ Not underestimate the equal importance of disseminative capabilities for overall effective knowledge sharing in addition to absorptive capabilities and address capability gaps in manufacturing or quality control accordingly.

Furthermore, organizational aspects and the structural set-up have been recognized to effect and facilitate cross-departmental collaboration across manufacturing and quality control. OPEX management should:

- ✓ Introduce cross-functional centers of excellence and knowledge nodes establishing organizational ties.
- ✓ Co-locate departmental optimization teams, offer shared meeting spaces across departments and introduce job rotation for departmental OPEX resources.
- ✓ Define, formalize, and systematize a combined knowledge architecture of integration and partition to address the trade-off between depth in departmental knowledge and breadth in cross-functional knowledge.
- ✓ Establish an integrated cross-departmental QMS with a focus on monitoring process quality instead of managing documents alongside with interdepartmental indicators.
- ✓ Install local middle management positions overseeing both departments to ensure strategy alignment completing – but not replacing – the separated reporting lines to departmental senior management on the above-site level.

Finally, several concrete practices and mechanisms for cross-departmental knowledge management and capability dispersion between manufacturing and quality control have been identified. OPEX management should:

- ✓ Enable direct person-to-person communication across both departments as part of the everyday job by appropriate infrastructure and beyond dedicated sharing conferences.
- ✓ Establish a shared organizational culture by putting a common company language, values, and vision in place.
- ✓ Ensure trust by enforcing joint ownership & responsibilities, preventing departmental competition, and demanding full transparency on failures & learnings without any blame.

- ✓ Support the creation of private & personal relationships beyond own departments through allocating budgets for cross-departmental team building and networking events.
- ✓ Incentivize & motivate individuals to share knowledge by integrated target setting processes and joint recognition systems.
- ✓ Measure and reward contributions towards other departments based on dedicated indicators.
- ✓ Show active managerial initiative to align departments and harmonize line management's specific routines such as huddle meetings or improvement project execution planning.
- ✓ Run internal and external benchmarking to create transparency, make gaps visual and uncover present successful practices across departments.
- ✓ Foster joint, collaborative problem solving of department-specific problems and introduce cross-departmental process improvement groups.
- ✓ Evaluate capabilities prior to start the knowledge transfer, while balancing efforts of the transfer process with applicability and importance to the target department.
- ✓ Understand knowledge creation beyond pure knowledge sharing and pay attention on internalization of acquired capabilities, what also comprises defined departmental measures for crystallization, adaption, and application of knowledge.
- ✓ Use innovation projects in generalizable common fields of interest as catalysator and multiplier for cross-departmental collaboration.

5 Proven Successful Practices in Pharmaceutical Production

Chapter 5 aims to complement and confirm the implications drawn from quantitative analyses based on the benchmarking databases (cf. chapter 3) and literature inputs revealed from desk research (cf. chapter 4). Previous analyses of the benchmarking originated from the departments manufacturing and quality control: Data attributes, such as performance indicators or maturity levels, are gathered departmental in the benchmarking programs. These have been normalized, unified, integrated, and analyzed across both departments researching for associations and interplay. Differently, literature review started from an interorganizational and interdepartmental perspective: Barriers, structural set-ups, and levers for collaboration have been uncovered, assessed, and finally discussed in particular for applicability to the cross-departmental OPEX management of pharmaceutical manufacturing and quality control.

Supplementary and complementary, chapter 5 at hand focuses on researching the integrated management of OPEX in manufacturing and quality control. Thus, subsequent passages examine how OPEX is successfully managed across departments in an integrated manner rather than highlighting the association and interplay of both departments. For this purpose, a survey is conducted across OPEX functions in pharmaceutical production. Outcomes of the survey contribute to the research twofold: At first, insights on how to comprehensively manage OPEX while involving production and laboratories are revealed. Furthermore, responses gathered allow to select cases for additional in-depth follow-up interviews on certain topics uncovered in the survey. This chapter addresses SRQ 3 *How do successful pharmaceutical production sites achieve excellent performance across manufacturing & quality control?* (cf. chapter 1.2.2) and phase 3 *Confirmation* (cf. chapter 1.2.4) of the overall research procedure. Following the iterative approach, the survey study set-up was continuously informed by the learnings from the quantitative analyses in phase 1 and the desk research in phase 2.

Methods and procedure of the following parts are introduced in chapter 5.1. Afterwards, chapter 5.2 outlines the survey set-up used for the study and provides an overview on the sample of respondents. Outcomes of the survey study are presented and discussed within chapter 5.3. On this basis, patterns across answers are identified, particular interesting practices highlighted and cases for follow-up interviews selected. Subsequently, chapter 5.4 expounds findings of the case study interviews. Finally, implications for OPEX management are derived based on findings from both the survey-based study and the supplementary case studies in chapter 5.5. These implications contribute to the overarching research problem and the MRQ (cf. chapter 1.2.2) of the present thesis.

5.1 Methods

Following the mixed-methods research approach of the thesis (cf. chapter 1.2.4), subsequent chapters are applying qualitative methods to complement and deepen the implications drawn from the previous quantitative analyses (cf. chapter 3). Unlike quantitative statistical explorations, case studies primarily focus on explaining phenomena by investigating the how and why (Stuart et al., 2002, p. 426). Explanation of quantitative findings and theory formed based on those findings need finally to be substantiated by qualitative understanding (Meredith, 1998, p. 493). Accordingly, case study research is suitable to address SRQ 3 of the research at hand and applied in the following. The method is supplemented with a survey-based study conducted beforehand to allow for successful practice identification and case selection. Procedures of both research steps are introduced in the following.

5.1.1 Survey-Based Study

Surveys are a widely used self-report method for data collection. Data is gathered in a standardized way and allows to gain empirical insights to explore real-world phenomena. Consequently, surveys are well suited to descriptive studies but can additionally be applied to explore observations or seek explanation for occurrences. In that way, survey research reduces the gap between management theory and practice in OM, it increases the usefulness of findings for practitioners. (Ellram, 1996, p. 96; Forza, 2002, p. 152; Kelley et al., 2003, p. 261; Rosenthal & Rosnow, 2008, p. 172) In the recent past, survey research has often been associated with very rigid and rigorous quantitative research set-ups including formalized approaches for conceptualization, sampling, and distribution. Nevertheless, survey research in general can still represent a broad range of different aims, data collection instruments, and procedures as well as corresponding strategies for responses recruitment and survey administration. (Ponto, 2015, p. 169)

Most researchers classify survey research as a quantitative method striving to collect numerical data as baseline for statistical exploration. Statistical survey research is regularly applied in Operations, Quality, Supply, or Technology Management research. (Edmondson & McManus, 2007, p. 1162; Ellram, 1996, p. 96; Meredith, 1998, p. 442; Tomczak, 1992, p. 82) The survey-based study in the present research phase is conducted for a different purpose: Since the benchmarking databases already allowed for comprehensive statistical analyses and led to implications based on operational metrics (cf. chapter 3), the survey is focused on contextual categorial items and open-ended questions to uncover and collect underlying practices. Following SRQ 3, it particularly investigates the *How*. According to Ponto (2015, p. 168 ff.), such types of surveys can be categorized as qualitative method and contribute to exploring constructs of interest in qualitative research designs. Qualitative surveys do not research quantitative parameters but determine the

diversity of topics within a population and establish meaningful variation. (Jansen, 2010, p. 2)

Jansen (2010, p. 6) summarizes four key process steps to organize survey research applicable to both statistical and qualitative survey studies: Defining knowledge aims, sampling, data collection, and analysis. All steps are subsequently elaborated in the very context of the research at hand.

The knowledge aims of the study are derived from SRQ 3 (cf. chapter 1.2.2) of the overarching research project: Uncovering how successful sites already manage OPEX across manufacturing and quality control in pharmaceutical production. Consequently, the survey set-up must allow to identify successful sites based on the response items and recognize differences compared to the rest of the sample. Furthermore, focus on the practices applied is needed to explore how these sites achieved the level of excellence observed.

Sampling is organized according to the data gathering strategy outlined in chapter 1.2.5. Recent participants of the St.Gallen benchmarking programs are invited to take the survey alongside with members of the St.Gallen Industrial Research & Exchange Groups. A clear focus on OPEX executives that are capable and knowledgeable to answer representatively on behalf of production sites is defined (cf. chapter 5.2).

Detailing the data collection instrument of the study comprises the development of the survey's structure, formulation of the questions according to the knowledge aims stated and definition of appropriate answer scales. For this purpose, a study model to structure the survey is compiled in a first step and operationalized by a set of concrete questions afterwards. Thereby, particular attention is spent on deriving suitable answer options informed by intermediate findings of research phases 1 & 2 according to the iterative research approach (cf. chapter 1.2.4). The survey is presented in appendix A.6.

Results of the survey-based study are analyzed with regard to the objectives set for research phase 3 *Confirmation*. A descriptive review of the answer distribution across the different survey sections reveals insights on how successful pharmaceutical production sites align OPEX across manufacturing and quality control. Furthermore, the organizational set-up and contextual factors questioned allow to identify profiles of production sites more successful than others. Dependencies of the different items analyzed and patterns across questions uncover the levers for impactful cross-departmental OPEX approaches. Lastly, in-depth exploration of all free text answers by identifying key words, reviewing descriptions, and evaluating their generalizability allow to select practices for further exploration.

Testing the data gathering instrument prior to application in the field is an important success factor of survey-based research designs (Rosenthal & Rosnow, 2008, p. 173). Hence, the survey used for the research at hand has been developed, revised,

and finalized in an iterative manner along the meeting series of the St.Gallen Industrial Research and Exchange Groups: The initial study model was presented to the industry experts in spring 2020. Direct feedbacks and outcomes of workshop sessions informed an adapted version of the survey structure and a draft set of questions presented to the groups again in June 2020. Before rolling out the study and distributing the survey to the target audience, a third round of discussion in both groups confirmed relevance and accuracy of the fully operationalized final survey during October and November 2020.

Survey methods are appropriate to explore observations and compare results within the same context. These methods may be less applicable to compare between organizations operating in different context or reveal specific insights depending on the present context in detail. (Stuart et al., 2002, p. 420) Addressing this challenge for study designs, mixed-method research can successfully combine survey and case study research in a holistic data collection strategy according to Yin (2018, p. 64). While surveys could be used as research instruments within case studies, the techniques can also be coupled the other way around and researchers make use of case studies to enrich survey projects by revealing additional insights. That is why the approach applied in the chapter at hand complements findings from the survey-based study by case studies compiled based on semi-structured interviews with selected respondents. This method is introduced in chapter 5.1.2.

5.1.2 Case Study Research

Case research is one of the most powerful research methods in OM. Beyond investigating how and why questions, it can also support to develop new ideas and fields of application. (Voss et al., 2002, p. 195 f.) Thus, case study interviews are conducted by researchers to derive insights from practice (cf. Creswell, 2014; Ellram, 1996; Yin, 2018). Eisenhardt (1989, p. 535) depicts that case study research can be used to fulfill various aims: Generate theory, test theory or provide context, and descriptions of phenomena.

Following the latter aim, the method is applied in the research at hand and deemed useful since it is capable to explore and describe how successful procedures are conducted in the industry. Due to the high validity of real-world insights gained from practice, findings from case study research usually lead to impactful and directly applicable implications for industry practitioners. (Gassmann, 1999, p. 11; Voss et al., 2002, p. 195) Furthermore, case studies can inform triangulation of multiple data sources in a mixed-method approach and thus positively contribute to substantiation of constructs and hypotheses (Eisenhardt, 1989, p. 538). Consequently, case study research is applied to complement the previously gathered implications and semi-structured interviews are conducted for this purpose.

Yin (2018, p. 47 ff.) introduces four basic types of case study design: Holistic single case studies, holistic multiple case studies, embedded single case studies, and embedded multiple case studies. Single and multiple case studies are distinguished by the number of organizations in scope of the research, while holistic vs. embedded types follow different focuses within each organization analyzed: Holistic case study designs strive to investigate the entire organization at once, while the embedded approach differentiates between subunits within the organization that are individually examined in the case. Single case studies are especially favored by researchers to critically test existing theory in extreme or unusual circumstances. Furthermore, such studies are suitable to gain longitudinal insights. Unlike that, multiple cases are more appropriate when striving to confirm observations by similar results comparing several cases to each other or to underline context dependent differences by contrasting results across cases. If accessibility to several organizations is given to the researcher, multiple case study designs are preferred over single-case studies and likely lead to more credible results. (Yin, 2018, p. 54 ff.)

The research procedure within the present chapter follows a holistic multiple case study approach. Respondents of the survey-based study form a broad sample of accessible companies, reasonable selection of multiple cases can be made and justified based on the outcomes of the study (cf. chapter 5.3). Since all individual cases comprehensively evaluate the interplay of both departments manufacturing and quality control in addition to their relation with the OPEX organization at site, the design chosen can be characterized as holistic study.

According to Voss et al. (2002, p. 206), case study research design itself could combine multiple methods of field data collection such as direct observations, content analysis of documents, archival research, questionnaires, or interviews to allow for triangulation. In the dedicated case study section (cf. chapter 5.4) of the research presented in this thesis, the scope is intentionally limited to conducting, presenting, and discussing interviews of the multiple cases. The survey-based study performed and evaluated beforehand already serves as supplementing and enriching data source complementing all cases.

Addressing the objective of detailing the successful practices for cross-departmental management, all interviews are conducted in a semi-structured manner. The interview guideline is presented in appendix A.7. Unlike structured interviews, which are strictly limited to predetermined questions and prioritize quantifiability and comparability of statements across cases, semi-structured interviews are suitable for inductive exploration of defined subject areas. Semi-structured interviews are characterized by a set of sequential questions to be used as an interview guide but also include spontaneously introduced follow-up questions by the interviewer. In that way of approaching the interview as a controlled discussion, advantages of unstructured and structured interviews are combined: Guiding questions ensure focus on the pre-

defined topics in scope, but the open conversation still allows to obtain as much information on the investigated phenomena as possible. (Cachia & Millward, 2011, p. 268)

Based on the outcomes of the survey-based study, an individual focus is derived for each case study interview. Since the interviews aim to explore the different successful practices uncovered by the survey responses of all case sites in detail, the case-specific interview guidelines are tailored accordingly and include specific questions on the individual responses. However, all case interviews commonly start with a series of questions on the site's approach to OPEX across departments. This allows to understand the broader context of the successful practices obtained. The interviews are held as online video conferences, this mode of operation supports a trusted environment for exchange and allows to discuss supplementary material displayed on a shared screen in addition to audio-only conversations. Upon agreement of all attendees, the interviews are recorded, subsequently documented, and summarized in the case studies outlined in chapter 5.4.

Due to the individual and tailored focus of every case interview, no explicit and formalized cross-case analysis is performed as suggested by Eisenhardt (1989, p. 540). Instead, the scope of evaluation is intentionally limited to comprehensive within case analyses (cf. chapter 5.4) according to the focus of each case. Following CT as one of the research theories guiding this dissertation (cf. chapter 1.2.1), special attention is paid on exploring the context, in which the identified practices are successful in, and outlining the contingencies of the different cases. Finally, all case sites contribute with their successful practices to the overarching implications for OPEX management (cf. chapter 5.5) in conjunction with the results of the survey-based study (cf. chapter 5.3). Summarized in other words, the case study interviews at hand strive for exploring the case-individual successful practices and thereby enriching the overarching implications from the various angles of multiple case organizations, rather than comparing the cases to each other.

5.2 Data Gathering & Sample Overview

Following the objective to complement the empiricism for the present research, the survey study is limited to gathering responses to qualitative questions rather than collecting data points as in the benchmarking exercises (cf. chapter 3). The survey comprises 38 questions in total.

All questions directly or indirectly address the interplay of OPEX across manufacturing and quality control. Thus, answer options comprise either responses for both departments, or ratings between departments are questioned. Tailored questionnaire items additionally ask the respondent to select or prioritize between both departments. The majority of questions uses a multiple-choice scale with single response options. Additionally, study participants are asked to indicate starting times

of OPEX initiatives and application of selected practices in manufacturing and quality control at their production sites. Furthermore, free text fields allow to state brief descriptions of applied procedures to allocate OPEX resources and embedding a culture of Continuous Improvement. Appendix A.6 depicts the full survey including all answer options.

For this purpose, a study model structuring the survey and all underlying questions has been developed. It contains the three major categories *Structural Context & Infrastructure*, *Level of Excellence* and *Barriers & Levers*. The study model is shown in Figure 85.

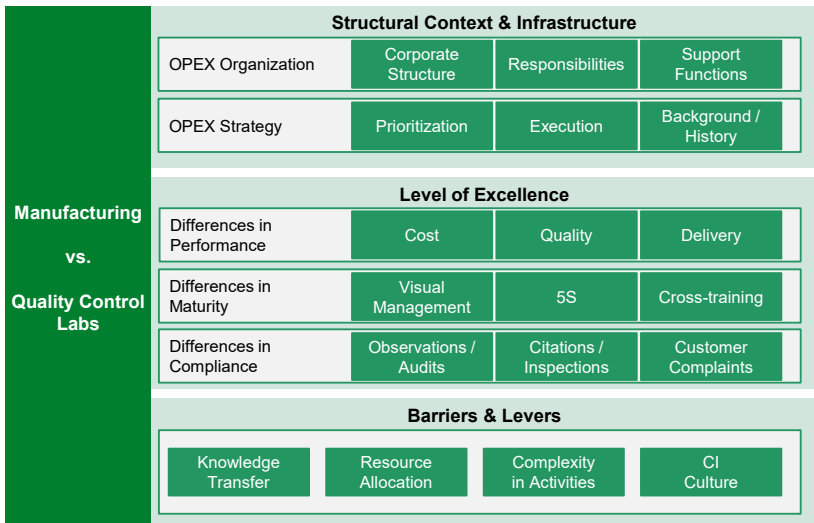


Figure 85: Survey Structure and Categories

Each category summarizes several underlying subject fields and questions allowing to identify patterns within and across the categories. Content-wise focus within the categories has been selected based on observations from the benchmarking studies, learnings from industrial collaboration projects¹⁴ and was additionally informed by discussions and workshop outcomes of both St.Gallen Industrial Research & Exchange Groups (cf. chapter 1.2.5).

The first category *Structural Context & Infrastructure* investigates the organizational set-up and the strategy to Operational Excellence in manufacturing, quality control, and across departments. Responsibilities for driving, planning, and executing

¹⁴ In his role as Research Associate at the University of St.Gallen, the author consulted different pharmaceutical companies in launching & maintaining OPEX initiatives, designing KPI systems, implementing Production Systems, and optimizing shop-floor routines.

improvement projects in both departments are questioned alongside with availability of resources and support provided by site or corporate functions. Particular attention is paid on whether OPEX initiatives follow a comprehensive strategy considering cross-departmental targets and their interplay. Furthermore, study participants are asked to indicate the starting year of having rolled out first OPEX initiatives in manufacturing and quality control at their production sites. The history of a site and its departments can indicate both the experience with OPEX practices and the priority assigned to this subject field in manufacturing or quality control. Furthermore, responses allow to evaluate whether the OPEX philosophy was rolled-out sequentially in departments or in parallel across the entire production site.

Subsequently, the next category *Level of Excellence* provides insights on the existing status of performance, maturity, and compliance. All subject fields are self-evaluated by the respondent. Fundamentally different to the benchmarking programs, the survey does not include measurement instruments to quantify department's or site's performance compared to external peers. Instead, the participating site is asked to simply self-assess performance, maturity, and compliance in a direct pairwise comparison of manufacturing and quality control within the production site. Keeping the balance and considering trade-offs ensures the comprehensiveness of comparisons within each subject field: Performance reflects all cost, quality, and delivery. Maturity summarizes the fundamental OPEX enablers 5S, Visual Management, and Cross-training of employees (cf. chapters 3 and 4). Compliance¹⁵ discusses outcomes of regulatory inspections, internal audits, and customer complaints on products in the market.

Finally, the third main study category *Barriers & Levers* addresses concrete challenges for cross-departmental alignment of OPEX initiatives and asks for production sites' approaches to overcome these. Following the iterative research approach of this thesis, it strives to confirm relevance and applicability of previous identified hurdles (cf. chapter 4.4) such as structured knowledge transfer, resource allocation and different cultures across pharmaceutical manufacturing and quality control. Levers for improvement are explored by free text descriptions of site's approaches to tackle these challenges and allow to uncover already existing successful practices in industry. Furthermore, the free text field questions comprise brief descriptions of approaches to allocate OPEX resources and embedding a culture of Continuous Improvement.

The survey has been realized using the online platform Unipark to easily allow respondents to provide answers and to make participation as convenient as possible. According to the data gathering strategy of the thesis (cf. chapter 1.2.5), the survey

¹⁵ Different to chapter 3.2, compliance does not solely focus regulatory compliance and outcomes of authority surveillance. As company internal audits and customer complaints are incorporated as well, the subject field summarizes all direct or indirect external evaluations of product and process quality.

has been rolled out across selected OPEX functions in manufacturing and quality control, previous benchmarking program participants, and members of the St.Gallen Industrial Research and Exchange Groups. As the scope of the questionnaire was defined to covering an individual pharmaceutical production site, participation of multiple sites from the same company required to fill one survey for each facility. This has been clearly communicated to all respondents.

Consequently, site leaders, local heads of production/quality, or site OPEX specialists have been the primarily target audience and preferred responding functions. However, above-site functions were deemed eligible to answer on behalf of specific sites they are particularly knowledgeable of. These corporate contacts have also been involved in the study distribution and acted as multipliers to engage production sites of their company's networks to participate.

All responses to the survey have been gathered between November 2020 and March 2021. Thus, the sample contains only recent data and accurately represents the current status in pharmaceutical production. In total, 27 pharmaceutical production sites from 13 companies around the globe participated in the study and completed the questionnaire. Figure 86 presents the geographical distribution of the sample: The majority of participating production sites is located in Europe, while North America, South America and Asia are represented by smaller proportions. Thus, the regional set-up of the sample is similar to the St.Gallen benchmarking databases (cf. chapter 3.2), what ensures credibility of overarching findings based on triangulation of implications drawn from different data sources throughout the thesis.

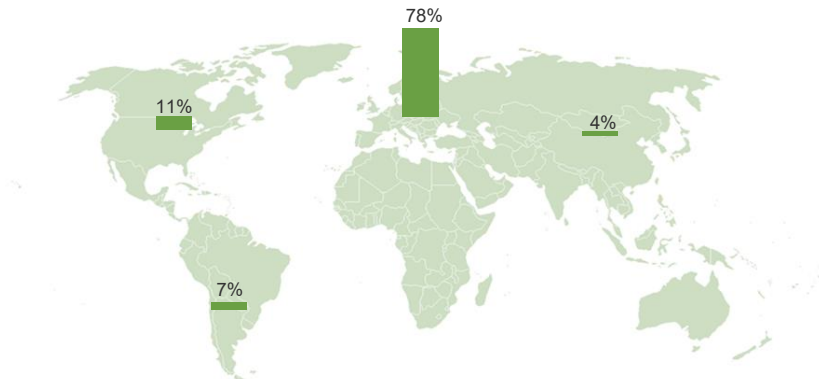


Figure 86: Survey Based Study – Sites per Region

The population includes producer of branded pharmaceutical products, generic drugs and CMOs. Furthermore, different types of production technologies are covered as depicted in Figure 87.

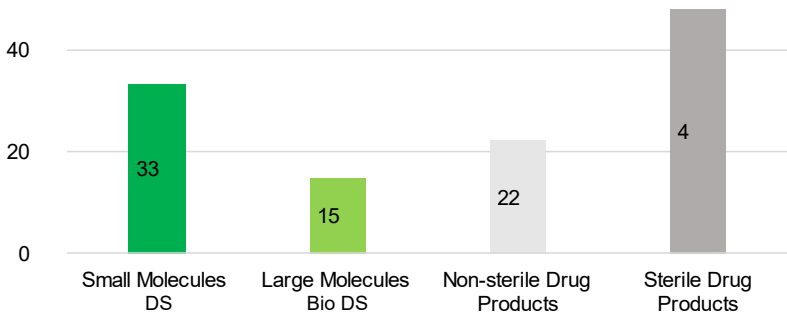


Figure 87: Survey Based Study – Production Technologies

Additionally, the profiles concerning centralized and decentralized testing operations (cf. chapter 3.2.1) can act as indicator for the sites' roles in their company network. As visualized in Figure 88, the majority of participants focuses on dedicated local testing, while almost a third of production sites is taking responsibility to serve the network with centralized testing in addition.

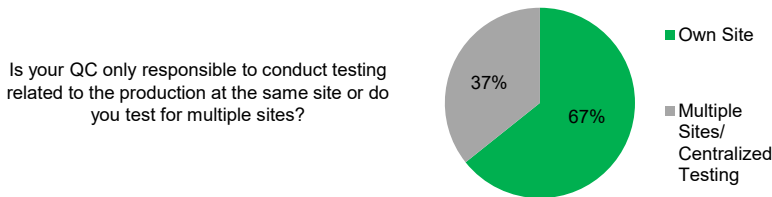


Figure 88: Survey Based Study – Centralized & Decentralized Testing

Consequently, a diverse set of manufacturing sites representing different types of pharmaceutical production contributed to the study. The number of participants $n = 27$ is deemed sufficient to make use of the survey responses twofold: Comparing, analyzing, and discussing responses across the sample allows to draw conclusions on the current status of embedding integrated OPEX management across departments (cf. chapter 5.3) in industry. Besides that, successful practices for aligning manufacturing and quality control can be identified based on the procedures uncovered and serve as basis for subsequent discussion within the case studies (cf. chapter 5.4).

5.3 Results, Discussion & Case Selection

Outcomes of the survey-based study on OPEX across manufacturing and quality control are presented and discussed in the following. All results are outlined according to the study model introduced in chapter 5.2, subsequent passages are structured along its main categories *Structural Context*, *Level of Excellence* and *Barriers & Levers*. Discussion of the outcomes is additionally informed by conversations and workshop sessions during meetings of the St.Gallen Industrial Research & Exchange Groups (cf. chapter 1.2.5). Finally, cases for detailed successful practice interviews are selected based on their survey responses.

Structural Context – OPEX Organization and Strategy

At first, a series of questions investigates organizational set-ups and strategies to Operational Excellence in the pharmaceutical industry. In addition to exploring different approaches for prioritization and execution of OPEX initiatives at the surveyed sites, the companies' above-site OPEX resources and corporate support provided are considered as well.

Figure 89 reveals the proportion of production sites belonging to companies that operate an above-site OPEX organization. Any kinds of central OPEX organization are considered, regardless of the specific nature or aim.

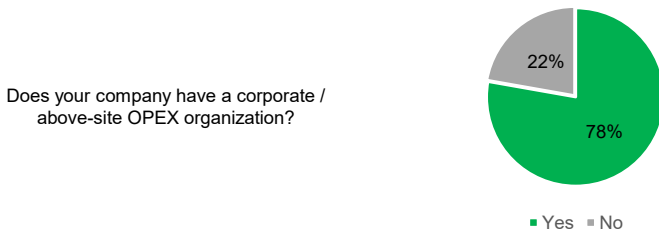


Figure 89: Corporate OPEX Organization

Operating central OPEX organizations has become common in pharmaceutical production. Around four out of five corporations run such organizations, usually as integral part of the global technical operations unit. Historically, OPEX organizations in pharmaceutical companies showed a focus on manufacturing operations in general. A need for OPEX in further departments evolved in the more recent past. Ramping-up dedicated above-site organizations, or splitting and tailoring overarching OPEX organizations, has been driven by the current focus on OPEX in quality control (cf. chapter 1.1.1) among further contributing factors. The as-is presence of departmental OPEX organizations dedicated to manufacturing and quality control in the industry is outlined in Figure 90.

Besides the general OPEX organization:
Does your company run a corporate / above site organization dedicated to OPEX per department manufacturing or quality control?



Figure 90: Corporate OPEX Organization Dedicated to Departments

Almost the half of the production sites are part of corporations that operate above-site OPEX organizations dedicated to either manufacturing or quality control, while a higher proportion of departmental organizations is dedicated to manufacturing than to quality control. None of the responding sites indicated that their company is operating a dedicated QC organization but no counterpart for manufacturing. Thus, observations are in line with the assumption that dedication to QC is newly evolving from – or in addition to – general above-site organizations. Dedicated QC OPEX organizations usually build on established initiatives for manufacturing.

However, providing specific corporate OPEX support to departments at production sites does not necessarily require a formalized and dedicated above-site organization. Figure 91 presents the corresponding survey item.

Does your company provide corporate / above-site support (e.g. training, tools) to drive forward OPEX in manufacturing and quality control at your site?



Figure 91: Corporate OPEX Support Dedicated to Departments

Although above-site OPEX organizations dedicated to quality control are less common than organizations assigned to manufacturing, both departments are nearly equally often supported by corporate in any way within the sample sites. The discrepancy between both questions can be explained by the role of above-site quality

organizations in pharmaceutical networks: Even if not formally dedicated to OPEX, global quality roles can also contribute with expertise and support production sites in optimizing their quality control procedures according to the principles of Continuous Improvement.

Despite the availability of OPEX support by above-site resources, responsibilities and ownership for Operational Excellence can be taken by different functions either on site or corporate level. Approaches differ across production sites determined by the degree of autonomy from corporate functions, the individual site role in the network, the experience and maturity of the site, or its management culture. In case responsibilities are assigned to site level functions, this can involve either site-wide OPEX organizations, dedicated departmental OPEX functions at the site, or selected departmental employees not dedicated to OPEX but taking ownership for Continuous Improvement as part of their job in addition to other tasks. None of the different options for allocating responsibilities can be recommended in general terms, suitability heavily depends on the present context of the individual sites. However, it is important that ownership is defined and responsibilities are fulfilled accordingly. There must be a clear and common understanding across all roles contributing either operatively or strategically to the OPEX program. Figure 92 shows the distribution across pharmaceutical production sites highlighting differences between manufacturing and quality control.

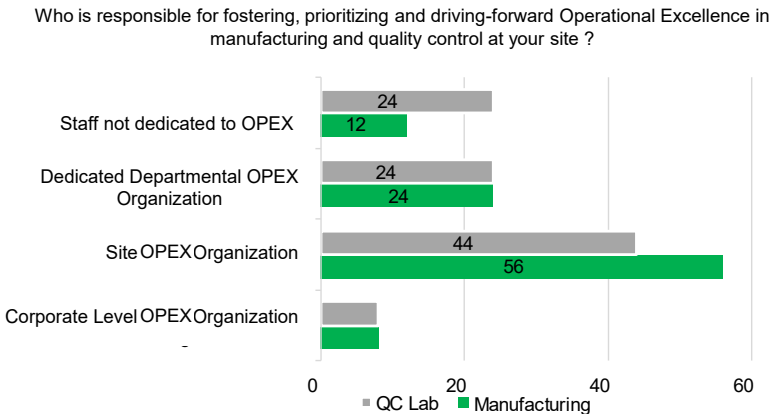


Figure 92: OPEX Responsibilities

In most cases, OPEX programs are driven and prioritized by site level organizations. Only few production sites indicated the above-site organizations taking the lead to define the site's priorities. This observation generally holds true for manufacturing and quality control related OPEX topics, while responsibilities are more often delegated to employees not dedicated to OPEX in quality control than in production.

Analogously, the execution of improvement projects in manufacturing and quality control is analyzed across the different sites and departments. Taking responsibility for defining OPEX priorities and ownership for the OPEX program does not necessarily comprise the implementation and realization of defined improvement measures in the departments. Depending on the overarching organizational set-up, these tasks are fulfilled by different roles. An overview across the survey sample is given in Figure 93.

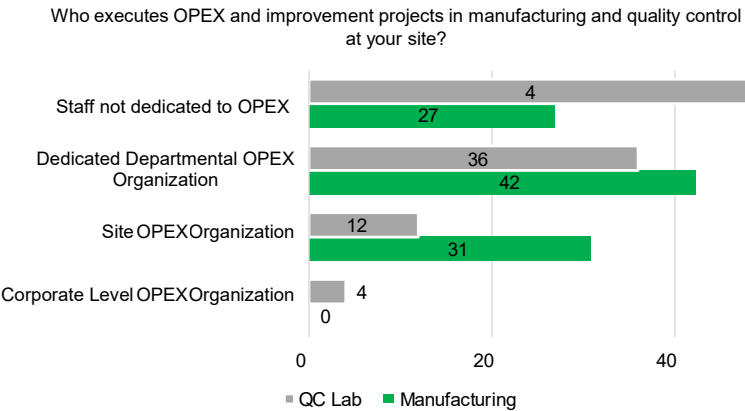


Figure 93: OPEX Execution

Compared to taking responsibility for setting priorities of the OPEX program, project execution is primarily approached by the individual departments. However, different distributions across manufacturing and quality control are observable: While execution within manufacturing is noticeably supported by resources of the site OPEX organizations, much more efforts are spent on OPEX projects by not dedicated employees in quality control. The pattern confirms the perception that central OPEX organizations are still more focused on manufacturing than quality control. This can be caused by either the history of the programs originated from production or the more specific expertise required within laboratories.

In the following, the history of OPEX approaches across the different production sites is outlined. Running OPEX initiatives on site level or departmental level is not entirely new to the pharmaceutical industry, but starting periods differ across sites and departments. Figure 94 provides a summary of the production sites in the survey sample, which stated the year of initially starting activities in manufacturing and quality control.

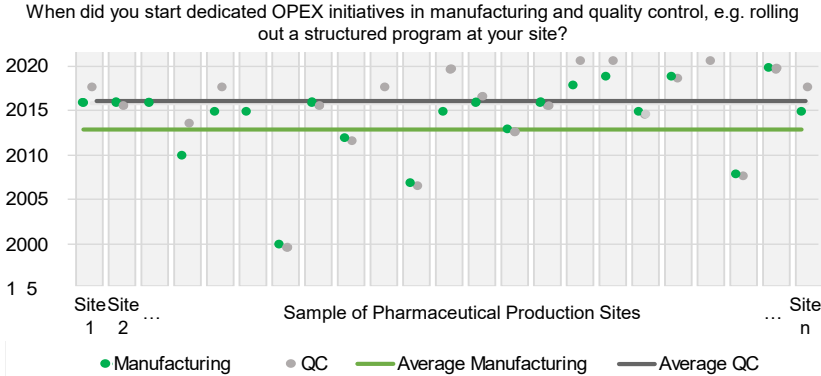


Figure 94: Start of OPEX Programs within Manufacturing and Quality Control

Most of the production plants started their OPEX programs after 2010. About the half of the sites already launched cross-departmental programs integrating manufacturing and quality control or started respective departmental programs in parallel. All other sites started with initiatives in manufacturing and followed-up in quality control at a later point of time. No cases of production sites starting OPEX initiatives in quality control prior to manufacturing can be observed.

Roadmaps are one of the available methods to formalize the OPEX strategy and the aspired direction of the program for a short, mid, and long-term horizon. Formalizing roadmaps can either act as integrated part of the OPEX program or the site's strategy process beyond Operational Excellence. The current status of applying OPEX roadmaps in the participating pharmaceutical production sites is depicted in Figure 95.

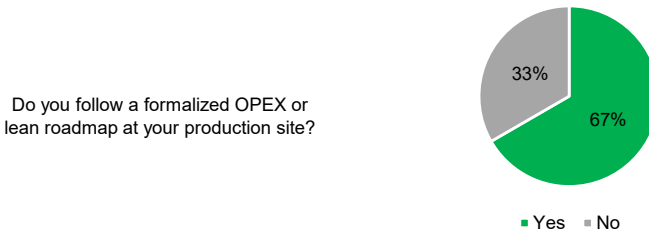


Figure 95: Application of OPEX Roadmaps

Most of the responding production sites formalize their OPEX initiatives in roadmaps. Such roadmaps can be set-up in very different ways and comprise varying levels of detail: Depending on focus and integration with the OPEX approach, roadmaps also include departmental targets in addition to documenting and

scheduling priorities. Responses to the question of whether industry's current roadmaps comprise specific targets are summarized in Figure 96.

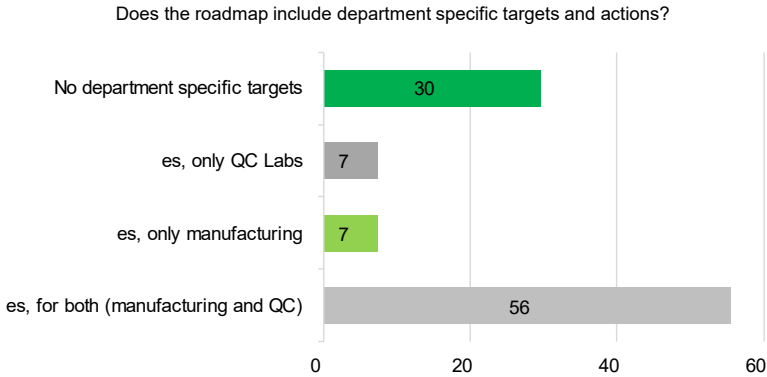


Figure 96: Target Setting within OPEX Roadmaps

70 % of respondents include specific departmental targets in their OPEX roadmaps. Since only a minority limits target setting to either manufacturing or quality control and no higher attention on one of the departments can be observed, it seems like roadmaps are usually formalized in an integrated manner and linked to the site strategy rather than acting as isolated framework for departmental execution.

Summarizing the OPEX structure and strategy of the survey study participants, most companies operate an above-site OPEX organization. In addition to that, more than the half of the companies generally provide above-site support related to OPEX dedicated to manufacturing and quality control. While the proportion of dedicated support provided by corporate is on a comparable level across departments regardless of the organizational structure, it is much more common in industry to establish formal OPEX organizations dedicated to manufacturing than its counterparts dedicated to quality control.

At the site level, most OPEX programs have been started after the year 2010. All sites not having launched initiatives concerning manufacturing and quality control in parallel approached production first and broadened the scope to laboratories at later points of time. Two of three establishments organize their OPEX programs according to a formalized roadmap that comprises specific targets for manufacturing and quality control. While prioritization of OPEX is similarly driven by the site OPEX organization in both departments, implementation differs between manufacturing and quality control: Execution of OPEX activities is more often performed by non-dedicated employees in the laboratories. Unlike that, improvement projects in manufacturing are usually executed by site or departmental resources dedicated to OPEX.

Level of Excellence – Differences in Performance, Maturity and Compliance

The next category of the survey aims to reveal the current status of Operational Excellence and its impact in manufacturing and quality control at the production sites. This comprises self-evaluation of quality, delivery performance, and cost efficiency operationalized by directly ranking manufacturing and quality control against each other. Furthermore, the level of maturity in departments is evaluated in the elements 5S, Visual Management, and Cross-functional Qualification alongside with the departmental outcomes of audits and inspections.

Quantitative research based on the St.Gallen benchmarking databases identified deviation rates as important indicators for process quality within and across manufacturing and quality control (cf. chapter 3.2). That is why deviations are used as simplified measure to question process quality related issues in the survey study. Outcomes are presented in Figure 97.

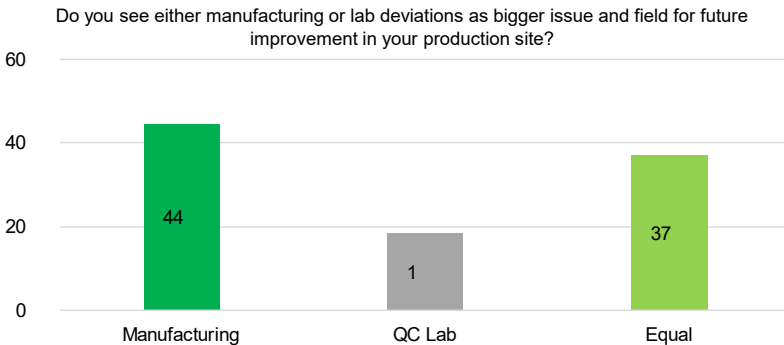


Figure 97: Deviations in Manufacturing and Quality Control

More than double of responding sites indicated deviations in manufacturing processes as bigger issues compared to QC lab deviations. However, almost one third of all sites rates the need for improvements with regard to deviations in both departments on an equal level.

Approaching departments' contribution to the value chain and delivery performance from a site perspective, the relative criticality of manufacturing and quality control for supplying on time is questioned. Answer distributions are depicted in Figure 98.

What part of the site internal value chain (and respective department) do you consider especially as bottleneck for on-time release and delivery?

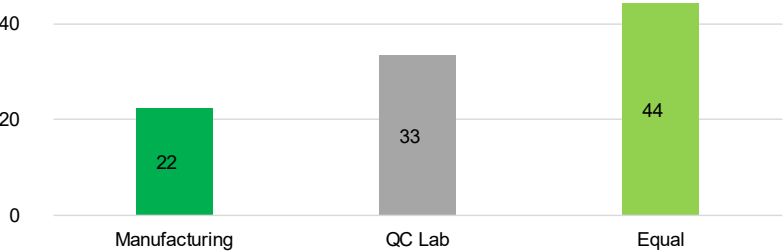


Figure 98: Release and Delivery Bottlenecks

Underlining the importance of integrated management across manufacturing and quality control, the majority of production sites considers both departments as equally important for on-time release and delivery. However, a slight tendency for experiencing quality control more often as a bottleneck can be observed.

Informed by the Quality Benchmarking Study (cf. chapter 3.3), adhering to defined standard lead times is a key success factor for delivering on-time in full. That is why ATL is evaluated across departments in Figure 99. In this way, challenges production sites are particularly facing along their internal value chain are uncovered.

In case there are defined lead times for production and testing processes: Do you see a better average adherence to defined standard lead times (ATL) in manufacturing or quality control?

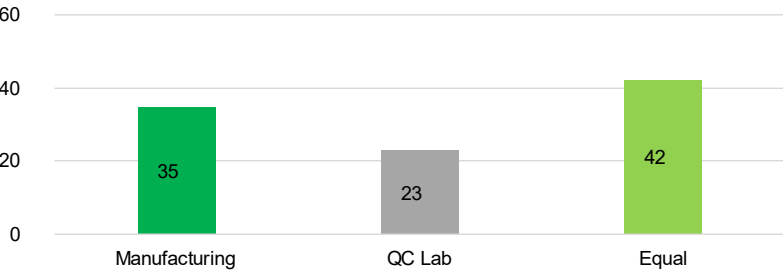


Figure 99: Adherence to Lead Time in Manufacturing and Quality Control

Following the Just-in-Time philosophy, most producers constantly reduce inventories of raw materials, finished goods, and intermediates. Consequently, discrepancies from the planned schedule in any process step negatively impact the entire value chain. There are no major differences in ATL performance recognizable across the sample. However, in line with findings of the previous question, more production sites are reporting a better ATL in manufacturing. This leads to the conclusion that quality control is struggling more often with fulfilling the planned schedules.

Complementing the performance related set of questions, perceptions on especially prioritizing cost efficiency in either manufacturing or quality control are compared to each other. Figure 100 shows the ranking across the sample of production sites participating in the study.

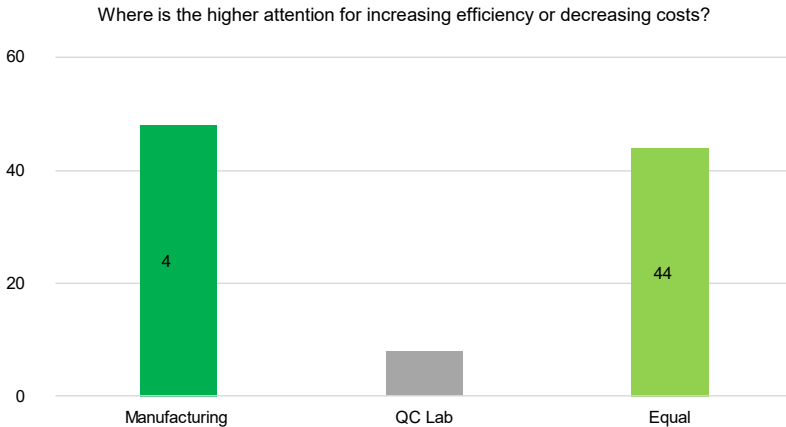


Figure 100: Attention on Cost Efficiency in Manufacturing and Quality Control

The answers reveal a higher pressure for decreasing costs in manufacturing than in quality control. Due to the role as quality safeguard and its regulatory relevance, companies still optimize cost structures in quality control with more caution than in manufacturing. However, almost half of respondents answered that there is equal attention on decreasing cost in quality control. Unlike in the past, striving for more efficiency has been one of the drivers for recently evolving excellence initiatives dedicated to the laboratory operations of pharmaceutical production sites.

The just discussed pressure to decrease costs in both parts of the organization usually comes along with saving targets defined by upper site level or above-site management. Depending on the nature and comprehensiveness of OPEX programs, such targets are built into improvement roadmaps and linked to achievements from optimization projects or separately driven by controlling functions. Both approaches are well established in the pharmaceutical industry and can lead to a different positioning and understanding of OPEX initiatives in the organization. Resulting differences impact employee's motivation to contribute to improvement projects within and across their departments (cf. chapter 4.4). The current status of departmental cost target setting across the survey sample is presented in Figure 101.

Do you currently follow active, specific targets for increasing efficiency or decreasing costs in manufacturing and quality control?



Figure 101: Efficiency Targets in Manufacturing and Quality Control

In line with the previous observations on the level of attention for cost efficiency, the majority of production sites follows specific targets to increase cost efficiency in both departments. Slightly more respondents report active targets in the area of manufacturing compared to quality control. Hence, even if cost efficiency is a priority across the entire sites, the initial statement on more reluctance to aggressive cost cutting in quality departments is visible in the answer distributions.

After having discussed performance differences across manufacturing and quality control, subsequent passages focus on maturity levels at the production sites. 5S is one of the fundamental and most often applied improvement principles of OPEX initiatives and Production Systems. Figure 102 shows the current status of application in manufacturing and quality control based on the survey study.

Did or do you actively apply 5S principles in manufacturing and quality control at your site?



Figure 102: 5S Application in Manufacturing and Quality Control

Three of four production sites have implemented 5S across both departments manufacturing and quality control. No remarkable differences in distributions are visible. Further investigating the site's perspectives on the 5S methodology, Figure 103 discusses differences in the 5S maturity for the group of production sites having reported to apply 5S in both departments.

Where do you see the higher maturity in applying 5S principles (e.g. shadow boards) at your site?

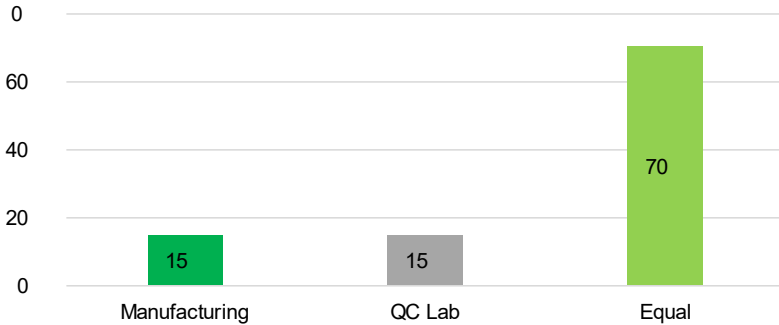


Figure 103: 5S Maturity in Manufacturing and Quality Control

Absolutely no differences in maturity levels are revealed. Even the sites that did not attest an equal level of 5S maturity to their production areas and laboratories, show an equal distribution between higher rankings of manufacturing or quality control. These findings are in line with the analyses of the St.Gallen benchmarking databases: Housekeeping has been found an enabler category significantly associated across the departments manufacturing and quality control (cf. chapter 3.2).

Nevertheless, similar levels of maturity can be reached by different approaches to implementation. Researching the present level of OPEX integration across manufacturing and quality control, the next question asks for cross-departmental standardization of 5S implementation. Outcomes are depicted in Figure 104.

Do you follow a corporate or site-level standard to implement and sustain 5S? Or do approaches across departments differ?

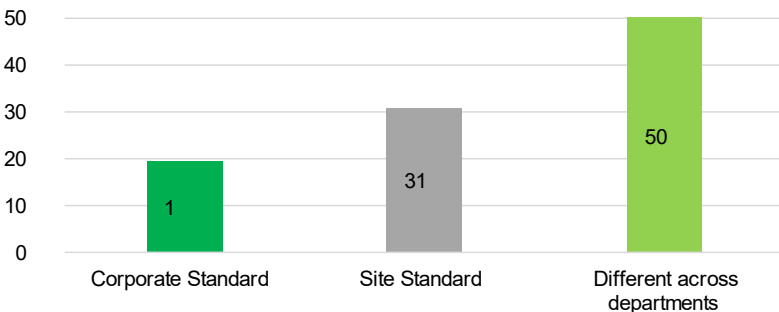


Figure 104: 5S Standards across Departments

The sample shows diversity in approaching and aligning 5S across departments. Half of production sites answered to follow different procedures across departments, while the rest of the production sites adheres to site or corporate standards for 5S

in manufacturing and quality control. Interestingly, all these different approaches seem to result in equal levels of maturity. Hence, the need for either standardization or departmental adaption of approaches to 5S implementation is determined by the individual context of the production site.

Completing the series of 5S related questions, the time period of implementation in manufacturing and quality control is presented in Figure 105. Considering the consistency in maturity levels and understanding 5S as one of the foundational elements of OPEX initiatives, rather early implementation compared to other tools and methods is expected.

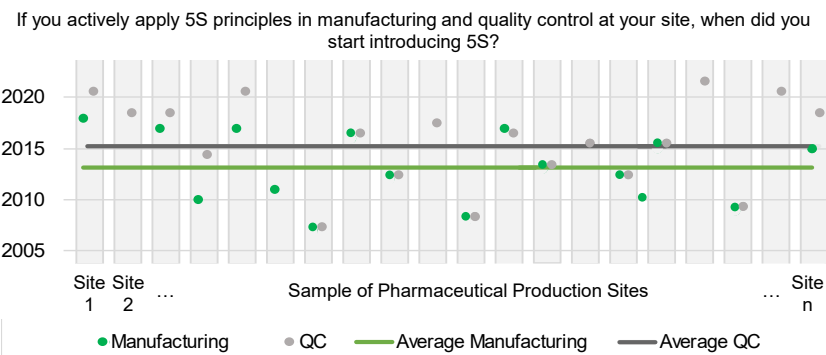


Figure 105: 5S Introduction in Manufacturing and Quality Control

Answers from the surveyed production sites confirm the assumption. 5S implementation has been started early and in the same timeframes of generally launching structured OPEX initiatives for the first time. However, the cross-comparison of manufacturing and quality control echoes the diversity of approaches to 5S implementation: Only a few production sites started approaching 5S in parallel within both departments. Usually, 5S has been implemented in manufacturing first and subsequently transferred to quality control. Since these sequential approaches mostly started years ago from today, this observation does not contradict the equal level of maturity observed in production areas and laboratories. Compared to other OPEX enablers, 5S initiatives are rather simple to organize and can be realized in reasonable time horizons. Hence, even if laboratories started later, 5S implementation seems to be completed in these areas analogously to manufacturing.

As additional enabler besides 5S, the application of Visual Management and usage of corresponding boards is discussed. Visual Management is one of the most insightful OPEX enablers since it combines technical and managerial maturity: Having introduced performance indicators and visualizing them at the floor also comes along with management routines to steer operations accordingly, i.e. by conducting

stand-up meetings. The current status of Visual Management usage in industry is summarized in Figure 106.

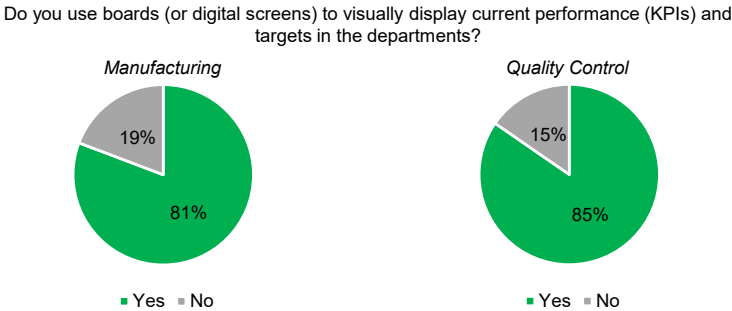


Figure 106: Visual Management Application in Manufacturing and Quality Control

Similar to the previously discussed application of 5S methods, Visual Management is widely used in the industry and no differences across manufacturing and quality control can be identified. Moreover, Figure 107 reveals ratings of maturity in Visual Management comparing both departments.

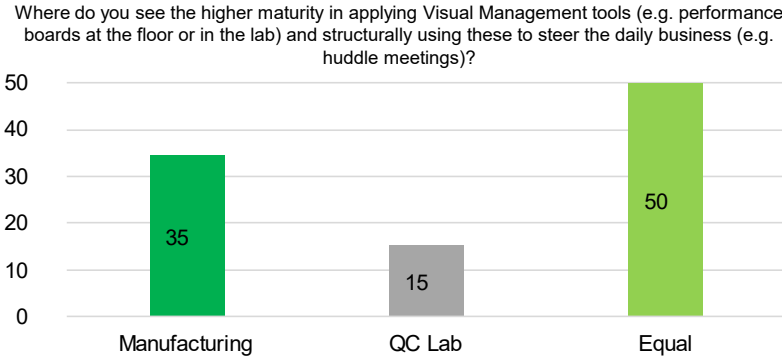


Figure 107: Visual Management Maturity in Manufacturing and Quality Control

The half of production sites indicated equal levels of maturity in applying Visual Management within manufacturing and quality control. Out of all production sites reporting differences in maturity, the proportion of facilities being more mature in manufacturing doubles the sites indicating a higher maturity in quality control.

Striving to understand the underlying drivers for Visual Management implementation and the way of execution, a follow-up question investigates whether sites define cross-departmental standards, adhere to corporate procedures, or design their Visual Management departmental. Results are outlined in Figure 108.

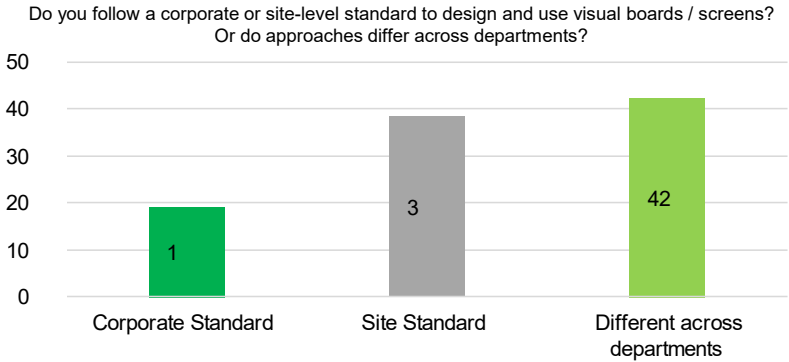


Figure 108: Visual Management Standards across Departments

There is a similar number of production sites following a site standard for Visual Management and sites approaching the enabler differently across departments. Thus, compared to 5S, Visual Management is rolled-out more standardized across departments. This observation can be explained by the managerial component of Visual Management: Huddle meetings are often performed as part of a site-wide tier meeting cascade also comprising cross-departmental stand-up meetings and boards. Consistency in Visual Management application along the cascade also motivates cross-departmental standardization of procedures within departments.

Reviewing the history of Visual Management application, the point of time for introduction in manufacturing and quality control has been questioned. The sample's distribution is presented in Figure 109.

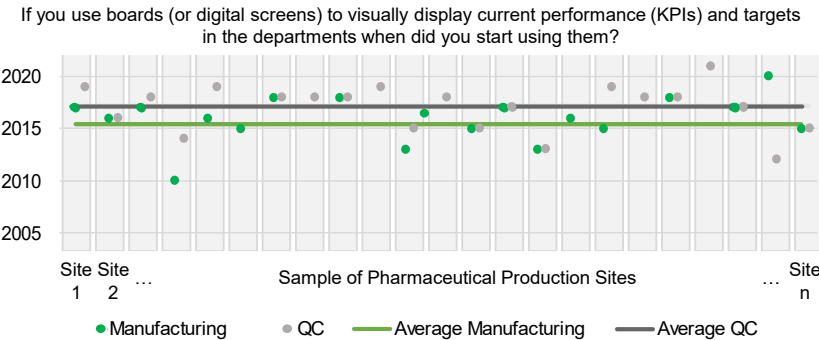


Figure 109: Visual Management Introduction in Manufacturing and Quality Control

Compared to 5S implementation, the systematic introduction of Visual Managements has been started later in industry. The higher degree of cross-departmental

standardization in Visual Management is also visible in the timeline overview: Visual Management has often been implemented in parallel. If not, application usually started in manufacturing prior to quality control.

The third OPEX enabler included in the survey-based study explores cross-training of staff in manufacturing and quality control. Corresponding answers of participating production sites are depicted in Figure 111.

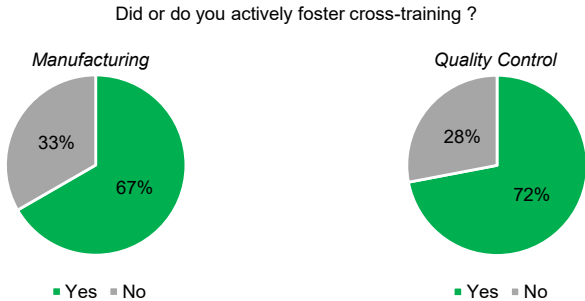


Figure 110: Cross-Training in Manufacturing and Quality Control

Cross-training is similarly fostered in manufacturing and quality control. Evaluating if employees are capable and qualified to fulfill multiple roles within their department, the level of cross-training can reveal insights on the flexibility of the organization to react to discrepancies or cope with limited resources in peak times. Figure 111 presents the observed level of cross-training in manufacturing and quality control.

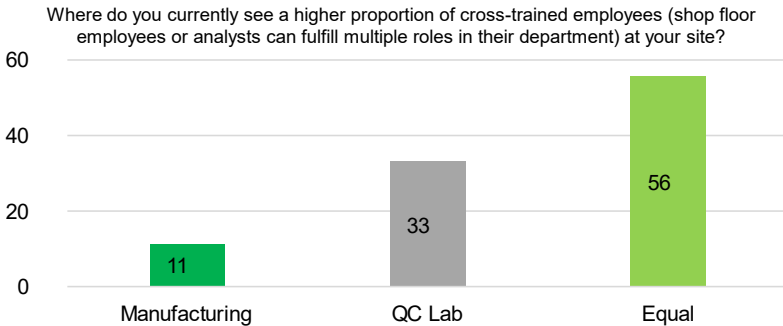


Figure 111: Proportion of Cross-Trained Employees in Manufacturing and Quality Control

Slightly higher levels of cross-training can be stated for quality control. However, most sites reported equal proportions of cross-training for manufacturing and quality control. Detailing this subject field, Figure 112 discusses how targets for cross-training are defined at the surveyed production sites and whether the target setting process differs for production areas and laboratories.

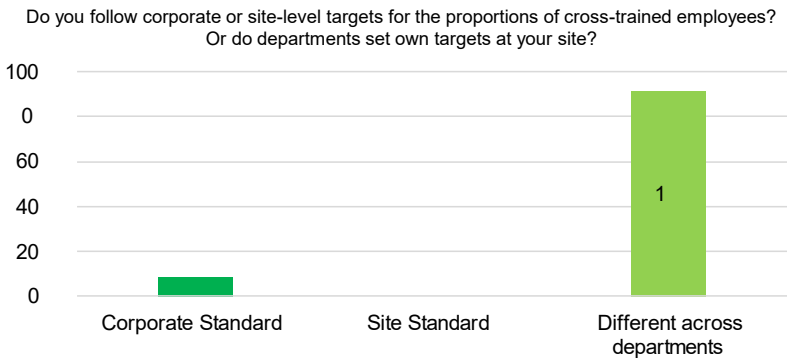


Figure 112: Cross-Training Standards across Departments

Apart from three production sites referring to corporate standards for cross-training, all facilities reported that targets for cross-training are defined differently across departments. This pattern can lead back to the individual task profiles within the departments. Depending on the site's nature and its operational profile, the need for flexible labor differs between departments. While cross-trained labor might be required in the set-up of a site's quality control, that does not have to be the case in manufacturing. One ostensive example is centralized testing performed for the network by the local quality control department. A broader test profile in laboratories due to the support of the network does not impact the qualification profiles required in manufacturing departments of production sites.

Analogous to 5S and Visual Management, the survey asked since when cross-training is actively fostered and a priority in manufacturing and quality control. Responses are summarized in Figure 113.

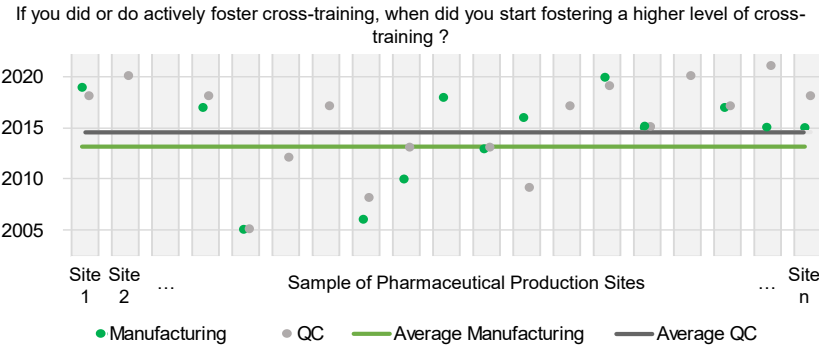


Figure 113: Cross-Training Introduction in Manufacturing and Quality Control

The time-wise distribution of evolving focus on cross-training does not show clear patterns across manufacturing and quality control. There seems to be less consistency with the timelines for generally introducing OPEX programs compared to 5S and Visual Management: Even if cross-training is an OPEX enabler, it does not necessarily have to be approached under the umbrella of an excellence initiative. Unlike 5S or Visual Management, fostering cross-training within and across departments can also be simply driven by the operational need for broadly qualified labor and trace back to the variety of tasks caused by the facilities' portfolio.

Completing the study category *Level of Excellence*, differences in compliance between manufacturing and quality control are investigated in addition to performance and maturity. As earlier indicated, the section compliance summarizes the perspectives of internal audits, inspections, and customer complaints related to products in the field. At first, it has been surveyed if the production sites are audited by corporate functions in manufacturing and quality control. Figure 114 outlines the answer distribution.

Does your company run an internal corporate audit program for manufacturing areas and quality control labs?



Figure 114: Corporate Audits in Manufacturing and Quality Control

Almost all production sites are audited by above-site organizations. Since most of the facilities are part of company networks and multinational corporations, experiencing audits is very common and part of regular routines. This observation holds true for audits concerning either manufacturing or quality control.

Corporate audits are regularly performed to review compliance with defined standards and procedures. Like authority inspections, audits can provide an enriching perspective for evaluating the overall health of production sites in addition to review performance indicators and perform maturity assessments (Friedli et al., 2019, p. 67). Consequently, outcomes of corporate audits and their breakdown in the departments manufacturing and quality control have been explored as part of the survey-based study. The comparison of audit results between production areas and laboratories is expounded in Figure 115.

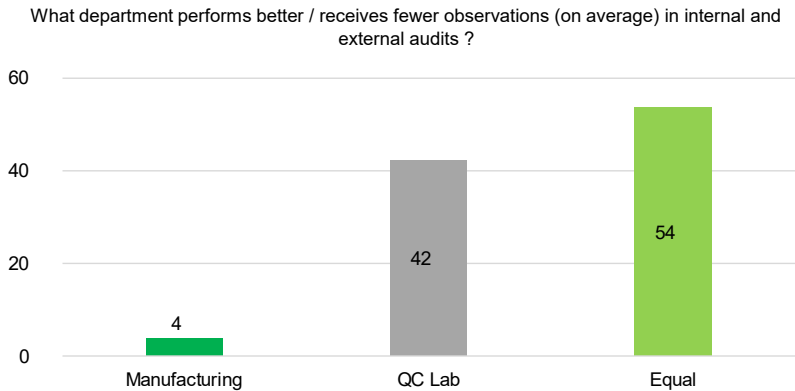


Figure 115: Audit Outcomes in Manufacturing and Quality Control

More than the half of production do not indicate differences in audit performance across manufacturing and quality control. Focusing the other half of the sample, almost all production sites reported more favorable audit outcomes in quality control. Analogously, Figure 116 presents the questioned outcomes of regulatory inspections, especially focusing on inspection results that comprised citations related to a specific department.

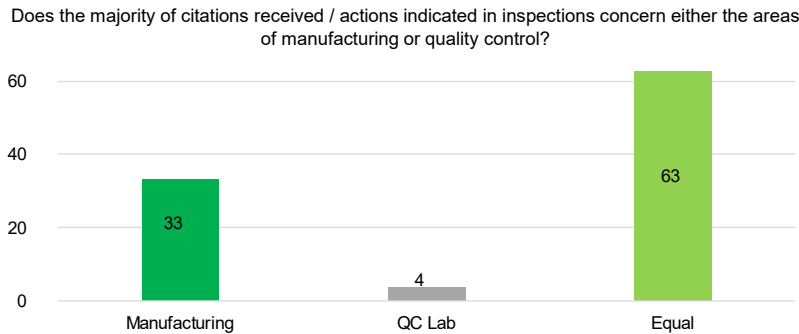


Figure 116: Inspection Outcomes in Manufacturing and Quality Control

Responses reveal a pattern similar to the corporate audit outcomes: The majority of production sites does not report a tendency of better inspection results for either manufacturing or quality control. However, in case of differences indicated, most of citations concern the production area, while only one single establishment answered that it is struggling more with citations related to quality control.

All customer complaints concerning products produced at site require actions of the facility according to defined procedures. After having initially justified the complaint

and traced it back to an area, the respective department investigates causes and starts to eliminate potential failure sources. The proportions of reactions on customer complaints within manufacturing and quality control across the sample are depicted in Figure 117.

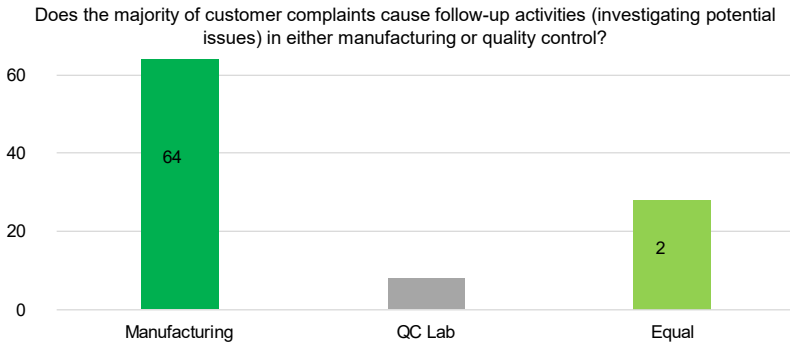


Figure 117: Customer Complaints in Manufacturing and Quality Control

Unlike audit and inspection outcomes, customer complaints show a clear tendency of being mostly related to manufacturing operations. Since justified customer complaints concern product instead of process quality, such a pattern is in line with expectations. Laboratory issues are usually not visible to the customer.

Summarizing outcomes of the second study category *Level of Excellence*, a set of commonalities and differences across manufacturing and quality control has been observed. All three sections performance, maturity, and compliance have revealed insightful patterns supporting and confirming findings of the quantitative analyses based on the benchmarking databases (cf. chapter 3).

Deviations challenge production sites mostly in manufacturing, while quality control shows a weaker adherence to standard lead times and is more often considered as bottleneck for on-time release and delivery. 5S and Visual Management are broadly implemented in the industry regardless of manufacturing or quality control. However, standards and specifications are not necessarily aligned along the value chain. Different to Visual Management, the procedures for 5S implementation are individually specified and driven by departments. Only a few production sites follow above-site standards for application of both OPEX tools. Cross-training of employees is heavily focused by respondents across the sample, no higher or lower importance for manufacturing or quality control is remarkable even if slightly more production sites indicated a higher maturity in laboratories. Both departments are regularly audited by corporate functions and inspected by authorities. In case of departmental differences in audit and inspection outcomes, surveyed production sites report more concerns related to manufacturing. In line with this pattern, most customer complaints lead to follow-up activities in production areas and concern quality control less often.

Barriers and Levers

The third category of the survey-based study particularly addresses barriers and levers for cross-departmental alignment and integrated OPEX management. It comprises questions related to information & knowledge exchange, resource allocation, and the CI culture at site. In addition to the answer distributions presented and discussed in the following, open-ended free text questions have allowed respondents to briefly describe how the subjects are addressed at the respective production sites. Among the answers given to the categorial questions, these descriptions allow for subsequent identification of successful practices and selection of cases.

Information and knowledge transfer across departments does not only happen accidentally but can be actively addressed by OPEX management (cf. chapter 4.4). Consequently, the survey asks production site for their approaches. Responses are summarized in Figure 118.

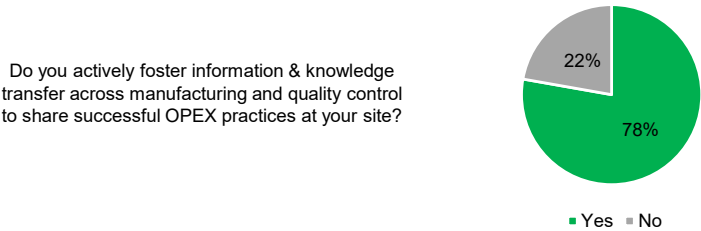


Figure 118: Information & Knowledge Transfer across Manufacturing and Quality Control

Almost four of five production sites reported to actively foster information & knowledge transfer across manufacturing and quality control. Based on the descriptions provided, selected successful practices to do so are latterly detailed in the case studies presented in the next chapter. Effectiveness of the applied procedures for information & knowledge transfer is evaluated in Figure 119.

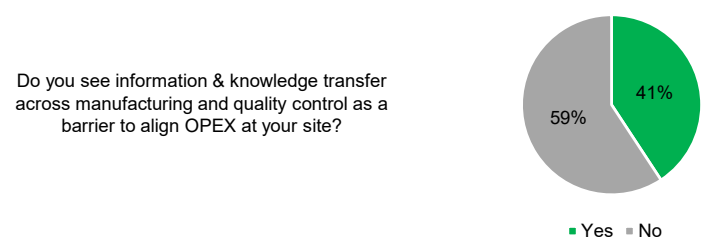


Figure 119: Importance of Information & Knowledge Transfer

Even if roughly 80% of production sites indicate to actively foster knowledge management across manufacturing and quality control, more than 40% still see the subject field as a barrier for OPEX alignment. Consequently, current procedures seem to be not solely sufficient and there is a need to revisit and strengthen cross-departmental exchange across the sample of production sites.

Availability of resources is regularly raised as a pain point by OPEX executives in both St.Gallen Industrial Research & Exchange Groups. Figure 120 depicts the perception of study participants distinguishing OPEX resources dedicated to the departments manufacturing and quality control.

Do your manufacturing and quality control departments struggle with driving OPEX due to lack of dedicated resources?



Figure 120: Lack of Dedicated OPEX Resources in Manufacturing and Quality Control

A lack of resources is clearly confirmed for both departments. However, twice as many production facilities is not concerned by resource availability in manufacturing compared to production sites reporting not to struggle with OPEX resources in quality control. Thus, more dedicated OPEX resources are available to manufacturing in the sample sites.

This observation can also explain the previously uncovered differences in execution of improvement projects across departments: Compared to manufacturing, OPEX projects are much more often executed by non-dedicated staff in quality control. Accordingly, the next survey question investigates whether OPEX resources are allocated and distributed in an integrated manner across the site. Outcomes are presented in Figure 121.

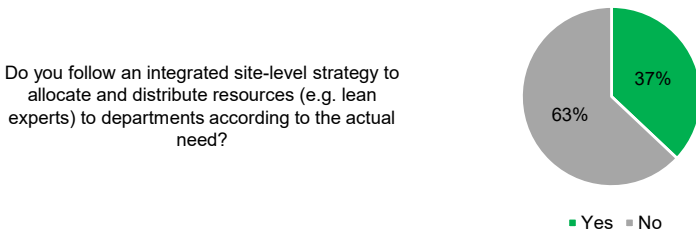


Figure 121: Site Strategy for Resource Allocation

Compared to production areas, QC labs are struggling more with OPEX resources, while executing improvement projects more often by departmental employees not dedicated to OPEX. Both effects can be caused by each other and would require a more balanced resource allocation along the value chain. However, only one of three pharmaceutical production sites follow a site level strategy to do so. This mismatch needs to be addressed as part of a comprehensive approach to OPEX management across manufacturing and quality control.

Literature revealed establishing a culture of Continuous Improvement across the entire organization as a further lever for aligning departments (cf. chapter 4.4). The current prioritization of cultural CI aspects in departments of pharmaceutical production is presented in Figure 122.

Is embedding a continuous improvement culture a current priority in either your manufacturing areas or QC labs (running structured initiatives to proactively engage operators and analysts)?

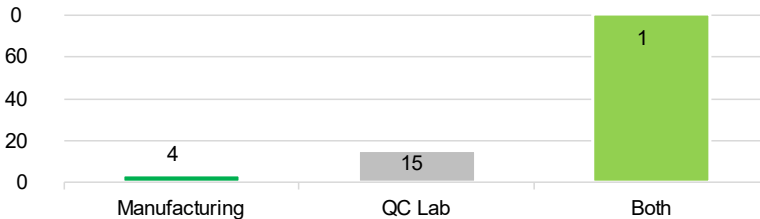


Figure 122: Prioritizing CI in Manufacturing and Quality Control

Surveyed production sites state embedding a culture of improvement as priority in manufacturing and quality control across the board. Responses show the clearest pattern of the entire survey-based study and confirm the current attention on cultural components of OPEX management for both departments. In addition to the importance of cultural readiness, the perception of the current status in departments across production sites is outlined in Figure 123.

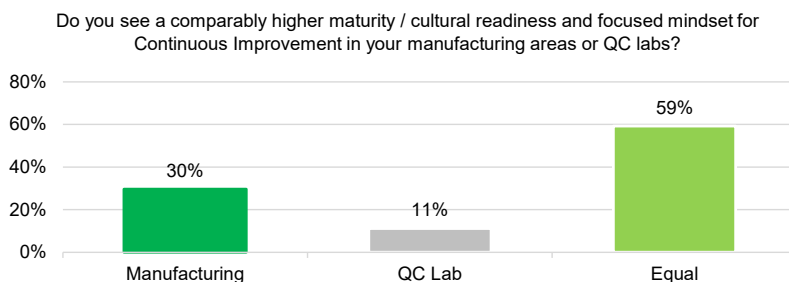


Figure 123: Cultural Readiness for CI in Manufacturing and Quality Control

More than the half of production sites attest equal readiness for Continuous Improvement across their production areas and laboratories. Among all other sites, a higher readiness in manufacturing is stated more often. This observation is in line with outcomes of discussions and workshop sessions in the St.Gallen Industrial Research & Exchange Groups: Even if manufacturing staff historically shows a higher affinity to the philosophy of Continuous Improvement, the recent attention on OPEX in quality control already pays off in a corresponding mindset.

Summarizing outcomes of the lastly discussed survey category *Barriers & Levers*, pharmaceutical production sites are still concerned by successfully transferring information and knowledge across departments, even if this subject field is already actively addressed. Furthermore, especially laboratories struggle with resources dedicated to Operational Excellence. Manufacturing areas indicated a lack of resources as well, but less often compared to the quality control departments. However, only a minority of production facilities follows an integrated, cross-departmental strategy to allocate resources along the site's value chain. An equal high attention on embedding a culture of Continuous Improvement is observable for manufacturing and quality control.

Patterns across Structural Context, Level of Excellence and Barriers & Levers

The above presented review of outcomes guided by the study model, individual analyses of its categories, and the discussion of underlying sections have revealed the current status of comprehensive OPEX management across manufacturing and quality control in the pharmaceutical industry. Following the aim of the present chapter and SRQ 3 of the thesis, answers to the entire set of questions along the study allow to identify patterns of production sites. These patterns contribute to understanding how excellence is achieved across manufacturing and quality control. Based on the sections performance, maturity, and compliance, the degree of cross-departmental alignment resulting from responding site's approaches to OPEX can be evaluated. Moreover, responses in the sections OPEX organization and OPEX strategy provide background on how OPEX is structured at the sites and inform perceptions what may cause the differences observed in the other categories of the

study. Different to the benchmarking data bases analyzed in chapter 3, the nature of the survey and its scales do not allow for statistical exploration across the categories. Instead, a content-driven qualitative review of site profiles based on their answers in different categories leads to the observation of dependencies between the sections. Production sites realizing a consistent Level of Excellence are characterized by achieving a high degree of alignment between manufacturing and quality control in the three sections performance, maturity, and compliance. These sites show a set of commonalities in the further two study categories Structural Context and Barriers & Levers.

Consistent performance across manufacturing and quality control is associated with maintaining a formalized OPEX roadmap and allocating OPEX resources following an integrated site level strategy. Furthermore, all sites indicating alignment in quality, delivery, and cost efficiency performance, actively foster information and knowledge sharing, what is additionally identified as a key lever to prevent one of the departments becoming the bottleneck of the site-internal value chain. Conducting centralized testing seems to hamper adhering to defined standard lead times in quality control, also in the cases of production sites that are capable to manage lead times in manufacturing well.

Aligned maturity levels across manufacturing and quality control are in particular achieved by responding production sites having started their OPEX initiatives and the introduction of selected enablers in parallel across departments. These sites indicate a high proportion of cross-trained employees in all areas coming along with a strong mindset for Continuous Improvement embedded into the entire organization. While priorities are set by a site level OPEX organization, the execution of individual improvement projects is mostly handled by departmental employees. However, consistent maturity in production areas and laboratories is additionally associated with support provided by an above-site OPEX organization. Like achieving consistency in performance, production sites successful in aligning maturity levels maintain a site-wide OPEX roadmap and actively foster information and knowledge sharing through defined feedback procedures. Moreover, they are able to allocate additional OPEX resources to both departments for handling peak loads in improvement initiatives.

Since the study section compliance is interrelated with performance levels and maturity, most of the organizational aspects and improvement levers previously highlighted also contribute to cross-departmental alignment of favorable inspection and audit outcomes. Responses revealed a very clear relation of having embedded a CI mindset along the entire value chain, prioritizing cross-training of employees in both departments, and preventing compliance issues related to a single area of the production facility. Consequently, achieving and sustaining the aspired level of compliance through the entire organization seems to be rather people than system driven.

Furthermore, the way of perceiving barriers for cross-departmental alignment and utilizing levers for improvement is identified to be impacted by the organizational approach to OPEX and the site's strategy. Facilities that operate a site level OPEX organization responsible for prioritization of improvement projects according to an integrated roadmap struggle less to spread resources, information and knowledge across departments than sites relying on corporate OPEX organizations dedicated to manufacturing and quality control. Following an integrated site level OPEX roadmap occurs alongside with effective resource allocation between manufacturing and quality control within the sample of production sites. A strong CI mindset in both departments and willingness to actively disperse knowledge across the organization are guided and supported by an actionable OPEX strategy, which is operationalized with the help of a roadmap.

Case Selection & Uncovering Proven Successful Practices

Besides the above outlined patterns, the free text descriptions concerning knowledge transfer, resource allocation or different cultures across pharmaceutical manufacturing and quality control are analyzed. These descriptions reveal concrete measures the sites take to manage OPEX comprehensively and achieve the level of performance indicated in the other questions. On this basis, successful practices can be initially uncovered, determined, and selected for in-depth investigation during tailored interviews.

In addition to the review of answers across categories and the descriptions provided in the free text answers, a set of formal criteria is applied and informs the selection of production sites for successful practice interviews: A completeness rate of more than 90% of the study is required to offer comprehensive and representative insights across all categories allowing for reliably appraising the degree of alignment. Furthermore, all selected sites should actively address OPEX in manufacturing and quality control motivated by site level objectives for improvement instead of just doing so to fulfill corporate expectations and requirements. In that way, the thesis' focus is maintained: Individual production sites form the primary objects of consideration, rather than analysis of multi-plant corporations. Lastly, at least five years of experience in structurally approaching OPEX at the site by any kind of formal organization, program, or initiative is defined as a threshold. Consequently, robustness of observations is ensured when evaluating the outcomes and stating the impact of approaching OPEX in manufacturing and quality control.

The described process led to the selection of three production sites successfully managing OPEX across manufacturing and quality control in an integrated, comprehensive, and aligned manner. In addition to their answer patterns across the study, all sites indicated concrete procedures serving as powerful levers for increasing maturity and performance along the site internal value chain. These are deemed insightful for the research at hand and thus detailed and documented. All three sites

have been approached and agreed to contribute with a supplementary interview to discuss their way to OPEX in detail, especially focusing on the individual successful practice procedures uncovered during the review and selection process.

5.4 Detailed Case Studies

As outlined in chapter 5.3, the survey-based study revealed three outstanding production sites managing OPEX comprehensively across manufacturing and quality control. Based on their approaches to OPEX indicated by the respondents, these sites have been selected for supplementary deep dive interviews to fully understand, evaluate, and document the successful practices.

Subsequent passages present the outcomes of the interviews as individual case studies. At first, the case site is briefly introduced including a detailed explanation of the local OPEX organization set-up and a summary of its interplay with manufacturing and quality control. Afterwards, case-by-case selected practices for cross-departmental OPEX management informed by the responses provided in the survey are presented and discussed in detail. These aspects inform the implications drawn from the qualitative research at hand and contribute as proven successful practices in the pharmaceutical industry to the overarching guideline for OPEX management across manufacturing and quality control.

5.4.1 Case A – Focus: Cross-departmental Exchange

The first case discusses one of the larger pharmaceutical production sites of a multinational biopharmaceutical company located in Europe. Both sterile and non-sterile products are manufactured, tested, and released at this location to supply domestic and international markets involving approximately 100 target countries. Additionally, stability testing is centrally performed for the network, which comprises more than 20 sites in total. The quality control unit also serves as contract laboratories for R&D and external partners. Consequently, very diverse activities and a comparably high level of portfolio complexity characterize the site's operations.

Showing a high degree of alignment between manufacturing and quality control in the survey, the site has been identified as successful practice case. Different to other respondents, no struggles in the field of OPEX resources and its allocation to departments have been reported. Furthermore, the site does not consider cross-departmental information & knowledge exchange as a barrier anymore, as past efforts led to integration of these components into regular job routines across manufacturing and quality control.

Approach to OPEX in Manufacturing and Quality Control

In addition to business excellence organizations for R&D and procurement, the site relies on a dedicated OPEX organization for operations to drive Continuous

Improvement. At the production site, operations is broadly defined as the site's internal value chain related to commercial production and also comprises the quality departments. It is set-up as a team jointly driving OPEX across the different areas of operations in an integrated manner, but also providing dedicated support to areas accordingly. Each team member of the OPEX organization is in particular responsible for leading and supporting optimization projects in one area of operations: Bulk, Packaging, Internal Logistics and QA/QC. Furthermore, the described cross-functional OPEX site organization centrally maintains all interactions with the corporate OPEX teams and adapts global initiatives to the local production site.

This way of operationalizing and supporting OPEX on site leads back to the year 2013, when the entire company underwent a major transformation of demerging from an even larger sister organization. While reorganizing the new company after the demerger, the site's enterprise system architecture was decoupled from the legacy systems and carefully harmonized across departments. The new cross-departmental system landscape acts as basis for transparency along the site-internal value chain and allows for data-based optimization today. Furthermore, the independence from the legacy corporation led to a change in priorities and working climate, especially at the production site discussed. Striving for process robustness as the foundation for becoming a more flexible and agile organization triggered increased attention on the subject field OPEX. Since the time of demerging, the site does not follow an overarching, formalized OPEX initiative, program, or framework. Instead, it continuously defines, prioritizes, and executes optimization projects according to a regularly renewed OPEX roadmap, which is part of the site's yearly strategy. Mid- and long-term continuity is ensured by operating the site level OPEX organization elaborated above.

In the recent past, the production site was challenged by comparably high human error rates along the entire value chain. Consequently, the OPEX strategy has been especially focused on quality and contained to start a cross-departmental initiative to identify, address, and resolve the real root causes behind human errors through a set of practices and measures. Still ensuring the independence of departmental reporting lines for manufacturing and quality, the initiative is jointly sponsored and prioritized by top management of both production and quality.

Beyond the just introduced site OPEX organization, there are no dedicated OPEX roles defined within the different areas of operations. Hence, execution of improvement projects is carried out by departmental staff as part of their everyday jobs but led and supported by the site level OPEX organization, especially by the OPEX team member focusing on the respective area. However, a number of departmental colleagues known for their affinity to OPEX and expertise in improvement projects – so called OPEX advocates – serve as primary point of contacts in the departments. Thus, there is consistency in the departmental teams for implementation of OPEX projects.

While the responsibility for project definition and prioritization is clearly assigned to the site OPEX organization to ensure alignment across areas and with the overarching OPEX strategy, the degree of supporting the departmental OPEX advocates in implementation differs from project to project: It is not solely determined by the level of sophistication of the certain project and the specific OPEX expertise required, but also by its resource intensity. Consequently, there is a procedure in place for allocating additional site level OPEX resources to the individual areas according to the current needs and priorities, even if areas are generally responsible for project execution with their own workforce.

Based on its general approach to OPEX introduced above, the production site follows a set of concrete procedures that are considered as proven successful practices for comprehensively managing OPEX across manufacturing and quality control in an integrated manner. These are presented and outlined in the subsequent passages.

Standardized Exchange Meeting Cascade

The production site operates a standardized cascade of regular meetings within and across departments. This process is organized according to a tier escalation structure and standardized across all areas of operations including quality control. Daily and weekly huddle meetings are performed within areas to review current operational performance, set short-term priorities, and discuss anomalies. Furthermore, recent achievements are presented and documented during the meetings, what integrates the implicit collection of successful practices in everyday routines.

Summarized in other words, these huddle meetings serve as management routine to steer the corresponding daily business in a consistent and standardized way across all areas. Following the idea of a cascade, outcomes of the area specific huddle meetings are taken to the next tier level and presented there across areas in the same meeting mode. After that, the next higher tier meeting consolidates the outcomes of across area meetings in between departments, still adhering to the same meeting standard. Consequently, there is a strict but simple management meeting routine in place delivering several benefits across departments: Frequent reporting and discussion of the departmental as-is situation provides transparency and allows for immediate synchronization of activities. Any issues are directly escalated, therefore known, and can be addressed by management.

Furthermore, successful practices are automatically shared and disseminated across areas or departments due to the corresponding agenda slot in the regular meetings on all tier levels. Thus, cross-functional exchange and alignment has become part of everyday business and the way management steers its areas of responsibility. Interdepartmental exchange is simply built in the organization's way of operating and supersedes the need to launch any dedicated efforts for particular alignment at defined points of time. In the case of the production site discussed,

ensuring standardized cross-departmental exchange and alignment in the described way is enabled by two crucial preconditions that have been implemented prior to the meeting cascade: A wider management team and standardized Visual Management.

Widening the management team by introducing a supervisor structure as additional management layer in manufacturing and quality control ensures the presence of roles that are capable and willing to take responsibility for their areas in the tier meeting cascade. Moreover, sufficient time for aligning and exchanging according to the management routine is built in the new job profiles of supervisors. The site's decision to implement an additional management layer is remarkable since it is usually common sense in industry to strive for flattening hierarchies when pursuing excellence initiatives. However, the case at hand demonstrates that successfully introducing new procedures comes along with ensuring availability and dedication of associated resources. Depending on the legacy set-up, this can require establishing new roles.

Additionally, a robust and standardized Visual Management across all areas and departments provides structure to the meeting cascade: Boards allow to visually report, review, and discuss performance alongside with documenting actions. Applying the same types of visualization for this information in the entire organization and across all meetings of the cascade simplifies the communication and therefore fosters understanding, exchange and alignment of the involved functions.

Structured Idea Walks

Regularly conducting formalized cross-functional Gemba walks is one of the measures having evolved from the quality improvement initiative to address human errors. These walks follow several purposes: Department and site leadership show presence at the floor and are easily approachable for employees. Special attention is paid on identifying early indicators for quality issues by jointly reviewing all areas visited during the walks according to this focus. Additionally, the Gemba walks are proactively announced as idea walks to cross-functionally brainstorm improvement potentials.

Gemba walks are not entirely new to OPEX management in pharmaceutical production and broadly applied in the more mature sites of the industry. However, the approach to conduct Gemba walks at the case site discussed is unique because of its highly cross-functional set-up: While Gemba walks are usually performed by the upper departmental management within its areas of responsibility or by the site management across departments, the practice at hand is organized in a different way.

The site OPEX organization organizes, leads, and owns all Gemba walks across different areas and departments, which are visited by a cross-functional group in an alternating sequence. Walks are conducted in a fixed frequency according to a standardized procedure, the individual area visited is selected and announced by

the OPEX organization depending on current needs and priorities. The group performing the Gemba walks always comprises all members of the site OPEX organization regardless of their personal focus area and a broader core team with one or two attendees each from Bulk operations, Packaging, QC/QA, and Logistics. Furthermore, site management and EH&S (Abbreviation Environment, Health & Safety) functions regularly join the cross-departmental walks. Depending on the area visited, representatives from Maintenance and Engineering are invited to join upon request and bring-in technical expertise to immediately evaluate initial ideas for improvements during the walks on the floor.

The walks are clearly owned by the site OPEX organization to ensure the intended focus on Continuous Improvement. Walks aim to uncover opportunities to be considered in the OPEX strategy bottom-up, while using the broad expertise of the group for ad-hoc reviews of emerging ideas. That is why the Gemba walks are also referenced as idea walks internally. Furthermore, the cross-functional team benefits from direct interdepartmental exchange of new ideas and harmonization of approaches across areas is fostered at the same time. Thus, the interdepartmental walks complement the previously presented exchange meeting cascade and also contribute to cross-departmental alignment. Following-up on the achievements and successful practices regularly presented from different areas in the tier meetings, these practices can be experienced first-hand across departments during the next walk in the respective area.

Aligned Site OPEX Roadmap

The upper management of the discussed production site regularly states cross-departmental alignment as a priority. This priority is also actively addressed by formulating a joint site strategy across all departments once per year and communicating it in an all-employee meeting event. One part of the site strategy is the yearly OPEX roadmap which comprises targets, priorities, and initiatives for the upcoming period. Informed by the broader site strategy, the OPEX roadmap is developed and owned by the site OPEX organization.

On the one hand, the OPEX roadmap can be understood as first step of operationalizing the site strategy by defining actionable items. On the other hand, it is still of a strategic nature due to its cross-departmental scope. The roadmap contains the yearly priorities in the field of OPEX such as introduction and training of particular new methods, but also actively offers assistance of the site OPEX organization to the different departments. One example is stating available site level OPEX resources for data-backed process analysis, that can be taken up by the respective departments to support their own particular needs in the next year. Since objectives, priorities, initiatives, and offers for support are all formulated across departments, the roadmap is not only a powerful driver for alignment of OPEX execution across

manufacturing and quality control, but also ensures concordance with the overall site strategy beyond OPEX.

Integrated OPEX Idea Management System

While the site OPEX roadmap guarantees alignment from a top-down perspective, a newly launched integrated idea management system acts as bottom-up counterpart: The site just introduced an integrated idea management system that replaces and consolidates all legacy initiatives for directly collecting improvement potentials through different departmental suggestion systems and processes. It follows a simplified approach, which is not only harmonized at a site level but equally applied in other facilities of the company's network. The system aims to establish a corporation-wide baseline for exchanging ideas across establishments in the future. However, ideas are currently collected, evaluated, and transformed in actions individually per production site. An internal web-tool commonly used in all departments and areas of the production site allows every single employee to raise and document improvement ideas. While submitting an idea, the employee indicates the functional area or subject field addressed. According to this indication, ideas are assigned to responsible teams for an initial review and evaluation.

All ideas addressing improvements in manufacturing, quality control, or any processes across departments appear at the site OPEX organization. Depending on the nature of an idea provided and its initial evaluation, the site OPEX organization decides how to process the idea: It can inform the next upcoming OPEX roadmap and be broadly addressed across departments, it can trigger immediate realization by launching a project to grab low-hanging fruits in the individual area of the submitter, or a decision for no further consideration can be made. However, since evaluation and initiation of next steps is always up to the OPEX organization, alignment across manufacturing and quality control is permanently ensured. Compared to the legacy process of raising ideas within the departmental reporting line, this procedure prohibits the risk of lacking transparency about improvement ideas raised in one department that might be highly applicable and beneficial in other departments as well. Thus, the new idea management system fosters employee involvement. It helps to further drive the culture of Continuous Improvement, while making sure that individually acting on ideas is not redundant to broader OPEX initiatives or does even contradict the aligned OPEX strategy.

5.4.2 Case B – Focus: Integrated OPEX Management

The second case presents the approach to OPEX across manufacturing and quality control of a DP production site located in Europe. It manufactures a wide portfolio of products comprising more than 20 different small and large molecules and 2000 active SKUs (Abbreviation Stock Keeping Unit). Furthermore, the site's operations are characterized by a broad range of different packaging containers such as vials,

syringes, cartridges, bottles, and ampules. The case site is part of one of the largest pharmaceutical companies of the world with a headquarter in the United States, it serves as central pillar of the company's European business. Besides supplying almost all global markets, the site strategically assists other European facilities of the network.

Indicating a high degree of alignment between manufacturing and quality control in the survey, the site has been identified as successful practice case for the research at hand. In particular, the case site manages well the interface to the corporate OPEX program and benefits from the above-site support while tailoring, adapting, and applying it according to its certain needs at the same time. Furthermore, the case is strong in ensuring high and equal levels of OPEX maturity across manufacturing and quality control.

Approach to OPEX in Manufacturing and Quality Control

The case facility operates a comprehensive OPEX site level organization, which currently combines working streams originated from two corporate OPEX programs: A legacy program focused on process quality driven by Six Sigma and a more recent program focused on Lean Management based on the newly introduced corporate Production System. Both working streams are strictly approached across departments: Manufacturing and quality control are equally in scope of the site OPEX organization's activities in addition to further departments such as site internal logistics. Beyond the site level organization, dedicated area OPEX functions are installed within departments. These roles report into the departmental line management but work in close collaboration with the site OPEX organization. In total, all resources in departments dedicated to OPEX and the site OPEX organization jointly form 0.7 % of the entire site workforce, what represents the largest OPEX organization in the surveyed sample of pharmaceutical production sites.

First initiatives of the process quality related OPEX program have already been started in 2000. Thus, the site is looking back to a long history of OPEX compared to its peers. Since then, OPEX has always been driven in an integrated manner across manufacturing and quality control, regardless if the activities concern larger project initiatives or training of specific OPEX methods and tools. The newly introduced Production System has also been rolled out that way: After having initially confirmed applicability to the local conditions and evaluated value added by the system during a narrow prototype in one manufacturing area, the installment was planned in parallel across all departments related to commercial production. The OPEX site organization led the deployment in conjunction with the corporate Production System team. As a starting point, incubators selected by the corresponding line management were installed within manufacturing and quality control at the same time. Based on the established departmental incubators, the Production

System has been further spread within and across departments striving to broadly roll out all system elements in parallel in manufacturing and quality control.

At the case site, responsibilities are clearly defined and distinguished between the different types of OPEX functions: The site level OPEX organization defines priorities throughout the entire site together with a steering committee that comprises all department directors and the site leadership team. It coordinates interactions with the corporate Production System organization and oversees progress in OPEX projects across all departments. Furthermore, introduction and training of new methods and tools is facilitated by the central cross-departmental team. The central site OPEX organization additionally owns specialized expertise and provides it to areas, e.g. a full-time statistician is available to support projects within or across departments upon request.

Differently, the departmental OPEX resources are in charge of executing the defined improvement projects within their areas. This comprises specific planning and day-to-day project work related to implementation. Even if the functions are integrated into their area's organizations and report to the departmental line management rather than into the site level OPEX organization, all departmental roles are fully dedicated to OPEX and accordingly specified as deployment leads. The case production site intentionally chose this set-up for multiple purposes. Following the aim to sustain deployed improvements in the long-term, execution is organized departmental to ensure involvement of the areas and drive ownership for achievements. However, unlike most other pharmaceutical production sites delegating execution to the departmental staff (cf. chapter 5.3), a decision for dedicated OPEX functions in departments has been made. In that way availability of sufficient resources for project execution is ensured and trade-offs between OPEX and operational priorities are avoided. Considering the site's situation of continuously scaling up its sterile production business and heavily growing, any non-dedicated departmental staff would regularly face such trade-offs and finally need to prioritize supply related activities over working on Continuous Improvement.

Based on its general approach to OPEX introduced above, the production site follows a set of concrete procedures that are considered as proven successful practices for comprehensively managing OPEX across manufacturing and quality control in an integrated manner. These are presented and outlined in the subsequent passages.

Application and Adaption of Corporate OPEX Frameworks

As elaborated, the site's OPEX set-up evolved from two corporate OPEX programs: A well-established process quality improvement initiative and the recently introduced companywide Production System. Consequently, the site's high level of OPEX maturity also leads back to the corporate support and additional expertise

available from there. Site and corporate functions collaborate very closely in the case at hand.

The corporate OPEX organization has been extensively supporting the initial deployment of the Production Systems and its elements, that each comes with a comprehensive set of OPEX methods, tools, and practices increasing maturity across all departments. The implementation process has been formalized by measuring progress based on evaluating the proportion of defined standards successfully installed per element on site. After having achieved the required level of standard adherence, the initial deployment of the Production System was deemed completed with a certification.

However, the system itself is evolving and strives for Continuous Improvement: Having completed the deployment, the site now not only applies the elements and operates according to the installed standards, but also contributes to refinement and further optimization of the elements. Despite site specific adaption, this also includes a formalized feedback loop into the corporate Production System organization, which is appreciative of suggestions from the case site as one of the largest and most mature DP facilities in the network. Achievements and progress made beyond the initial deployment of the system are regularly evaluated by a maturity assessment also reviewing outcome performance metrics.

Close interaction with the above-site organization additionally strengthens the positioning of the OPEX organization within the case site. In that way, attention to OPEX priorities by the site leadership is ensured and reflected in the site strategy. High visibility of the OPEX program and organization to both site and above-site management provides access to resources and budgets. Furthermore, alignment and consistency across departments is ensured, while avoiding cherry picking of selected OPEX tools by departmental line management according to personal preferences. Instead, the set-up allows to force departments to strictly follow the overarching site and above-site priorities.

Formalized Feedback Process across OPEX in Manufacturing & QC

The present architecture of the cross-departmental site level OPEX organization and its responsibilities already fosters alignment of manufacturing and quality control. Additionally, the site follows a formalized process for exchange between the departmental OPEX resources.

A bi-weekly OPEX townhall meeting brings together both layers of the OPEX organization. All site level OPEX colleagues attend alongside with all departmental OPEX functions. Following a standard agenda, the departmental OPEX resources report current activities, progress in projects, and raise any issues occurred in the last two weeks for the purpose of transparency. Consequently, the area specific OPEX colleagues from manufacturing are well informed about the day-to-day status of OPEX in quality control and vice versa. The agenda of these meetings is not limited to

reporting, but also allows for discussion and immediate successful practice exchange on the operational levels. Furthermore, discussions are documented and concluded with defining actions to address specific issues in either manufacturing or quality control involving central or cross-departmental support if appropriate.

Analogously, a monthly OPEX steering committee meeting is owned and facilitated by the site OPEX organization. The meeting brings together the head of the site OPEX organization, the site leadership team, and the directors of all departments. Even if following a mode of operation according to a standard agenda similar to the one outlined for the OPEX townhall meeting, the purpose of the meeting is a different. Discussion of departmental OPEX execution is limited to any escalation felt necessary by either the OPEX organization or the departmental line management. Both can directly address all issues to the site leadership team. On that basis, the committee jointly reviews priorities, allocates resources, or defines any further measures as appropriate. Besides, the main purpose of the steering committee meeting is to discuss consequences of above-site priorities or initiatives for the site and continuously maintain a mid-term site OPEX strategy including objectives for periods of one to five years. The strategy concerns the entire case site in an integrated manner and thus further contributes to the alignment of manufacturing and quality control.

Summarizing the case site's structured feedback process, it successfully combines bottom-up and top-down management approaches. While the OPEX townhall meeting provides full transparency and offers a facilitated environment for exchange that supports execution of projects, the steering committee meeting ensures accurate priority setting and availability of resources according to an integrated site-wide strategy. Both feedback meetings include all relevant functions contributing in any way to OPEX at site, complement each other, and jointly ensure alignment of all OPEX activities in manufacturing and quality control.

Cross-Departmental Gemba Walks Tailored to OPEX Elements

Gemba walks are part of the case site's OPEX approach since the beginning of the first initiatives. It looks back to a comparably long history in applying this method. Nowadays, all Gemba walks are methodologically owned by the site level OPEX organization and follow standardized principles across manufacturing and quality control. However, unlike the usual application in pharmaceutical production and its own approach in earlier stages of the OPEX program, the site stopped specifying Gemba walks as a management tool and engaging site or departmental leadership to conduct walks. Instead, two different types of adapted Gemba walks are regularly performed.

The first type of Gemba walks is organized within departments and addresses the purpose of department internal synchronization and domain specific exchange between SMEs. A representative of the raw material laboratory visits the colleagues in

the microbial laboratory, or a supervisor of a packaging line goes on a walk through the filling area. Department internal Gemba walks conducted across the different areas of departments are alternatingly planned and scheduled by the departmental OPEX functions according to the site level OPEX principles.

Notwithstanding the above, the second type of Gemba walks is organized by the site level OPEX organization and detailed according to the elements of the newly introduced Production System. All elements, such as TPM or Visual Management, are owned by a central site specialist. This function performs Gemba walks particularly focusing on the element across manufacturing, quality control and all further departments in scope of the Production System. The walk is not part of the formal deploying and training program for the element, it is specified as regular touchpoint to observe the current status of application during everyday operations in the different departments. For this purpose, it is conducted once per week and the scope is rigorously limited to the element owned by the specialist. The alternating schedule of the element specific walk in different areas fosters attention and alignment across departments concerning this specific piece of the OPEX program.

Based on learnings from legacy approaches to Gemba walks at the site, both types have the following principles in common: All walks are intentionally specified to happen on a lower managerial level allowing for open exchange on an equal footing and prevent any impression of audits. Furthermore, the walk is always strictly limited to one visiting person. The latter addresses twofold purposes: Both types of Gemba walks aim for exchange between the visiting person and the visited department, not for interaction between different walkers. Moreover, operations visited during the walks are disturbed as little as possible compared to a group conducting the Gemba walk.

At a first glance, the just outlined procedure for Gemba walks at Case B seems to contradict the principles of the idea walks highlighted as successful practice in Case A. At that site, idea walks are conducted by a comparably large group including high-profile site management among cross-departmental representatives (cf. chapter 5.4.1). However, there is no opposition. Both practices are successful in addressing their respective aims in the different cases: While the idea walks in Case A are performed for cross-departmental exchange and brainstorming of new ideas, Case B differently addresses both aims as part of its structured feedback process comprising of the OPEX townhall and steering committee meeting. Unlike Case A, Case B conducts its Gemba walks for detailed observations on alignment within departments or cross-departmental application of a specific Production System element. Consequently, both set-ups are suitable to achieve the specific aims in the context of the different cases and contribute as successful practices to the integrated management of OPEX across manufacturing and quality control.

5.4.3 Case C – Focus: Product & People Centric Optimization

Lastly, a European DS production site of a pharmaceutical company is discussed as third case deepening the outcomes of the survey-based study. The company operates a diverse business across more than ten production plants in three continents of the world. Its portfolio is unique since it comprises both development and production of own patented products and CMO services for external products with a focus on commercializing and launching pre-developed early phase products. The same holds true for the site at hand, that also serves as headquarter of the company and home base of several above-site functions. Due to the CMO operations, the site is in particular challenged by varying demand and reveals a strong focus on all delivery related aspects in its approach to OPEX.

While the site shows less alignment in OPEX maturity between manufacturing and quality control than the two previously discussed cases, it has been deemed insightful for documenting successful practices due to a clear strategy of organizing operations along products instead of departments. Consequently, optimization projects consider the entire site internal value chain of a product and are set-up within or across manufacturing and quality control.

Approach to OPEX in Manufacturing and Quality Control

Unlike the two previously discussed cases, the production site does not operate an OPEX organization. Instead, it follows a project-based approach to Continuous Improvement closely linked to product-specific needs and operational priorities. These projects are launched either departmental or cross-departmental and supported by an above-site OPEX function. Consequently, no dedicated OPEX resources are installed in manufacturing or quality control. Execution of improvement projects according to the product and process specific architecture is integrated in the task profiles of departmental staff or approached as integral part of a comprehensive certification program. Furthermore, specialized external support from consultancies or implementation providers is sought if needed.

The outlined approach is successfully applied to all departments across the site since 2016. It has been chosen according to the operating portfolio of the site, which is especially focused on launching new CMO products among further activities. That is why everyday operations, primarily comprising ramping-up production of new products, producing campaigns of high complex legacy products, and transfer of launched products or methods to other sites of the network, are structured along individual products rather than volume production of a constant portfolio.

Thus, the site does not follow an overarching OPEX strategy or roadmap. Improvement projects are evolving from product specific needs. All potentials uncovered during everyday tasks are indicated by the project teams to the departmental management, evaluated for direct impact on the current product specific projects and

prioritized accordingly. In case of a favorable evaluation outcome, an improvement project is launched immediately and assigned to a specific project lead.

Based on its special approach to OPEX introduced above, the production site follows two defined procedures that are considered as proven successful practices for aligning manufacturing and quality control and realizing cross-departmental improvement potentials. These two procedures are presented and outlined in the subsequent passages.

Product Leadership Teams

The case site organizes its daily work following the concept of dedicated product leadership teams. These teams are formed across departments and jointly take ownership for the entire site value chain of the respective product including the definition of individual improvement projects. Team members include representatives from Method Development, Production, QC, QA, Business Development, and Regulatory Affairs in addition to a nominated product leader, who facilitates the product leadership team and coordinates all activities following standardized procedures, defined milestones, and specific deliverables. Regular exchange meetings dedicated to the product and owned by the team ensure synchronization of departmental activities and interfaces, also including aligned external communication with suppliers, customer, and regulators. The majority of qualified labor in manufacturing and quality control is part of multiple product leadership teams at the same time, daily operations within and across departments are organized accordingly.

Initially, this organizational form of cross-departmental collaboration evolved from R&D and has been designed to structure the commercialization of pre-developed customer products during the initial launch phase of production. After having successfully rolled-out the concept to larger projects concerning transfer of methods or products to other sites, the approach has also been adapted to commercial production. Due to its changing role in the company's network, the site's commercial production is nowadays limited to a few very complex products that are produced upon request in non-routine frequencies and small batches. Consequently, the case site only produces in campaigns according to specific orders and phased out all legacy make to stock operations. Thus, the fulfillment of every order can be approached as a time-centric project and is organized by a dedicated product leadership team.

Forming such teams, and strictly organizing all processes within and across departments along the product's value chain, is highlighted as successful practice for aligning manufacturing and quality at the production site at hand. Considering the unique portfolio of the site, the approach ensures integrated management across different functions, always directed by the customer specific order. This comprises certain practices within the product leadership teams such as very narrow production and release planning across manufacturing and quality control while producing the campaign. The planning process is facilitated in three regular meetings per week

bringing together the entire product leadership team. With the help of cross-functional planning boards, the product leadership team synchronizes the in- and outputs of all departmental steps along the value chain from raw materials to finished goods release, including material and information flows. Overall product centric organization bridges departmental gaps and is therefore a successful practice for managing OPEX across manufacturing and quality control in the specific context of the facility at hand.

Addressing Improvement Potentials by Structured Employee Qualification

As mentioned above, the case site does neither operate a site OPEX organization nor installs any functions dedicated to OPEX within the departments. However, improvement projects are conducted within and across manufacturing and quality control under the umbrella of employee qualification: A corporate program calls production sites and their departments to nominate selected personnel for participation in a structured training program, targeting especially to middle management positions such as team leaders. This qualification program is directly sponsored by the executive board and owned by the above-site OPEX function. In addition to visibility and reputation in the organization, program members can earn different lean belts among other certifications by successfully implementing an improvement project in their areas of work, closely supported by the above-site OPEX function.

Participation in the qualification program allows employees to dedicate 25% of the individual working time to executing the selected project and driving forward improvements in the department. Thus, the program does not only provide training to employees, but acts as organizational vehicle to freeze resources for Continuous Improvement and delivers at the same time value to the departments not regularly owning any OPEX resources. Furthermore, after having completed the certification, the individual is capable and asked to identify further improvement potentials and propose these to the line management. On this basis, improvement opportunities are considered for nomination as subsequent qualification program project or to be directly approached as part of the product centric organization. Thus, the qualification program aims to establish a baseline to start CI loops initiated by the newly qualified labor within departments, even if their job profile is still not dedicated to OPEX.

The qualification program is open to all departments of the production site, including representatives of manufacturing and quality control. Due to the certification process, regular project documentation, reporting and presentation of progress in qualification group meetings are required. Hence, the program's group meetings lead to transparency about on-going improvement projects across departments. At the same time, the program also provides an interdepartmental exchange platform facilitated by the corporate OPEX function.

Cross-departmental learnings or additional improvement potentials observed can also be transferred outside the qualification program. Product leadership teams decide to plan in evolving opportunities as specific projects during the next product cycle according to their mode of operation. Consequently, the approach combines definition and execution of improvement projects with qualification and certification, while narrowly coaching all improvement projects by corporate. This procedure ensures interdepartmental visibility across the production site, it is deemed a successful practice for OPEX management across manufacturing and quality control.

5.5 Implications for OPEX Management

Chapter 5 aimed to enrich the research project by identifying, evaluating, and documenting proven successful practices for managing OPEX across manufacturing and quality control in pharmaceutical production. Different to the analyses presented within chapter 3, that also built on real-world empiricism, a qualitative focus was chosen according to the objective of research phase 3 *Confirmation*.

For this purpose, a survey-based study was conceptualized (cf. chapter 5.2) incorporating findings of research phase 1 *Investigation* and Phase 2 *Recommendation* according to the iterative research approach. OPEX executives representing 27 pharmaceutical production plants took the survey and participated in the study. Outcomes of the survey responses were presented and discussed in chapter 5.3. Observations allowed to uncover successful practices, which were deepened based on selected case studies in chapter 5.4.

Consolidated outcomes of the qualitative research contribute to the MRQ of the thesis and answer in particular SRQ 3 – *How do successful pharmaceutical production sites achieve excellent performance across manufacturing & quality control?* A detailed review of the survey responses and in-depth analysis of the identified successful practices during supplementary case studies lead to below summarized implications for OPEX management across manufacturing and quality control. All implications are derived based on the intermediate summaries given for each survey category (cf. chapter 5.3), the patterns of production sites observed across the study model (cf. chapter 5.3), and the selected case study interviews (cf. chapter 5.4).

Interdependencies between the organizational OPEX set-ups of pharmaceutical production sites, application of procedures to overcoming barriers and foster alignment across manufacturing and quality control, and the achieved level of excellence have been identified. OPEX management should:

- ✓ Properly balance site and network level operations. High proportions of centralized testing in quality control hamper the synchronization with manufacturing for batch release of local products.

- ✓ Follow a comprehensive and integrated site strategy to allocate OPEX resources to manufacturing and quality control. In that way, not only local peak loads can be leveraged, but specific expertise offered to departments in addition. Furthermore, using synergies results in higher cost efficiency.
- ✓ Assign responsibility and accountability for identification, prioritization, and execution of improvement projects in manufacturing and quality control. Different organizational set-ups can be successful depending on the context of a site. However, roles or contributions must be clearly defined for above-site OPEX functions, the site level OPEX organization, departmental OPEX resources, and all staff not dedicated to OPEX.
- ✓ Roll out OPEX initiatives in parallel across departments. Avoid time gaps between implementation in manufacturing and quality control to achieve consistent maturity across the organization in the midterm. Limiting initiatives to manufacturing at first leads to disbalanced enabler implementation levels to the disadvantage of laboratories, which causes extra efforts for alignment later on.
- ✓ Foster alignment of departmental maturity in fundamental tools such as 5S or Visual Management. Compatible maturity levels across manufacturing and quality control are associated with preventing departmental bottlenecks for supply.
- ✓ Invest in cross-training of operators and analysts within manufacturing and quality control. Higher flexibility of broadly skilled departmental staff positively contributes to strengthen the mindset for Continuous Improvement along the value chain. Moreover, it is associated with achieving favorable audit and inspection results throughout the entire organization.

Furthermore, proven successful practices contributing to achieve excellence across manufacturing and quality control have been uncovered, explored, and detailed. At the production sites discussed in detail, all below mentioned procedures have contributed to achieving overall excellent performance. OPEX management should:

- ✓ Apply and adapt corporate OPEX frameworks such as Production Systems to benefit from above-site expertise in cross-departmental alignment. In addition to sharing experience and knowledge of comprehensive optimization set-ups, corporate systems or functions can provide manufacturing and quality control with access to additional resources.
- ✓ Maintain an integrated site level OPEX roadmap concerning both manufacturing and quality control. Ensure alignment with the overarching site and corporate strategy beyond Operational Excellence.
- ✓ Consider a project based, product centric organization of all processes in case of small and regularly changing portfolios. In that way, specifically synchronize

interfaces between manufacturing and quality control per product along the site value chain.

- ✓ Harmonize or properly integrate cross-departmental OPEX initiatives and employee qualification programs. Inform certification projects by current OPEX priorities and integrate the qualified labor in the strategy for OPEX execution.
- ✓ Establish a formalized feedback process between all departmental and cross-departmental roles concerned with owning, prioritizing, or executing OPEX initiatives in manufacturing and quality control. Define interfaces with the line management and ensure approachability of site leadership for OPEX related matters.
- ✓ Exploit knowledge of operators in manufacturing and analysts in quality control by running a robust bottom-up idea and suggestion system. Ensure cross-departmental processing and review of all ideas prior to departmental prioritization and execution to avoid optimizing silos.
- ✓ Facilitate regular meetings in manufacturing, quality control or across departments in a standardized way. Operate all huddle-meetings across the site supported by a proper Visual Management and introduce a tier meeting cascade to ensure synchronization along the value chain.
- ✓ Systematically organize Gemba walks in manufacturing and quality control to reduce distances in between shop floor processes, line management, and the OPEX organization. Tailor the Gemba walk set-up to addressing well-defined specific aims such as generating improvement ideas or experiencing application of certain OPEX tools and select participants accordingly.

6 Guideline for OPEX Management

Chapter 6 condenses the research findings previously outlined in chapters 3, 4, and 5. Implications for OPEX management have been derived in intermediate summaries at the end of the three core research phases *Investigation*, *Recommendation* and *Confirmation* completed beforehand (cf. chapters 3.4, 4.5, and 5.5). Already formulated in an actionable format, these implications jointly inform the following passages and add up to the overall product of the thesis at hand: A guideline for comprehensive OPEX management across manufacturing and quality control in pharmaceutical production. Thus, chapter 6 particularly addresses SRQ 4 *How to consolidate uncovered causes for performance differences, identified strategies for cross-departmental alignment, and proven successful practices in a guideline for interdepartmental OPEX management?* (cf. chapter 1.2.2) and presents the outcomes of research phase 4 *Conclusion* (cf. chapter 1.2.4).

According to Cambridge University Press (2021), a guideline is defined as information intended to advise people on how something should be done. Consequently, the implications derived from the present research are summarized for direct application by practitioners. As the guideline combines conclusions previously drawn from multiple perspectives grounded in quantitative empiricism, literature, and qualitative empiricism, the chapter at hand pays special attention on integrating and harmonizing the findings. This comprises to maintain consistency of the manifold implications contributing to the guideline and to ensure their interplay. Moreover, the overarching way of presenting implications and providing recommendations to management is modified: Whereas previous chapters have been structured along the observations made in research, chapter 6 rearranges the content in a suitable format for application by practitioners.

Even if designed for practitioners and addressing OPEX executives as primary target audience, the guideline builds on foundations of theory. In that way, credibility can be ensured and is underpinned by well-established research following the tradition of OM. Referring to the three research theories jointly providing the theoretical lenses of the present thesis (cf. chapter 1.2.1), the guideline is compiled respecting the following principles:

1. TDC: The guideline aims to equip management with capabilities to comprehensively manage Operational Excellence across manufacturing and quality control. In line with Teece et al. (1997) and Teece and Pisano (1994) these capabilities are understood as management's ability to provide and reconfigure resources, skills and competencies. They need to be dynamically built, renewed, and deployed across the organization to respond to its individual challenges.

2. TOC: The variety of implications contributing to the guideline and manifoldness of their subject areas underline the level of sophistication needed to comprehensively manage OPEX across manufacturing and quality control. Therefore, integrating and balancing the different aspects form the key factors for the guideline to be successful, since constraints determine overall performance of a system rather than its highest performing part (Goldratt, 1990; Rahman, 1998).
3. CT: Even if the guideline is intended for application by the entire community of OPEX professionals in pharmaceutical production, there is no way to ensure equal suitability for all sites. Complying with Donaldson (2001, 2006), effective organizational designs fit the contingencies of organizations. Consequently, the guideline must allow for adaption and adoption by the OPEX management of a specific production site and include advise accordingly.

The guideline for OPEX management is developed and presented in the following chapters. At first, the overall structure is derived and outlined in chapter 6.1. An overview allows practitioners to familiarize with the subject fields discussed in the guideline and to understand the interplay of its various modules. Subsequently, all guideline modules are detailed module by module within chapter 6.2. These passages cluster, integrate, and condense the previously discussed implications for OPEX management according to the various subject fields. Chapter 6.3 advises management on how to apply the guideline and creates awareness for pitfalls in practice. Lastly, chapter 6.4 summarizes the benefits and emphasizes reasons why OPEX management shall follow the guideline based on the findings of the thesis' core research phases 1, 2, and 3.

6.1 Overview & Structure

All implications drawn have been previously presented in the sequence of the research phases along the different empirical sources of the data gathering strategy (cf. chapter 1.2.5). Unlike this, the guideline for OPEX management clusters all recommendations content-wise according to subject fields to simplify application for practitioners. For this purpose, it is structured in multiple pillars and modules in order to address the manifoldness and diversity of aspects contributing to Operational Excellence across departments.

Three pillars provide the basic architecture and represent overarching fields of activity for comprehensively managing OPEX according to the guideline. Within these three pillars, five modules are situated to guide the practitioner. All five modules contain a set of managerial recommendations derived from the previously drawn implications and clustered according to the module's subject field. Furthermore, the

guideline modules do not solely contribute to Operational Excellence across manufacturing and quality control, but additionally interact with each other. Some modules are informed by the outcome of other modules or act as feedback loop, since the guideline aims to direct OPEX management reflecting the principal philosophy of Continuous Improvement (cf. chapter 2.1.1). Figure 124 visualizes the guideline's structure and introduces the five modules.

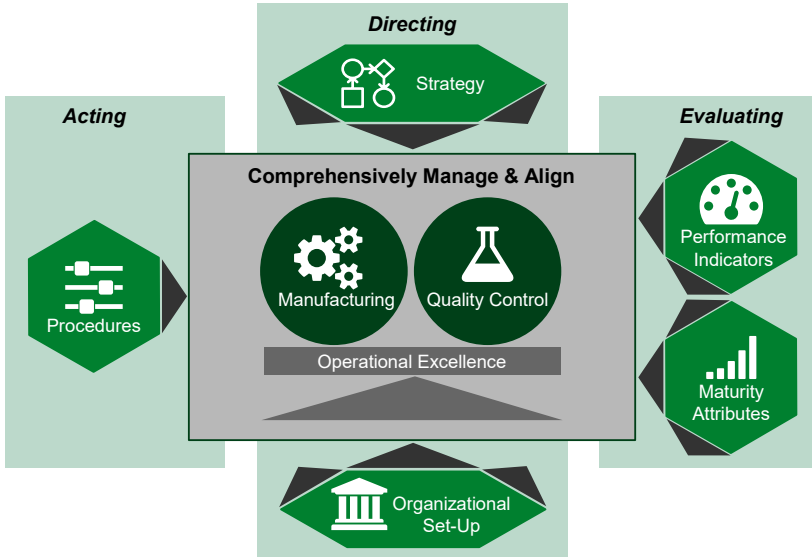


Figure 124: Guideline for OPEX Management across Manufacturing and Quality Control

The central pillar *Directing* comprises the first two modules of the guideline *Strategy* and *Organizational Set-Up*. Both modules directly impact comprehensiveness and alignment of OPEX approaches across departments, while shaping the further guidelines' modules situated within pillars *Acting* and *Evaluating* at the same time. Moreover, *Strategy* and *Organizational Set-up* are continuously evolving themselves: Even if setting an initial baseline for the site's approach to OPEX management, the modules are not designed to be applied only once. On the contrary, they need to be regularly refined and renewed based on the outcomes of evaluations.

Detailing the activities of managing and cross-departmentally aligning Operational Excellence in everyday operations of manufacturing and quality control, the pillar *Acting* summarizes specific *Procedures* to follow. It provides management with precise advices how to foster optimization along the value chain. The pillar is continuously informed and maintained by the modules *Strategy* and *Organizational Set-Up* during application of the guideline in practice.

Regularly *Evaluating* the current operational health within manufacturing and quality control as well as across departments of a production site completes the pillars of the management guideline. The pillar is defined in line with the St.Gallen understanding of Operational Excellence (cf. chapter 2.1.1): It is not limited to solely monitoring the fulfillment of targets set, but combines the two modules *Performance Indicators* and *Maturity Attributes* instead. In conjunction, these allow for a comprehensive and balanced evaluation of the current status of excellence. Both modules interact with each other, contribute as crucial instruments to managing Operational Excellence across manufacturing and quality control, and reflect the baseline established within the guideline modules *Strategy* and *Organizational Set-Up*. Vice versa, evaluations initiate a feedback loop and also continuously inform the pillar *Directing*.

6.2 Modules & Recommendations

The following chapters outline and detail the five modules of the guideline for OPEX management according to the structure introduced in chapter 6.1. Each individual module is a content-wise clustered, consolidated, and condensed compilation of the implications drawn within the core research phases of this thesis as presented in chapters 3.4, 4.5, and 5.5.

Even though stated for guidelines concerning clinical procedures or public health, HO's (2012, p. 48) basic advises on how to write guidelines are deemed applicable to the guideline at hand and followed accordingly: Recommendations made need to be clear, actionable, and presented in consistent language across the entire guideline. Following the iterative research approach (cf. chapter 1.2.4) and already targeting to finally inform the guideline for OPEX management, all implications have been formulated in a consistent and actionable manner across previous chapters. Hence, the guideline sticks to the priorly established way of stating recommendations as calls directly raised to OPEX management. This style of expression is subsequently followed to outline recommendations in all guideline modules in a concordant format. All calls are complemented with explanations for practitioners.

6.2.1 Strategy

The first module provides management with guidance on how to set-up the Operational Excellence strategy at pharmaceutical production sites. Referring to the overarching focus of the guideline, special attention is paid on strategy elements, which contribute to balancing and aligning the departments manufacturing and quality control. In doing so, the module comprises defining, specifying, and maintaining the approach to interdepartmental OPEX management at production sites.

Before Operational Excellence programs, initiatives, or projects are launched across departments, a clear and tailored strategy must be defined by management. For this purpose, individual priorities and needs of the production sites have to be identified

at first. After that, these priorities shall be specifically addressed in the strategy to guide execution of OPEX activities across manufacturing and quality control. Unlike the concrete practices later on discussed in the guideline module *Procedures*, the following recommendations do not directly improve performance, but allow management establishing the OPEX strategy in an actionable way:

- ✓ Tailor and adapt the strategy for performance alignment across manufacturing and quality control depending on the cross-departmental maturity level on site.
- ✓ Follow a comprehensive and integrated site strategy to allocate OPEX resources to manufacturing and quality control. In that way, not only local peak loads can be leveraged, but specific expertise offered to departments in addition.
- ✓ Roll out OPEX initiatives in parallel across departments. Avoid time gaps between implementation in manufacturing and quality control to achieve consistent maturity across the organization in the midterm. Limiting initiatives to manufacturing at first leads to disbalanced enabler implementation levels to the disadvantage of laboratories, which causes extra efforts for alignment later on.
- ✓ Harmonize or properly integrate cross-departmental OPEX initiatives and employee qualification programs. Inform certification projects by current OPEX priorities and integrate the qualified labor in the strategy for OPEX execution.

Transferring and sharing knowledge throughout the organization is a lever for cross-departmental synchronization and alignment of maturity levels. Consequently, setting directions for knowledge management is a key part of formulating and operationalizing the approach to cross-departmental Operational Excellence:

- ✓ Do not underestimate the equal importance of disseminative capabilities for overall effective knowledge sharing in addition to absorptive capabilities and address capability gaps in manufacturing or quality control accordingly.
- ✓ Define, formalize, and systematize a combined knowledge architecture of integration and partition to address the trade-off between depth in departmental knowledge and breadth in cross-functional knowledge.
- ✓ Understand knowledge creation beyond pure knowledge sharing and pay attention on internalization of acquired capabilities, what also comprises defined departmental measures for crystallization, adaption, and application of knowledge.

Moreover, formulating the strategy for cross-departmental Operational Excellence at production sites only once is not sufficient. It needs to be maintained, evaluated, and renewed by OPEX management on a regular basis:

- ✓ Run internal and external benchmarking to create transparency, make gaps visual and uncover present successful practices across departments.

- ✓ Maintain an integrated site level OPEX roadmap concerning both manufacturing and quality control. Ensure alignment with the overarching site and corporate strategy beyond Operational Excellence.
- ✓ Value the equal importance of maturity and outcome performance by considering measures and targets for both fields in cross-departmental OPEX initiatives since there is no direct association that would allow to surrogate one pillar through the other.

6.2.2 Organizational Set-Up

In addition to *Strategy*, the pillar *Directing* contains a dedicated module to provide guidance for favorable organizational set-ups, which enable to comprehensively manage Operational Excellence across manufacturing and quality control. Establishing conditions that allow for knowledge exchange and capability transfer is a key success factor of cross-departmental initiatives. For this purpose, production sites need to set-up OPEX organizations that are well aligned with the company's corporate architecture, foster visibility beyond departments, and clearly define roles contributing to Operational Excellence initiatives.

Most pharmaceutical companies operate above-site OPEX organizations. Aligning the site level approach to OPEX across manufacturing and quality control with the network-wide set-up does not only leverage synergies, but is additionally required to avoid unintended contradiction of parallel efforts. Interfaces to the corporate structure and other sites need to be well defined and actively maintained:

- ✓ Introduce cross-functional centers of excellence and knowledge nodes establishing organizational ties.
- ✓ Apply and adapt corporate OPEX frameworks such as Production Systems to benefit from above-site expertise in cross-departmental alignment. In addition to sharing experience and knowledge of comprehensive optimization set-ups, corporate systems or functions can provide manufacturing and quality control with access to additional resources.

Moreover, transparency between areas and visibility of all departments is crucial for uncovering successful practices as a prerequisite for transfer and alignment. The organizational set-up at site can force interaction and support unplanned exchange between OPEX functions in manufacturing and quality control during regular operations:

- ✓ Avoid isolation of departments within manufacturing sites and exclusion from cross-departmental exchange because of missing direct process interfaces.

- ✓ Enable direct person-to-person communication across both departments as part of the everyday job by appropriate infrastructure and beyond dedicated sharing conferences.
- ✓ Co-locate departmental optimization teams, offer shared meeting spaces across departments, and introduce job rotation for departmental OPEX resources.

Besides the structural conditions within departments and at site, the organizational set-up additionally defines roles contributing to Continuous Improvement across various functions. This includes providing resources and specifying ownership for programs, initiatives, and projects within or beyond manufacturing and quality control. A systematic staff management anchors Operational Excellence along the value chain:

- ✓ Install local middle management positions overseeing both departments to ensure strategy alignment completing – but not replacing – the separated reporting lines to departmental senior management on the above-site level.
- ✓ Assign responsibility and accountability for identification, prioritization, and execution of improvement projects in manufacturing and quality control. Different organizational set-ups can be successful depending on the context of a site. However, roles or contributions must be clearly defined for above-site OPEX functions, the site level OPEX organization, departmental OPEX resources, and all staff not dedicated to OPEX.

6.2.3 Procedures

OPEX management must actively foster alignment and contribute to comprehensively optimizing manufacturing and quality control. A set of routines to follow and procedures to apply is outlined in the following guideline module. In addition to employ specific managerial practices driving forward OPEX within departments, responsible functions are asked to personally act as role model and actively promote a culture of disseminating knowledge across the organization.

Management commitment is a key success factor for all OPEX initiatives. This holds especially true for the integration of approaches across manufacturing and quality control since the alignment of OPEX initiatives strives to overcome the natural paradigm of prioritizing and departmentally optimizing the personal area. Consequently, a clear message expressed through own managerial behavior is required:

- ✓ Prevent impression of lacking management buy-in, actively demonstrate commitment to cross-departmental collaboration by sponsoring initiatives and ensuring personnel visibility in interdepartmental projects.

- ✓ Show active managerial initiative to align departments and harmonize line management's specific routines such as huddle meetings or improvement project execution planning.

Even if the atmosphere and climate within production sites is often seen as given, it can be actively promoted, stimulated, and facilitated through targeted managerial actions. Hence, OPEX management is asked to manifest the cultural foundations for interdepartmental exchange:

- ✓ Establish a shared organizational culture by putting a common company language, values, and vision in place.
- ✓ Incentivize & motivate individuals to share knowledge by integrated target setting processes and joint recognition systems.
- ✓ Ensure trust by enforcing joint ownership & responsibilities, preventing departmental competition, and demanding full transparency on failures & learnings without any blame.
- ✓ Support the creation of private & personal relationships beyond own departments through allocating budgets for cross-departmental team building and networking events.

Certain practices particularly foster capability transfer, synchronization, and joint optimization across manufacturing and quality control. In this way, OPEX management can direct both departments to comprehensive Continuous Improvement by acting accordingly. Managers are advised to:

- ✓ Invest in cross-training of operators and analysts within manufacturing and quality control. Higher flexibility of broadly skilled departmental staff positively contributes to strengthen the mindset for Continuous Improvement along the value chain.
- ✓ Exploit knowledge of operators in manufacturing and analysts in quality control by running a robust bottom-up idea and suggestion system. Ensure cross-departmental processing and review of all ideas prior to departmental prioritization and execution to avoid optimizing silos.
- ✓ Use innovation projects in generalizable common fields of interest as catalysator and multiplier for cross-departmental collaboration.
- ✓ Facilitate regular meetings in manufacturing, quality control or across departments in a standardized way. Operate all huddle-meetings across the site supported by a proper Visual Management and introduce a tier meeting cascade to ensure synchronization along the value chain.
- ✓ Establish a formalized feedback process between all departmental and cross-departmental roles concerned with owning, prioritizing, or executing OPEX

initiatives in manufacturing and quality control. Define interfaces with the line management and ensure approachability of site leadership for OPEX related matters.

- ✓ Systematically organize Gemba walks in manufacturing and quality control to reduce distances in between shop floor processes, line management, and the OPEX organization. Tailor the Gemba walk set-up to addressing well-defined specific aims such as generating improvement ideas or experiencing application of certain OPEX tools and select participants accordingly.
- ✓ Foster joint, collaborative problem solving of department-specific problems and introduce cross-departmental process improvement groups.

6.2.4 Performance Indicators

Measuring the current level of operational performance is key to emphasize strengths, identify issues, and uncover improvement opportunities. Selecting appropriate measures to evaluate effectiveness and efficiency within manufacturing, quality control and across the organization forms the data-backed basis for managerial decision making by OPEX functions.

Comprehensively managing Operational Excellence across manufacturing and quality control requires a balanced approach to performance measurement. Thus, the system needs to systematically aim for synchronization and integration along the entire value chain instead of quantifying capability of specific processes within departmental silos:

- ✓ Measure and reward contributions towards other departments based on dedicated indicators.
- ✓ Consider efficiency to evaluate cross-departmental performance of production sites comprehensively since only evaluating robustness and stability does not uncover all performance determinators and their associations along the value chain.

The majority of pharmaceutical production sites already utilizes performance measurement systems and regularly evaluates KPIs. However, most indicators are selected based on line management's preferences or historic reporting requirements. To achieve excellence along the site internal value chain and comprehensively managing manufacturing and quality control, dedicated KPIs that are able to reveal performance beyond their own object of measurement need to be considered:

- ✓ Use Invalidated out of Specification Rate and the Share of Rejected Batches as simplified cross-departmental metric combination to measure effectiveness.

- ✓ Pay special attention to the plant's Customer Complaint Rate, Raw Material Turns, WIP Turns, Finished Good Turns, and OTIF. Anomalies in these metrics can also uncover issues in quality control quantifiable through Lab Deviations, Analytical RFT, iOOS Rates, Investigation Rates, Lead Times, Adherence to Lead Time, and Adherence to Schedule.
- ✓ Be mindful that Deviations/Batch, Deviation Closure Time, Share of Rejected Batches, and OTIF in manufacturing might also impact quality control's performance due to increased workload for Product Re-Test Due to Complaints or Investigations and therefore diminish lab efficiency in Batches processed/FTE or Cost/Test.

6.2.5 Maturity Attributes

Similar to *Performance Indicators*, guidance for regularly evaluating *Maturity Attributes* across production and laboratories is provided. The module does not solely complete the pillar *Evaluating* but additionally informs the overall managerial acting according to identified priorities in the field of cross-departmental Operational Excellence. OPEX maturity needs to be regularly assessed and capabilities examined. This shall take place in reasonable detail, include appropriate attributes, follow a systematic approach, and integrate observations from external compliance evaluations.

Maturity assessments are commonly performed in industry. However, comprehensively managing Operational Excellence across manufacturing and quality control shifts the focus from checking selected maturity attributes within departments to systematic evaluation along the site-internal value chain:

- ✓ Do not solely rely on aggregated departmental results of maturity assessments, but focus on evaluating maturity gaps across manufacturing and quality control in individual enabler categories to uncover the most powerful improvement levers.
- ✓ Avoid overemphasizing the importance of single enabler dimensions like Maintenance or Quality assuming these would particularly drive alignment across manufacturing and quality control to achieve higher combined maturity.

Choosing the maturity attributes for evaluation based on their expressiveness for the entire production site rather than departmental preferences narrows down the systematic approach to production and laboratories. Following selection of enabler categories is outstandingly contributing to enhancing cross-departmental maturity and requires consideration:

- ✓ Especially assess maturity of the plants concerning Housekeeping, Process Management, Cross-functional Product Development, and Direction Setting as

leveraging improvements in these categories can pay off in higher cross-departmental maturity and additionally drive improvements in quality control.

- ✓ Prioritize the levers Housekeeping, Technology Assessment & Usage, Layout Optimization, and Employee Involvement in quality control associated with higher maturity in the manufacturing plant.

Striving to align OPEX maturity across manufacturing and quality control includes to actively manage and transfer capabilities based on the observations made through maturity assessments. However, the transfer process itself needs to be properly maintained and supported considering the existing level of maturity in departments:

- ✓ Review present cross-departmental maturity at larger sites of the network first, hereby identify successful practices to enable excellence across departments and transfer these practices to the smaller production sites of the company.
- ✓ Evaluate capabilities prior to start the knowledge transfer, while balancing efforts of the transfer process with applicability and importance to the target department.
- ✓ Establish an integrated cross-departmental QMS with a focus on monitoring process quality instead of managing documents alongside with interdepartmental indicators.

Preparing for regulatory inquiries and addressing audit or inspection outcomes is compulsory to maintain the compliance status of pharmaceutical production sites. Nevertheless, actively incorporating these efforts required anyway in the OPEX assessment strategy can help management to move forward Operational Excellence throughout the entire organization. Outcomes of audits and inspections shall be used to complement maturity assessments. Furthermore, prospective foreign evaluations trigger dissemination of learnings across departments:

- ✓ Recognize regulatory surveillance as external driver for maturity of production sites and take inspections as opportunities for improvements, which not regulated sites are lacking.
- ✓ Understand that compliance evaluations do not reward outstanding performance beyond required levels in single areas but react on all observations below the expected standard across all departments.

6.3 Application & Adaption

The general guideline set-up, its modules, and the situated recommendations for cross-departmentally managing Operational Excellence have been introduced in chapter 6.1 and outlined in chapter 6.2. Subsequently, advice is given on how to make use of the guidance in practice and avoid pitfalls of employment.

Most importantly, managers need to understand that all guideline modules are highly interconnected and have to be applied in conjunction: *Strategy* and *Organizational Set-Up* determine the way *Procedures* are executed. *Performance Indicators* and *Maturity Attributes* generate important feedback to be permanently addressed in all further modules. Hence, the three pillars *Directing*, *Acting*, and *Evaluating* provide orientation to the practitioner but should not be understood as a sequential order of tasks. Differently, all underlying aspects contribute to improving interdepartmental performance in parallel and shall be jointly considered in day-to-day management.

The compiled guideline is designed for industry-wide application and has been derived based on empiricism including observations from a broad variety of pharmaceutical production sites (cf. chapters 3 and 5). However, OPEX management is encouraged to actively question all recommendations provided and adjust execution of the guideline according to the individual needs in the context of each production site. Considering their contingencies, not any two facilities in the world are alike and managed best in exactly the same way. Thus, it is required to tailor managerial acting to the situation at hand as stated in the guideline and to evaluate adaption of the specific approach to Operational Excellence even beyond the guideline. A special role of an establishment in its network, distinctive cultural barriers for Continuous Improvement caused by a history of unsuccessful optimization projects, or a unique product portfolio can necessitate to reprioritize or deviate from the guidance.

In case striving for integration of OPEX across manufacturing and quality control is not a local priority of a single production facility but entirely new to the company, larger production sites of the network are best candidates to pilot the approach. These facilities usually show a higher level of maturity and are in a position to dedicate resources accordingly. In contrast, small and specialized sites can benefit from product centric organizations, where interfaces between manufacturing and quality control are specifically synchronized per product along the site value chain. Regardless of the size and role of a production site, attention is required to properly balance site and network level operations when applying the guideline and beyond. In particular, the appropriateness of the guideline's focus on alignment can be determined by quality control's profile. A high proportion of centralized testing on site hampers the synchronization with manufacturing for batch release testing of local products. Further structural factors such as the geographical region of a production site or its portfolio complexity do not determine the applicability of the guideline in general terms. These aspects may be disregarded if there is no company-specific reason to act differently.

Considering departmental specialization and individual subcultures of departments is a key success factor for managing Operational Excellence across manufacturing and quality control according to the recommendations. Managers must carefully read the organization, show awareness of departmental haughtiness due to different

maturity levels, or address initial reluctance to any change caused by the strong GMP mindset. Finally, breaking up legacy silos acts as gamechanger to sustain a cross-departmental culture of Continuous Improvement: OPEX management needs to make all individuals in charge of optimization changing their priorities from projects immediately impacting the own area of work to projects contributing most to the value chain.

6.4 Summarized Outcomes & Anticipated Improvements

Completing the guideline for OPEX management, chapter 6.4 summarizes the benefits of its application in practice. Similar to all changes in how production sites are managed, pursuing a new path and revising the approach to Operational Excellence is not a purpose in itself. It must come with the prospect of tangible benefits, plausibly demonstrate the value added, and provide confidence that there is a return of efforts invested.

Observations made during the core research phases 1, 2, and 3 revealed differences in operational performance between production sites managing OPEX comprehensively according to the subject fields discussed in the guideline's modules and other sites that do not. These findings (cf. chapters 3, 4, and 5) evolved from real-world empiricism and can be justified based on benchmarking data and proven successful practice cases. Thus, credibility of the recommendations stated is given. In the following, achievable improvements associated with applying the guideline are evinced to practitioners: The underlying research allows to expect increased levels of effectiveness, efficiency, and compliance throughout the organization from adopting the presented guideline for comprehensively approaching and aligning OPEX across manufacturing and quality control. Among others, management can anticipate the subsequently summarized outcomes.

High process quality of laboratory operations demonstrated in various robustness measures is a crucial contributor to effective delivery and appropriate order fulfillment of the production site. At the same time, alignment of departmental maturity in fundamental tools such as 5S or Visual Management and synchronization across manufacturing and quality control comes along with eliminating bottlenecks. Consequently, approaching Operational Excellence comprehensively and follow the recommendations stated in the guideline positively impacts the supply performance, increases reliability, and contributes to preventing drug shortages.

Besides increasing effectiveness, quality control robustness indicators are significantly positive correlated with Just-in-Time measures in manufacturing. Hence, production's interplay with high performing laboratories does not solely ensure product quality and delivery on time, but can also act as competitive advantage to increase efficiency along the entire site value chain. Beyond the positive impact on overall productivity, following a comprehensive and integrated site strategy to allocate

OPEX resources to manufacturing and quality control leverages synergies across departments. Implementing the guideline and aligning Operational Excellence across departments results in a more streamlined organizational set-up associated with higher cost efficiency.

Furthermore, applying the guideline and optimizing departments in conjunction pays off in more favorable inspection outcomes. Consistent KPI scores across manufacturing and quality control jointly occur with a higher probability of mastering inspections without actions indicated by the regulators. Analogously, aligning maturity levels according to the recommendations prevents compliance issues. Production sites performing best in U.S. FDA inspections demonstrate a much higher correlation between OPEX enabler implementation levels across manufacturing and quality controls than establishments receiving citations. Above given guidance advocates to invest in cross-training, it puts the workforce in the center of striving for optimization within and across manufacturing and quality control. Reaching higher proportions of broadly skilled departmental staff as an outcome does not only strengthen the mindset for Continuous Improvement along the value chain, but also contributes to achieving positive inspection results throughout the entire organization.

7 Conclusion

Chapter 7 concludes the thesis. It summarizes the findings of the corresponding research project. Different to chapter 6, the section at hand does not aim to summarize all implications drawn, but to recap and reflect the research procedure. In doing so, findings are outlined within the chapter while referring to the aspired research objectives and the research design stated at the beginning (cf. chapter 1).

For this purpose, chapter 7.1 looks back at the outcomes of the dissertation project. It is structured according to the initially formulated research questions (cf. chapter 1.2.2) and corresponding research phases (cf. chapter 1.2.4). Subsequently, chapter 7.2 summarizes the contributions of this research to theory and practice. Thereby, the chapter reaffirms the relevance of the research stated at the beginning (cf. chapter 1.1) and concludingly elevates its benefits. As a legit research project, the thesis does not claim exhaustiveness. Therefore, chapter 7.3 illustrates limitations of the findings and encourages to consider these when acting upon the results presented. Finally, future research opportunities are highlighted in chapter 7.4. These might motivate scholars to prospectively expand the research field and build on the basis established within this thesis.

7.1 Summary

The present research aimed at informing industry how to optimize manufacturing and quality control in pharmaceutical production through comprehensive and aligned OPEX management. Legacy observations of inconsistencies in effectiveness between production and laboratories within facilities were confirmed based on recent and enlarged benchmarking databases. Triangulating these patterns with outcomes of qualitative research in the field and literature not limited to Operational Excellence in the pharmaceutical industry underlined the existing performance gap. Hence, the need for action and the opportunity to realize associated improvement potentials were further demonstrated, clarified, and detailed.

Striving to evince a way to addressing and leveraging these improvement potentials in practice, the five research phases (0) Grounding & Foundation, (1) Investigation, (2) Recommendation, (3) Confirmation, and (4) Conclusion successively delivered cornerstones to comprehensively manage Operational Excellence across manufacturing and quality control in this thesis. According to the originally defined research approach, the core research phases (1), (2), and (3) were executed in parallel to continuously inform and stimulate each other. Methods, procedures, and outcomes of this journey along the sub research questions are briefly recapped in the following. After that, the findings of the research in its entirety are illustrated in a retrospective setting by commenting on the main research question.

SRQ 1 – *What are causes for performance differences and drivers for alignment across manufacturing and quality control?*

Statistical exploration of the combined St.Gallen Benchmarking Database and the sample available from the Global Quality Benchmarking Study led to a data-backed understanding of performance patterns across different types of production sites. Testing six hypotheses clusters revealed implications within all layers of the benchmarking architecture KPIs, Enabler, and Structural Factors.

A selection of indicators showed cross-departmental association and was therefore identified as particularly suitable to assess performance along the entire pharmaceutical value chain. Furthermore, maturity levels in certain enabler categories in manufacturing revealed significant positive correlations with further maturity attributes in quality control and vice versa. Analyzing the role of the structural context for cross-departmental maturity, solely the size of production facilities demonstrated a considerable impact. Moreover, the evaluation detailed relations between aggregated departmental KPI scorings, overall enabler implementation, and the compliance status operationalized by regulatory inspection outcomes. Hence, the quantitative analyses based on the benchmarking databases uncovered causes for performance differences between departments, identified levers to increase cross-departmental maturity levels, and highlighted drivers for alignment of manufacturing and quality control:

Coupling iOOS Rates in laboratories and the Share of Reject Batches in production results in a simplified but powerful combination of metrics able to indicate effectiveness along the site internal value chain beyond the indicators themselves. Moreover, process quality in laboratories significantly contributes to delivery performance of the entire production site as apparent in the association with plant's JIT scores. An efficiency perspective needs to be incorporated to properly measure and facilitate cross-departmental performance throughout pharmaceutical production sites, as solely assessing effectiveness is not sufficient. Compared to Lab Robustness and Operational Stability, the OPEX and Lab Performance scores comprise a broader and more balanced set of indicators used in both departmental benchmarking programs. These aggregated scores expose a positive correlation coming along with a remarkable degree of cross-departmental determination.

Understanding differences between manufacturing and quality control in full requires to equally consider aggregated KPI scores and enabler implementation levels for both departments, since there is no direct association that would allow to surrogate one pillar through the other. However, the top half of production sites in cross-departmentally combined enabler implementation demonstrates a significant association of aggregated outcome performance scores between manufacturing and quality control, whereas the lower half does not. Establishing combined cross-departmental OPEX maturity is consequently helpful to leverage performance

differences between manufacturing and quality control. In addition to that, higher alignment in performance across departments is associated with mastering regulatory inspections without any actions indicated and thus achieving favorable evaluations by authorities.

SRQ 2 – *What are suitable strategies, approaches, and tools to overcome organizational barriers and dispense OPEX capabilities across departments?*

Aiming to enrich the research with knowledge from broader subject areas, the scope of considered research fields was extended in the second research phase of the dissertation project. A newly adapted process for systematically searching literature uncovered manifold concepts to foster cross-departmental optimization within production sites not limited to Operational Excellence nor to the pharmaceutical industry. All identified articles were clustered in the two categories interorganizational or interdepartmental collaboration, reviewed for further consideration, discussed in detail, and summarized emphasizing their individual key findings. Afterwards, applicability and adaptability of promising aspects and practices from literature to the specific research problem OPEX across manufacturing and quality control was evaluated within the categories Barriers & Boundaries, Organizational Set-Up & Structure, and Knowledge Management & Capability Transfer.

Departmental haughtiness because of different maturity levels, reluctance to change due to departmental specialization, lacking management buy-in, and gaps in disseminative capabilities form common barriers for cross-departmental alignment, which are also highly applicable to the research at hand and hamper collaboration between manufacturing and quality control. Among others, these boundaries need to be actively addressed by OPEX management to overcome performance and maturity differences in pharmaceutical production sites.

Certain organizational aspects and structural set-ups are identified to positively affect and facilitate cross-departmental collaboration. Adapted to the present research problem, establishing centers of excellence, installing local middle management positions overseeing both departments, co-location of departmental improvement teams, and job rotation involving OPEX functions, can support the alignment between manufacturing and quality control. Furthermore, a well-defined combined knowledge architecture, which clearly specifies the balance of departmental depth and cross-departmental breadth in competencies, forms the basis to structurally dispense capabilities throughout the organization.

Moreover, several concrete practices or mechanism, which are successfully utilized in other industries, were revealed by literature. These are deemed powerful to share and comprehensively manage capabilities between departments of pharmaceutical productions sites. This particularly comprises the structured support of knowledge creation beyond knowledge sharing. Hereby special attention is paid on the internalization of acquired capabilities and the systematic evaluation of capabilities prior

to randomly start transfer processes. Furthermore, integration of target setting processes, introduction of joint recognition systems, and definition of indicators quantifying contribution to other departments all facilitate knowledge sharing by incentivizing individuals and preventing departmental competition. In addition to the mechanisms summarized, literature suggests approaching the transfer of capabilities through facilitating everyday routines in an integrated manner. Organizing problem solving of departmental issues in collaborative cross-functional teams or harmonizing the way huddle meetings are performed within and across departments serve as two actionable examples. Both are fully applicable to fostering capability dispersion across pharmaceutical manufacturing and quality control.

SRQ 3 – How do successful pharmaceutical production sites achieve excellent performance across manufacturing & quality control?

Complementing the previous two core research phases, qualitative research methods were supplementary applied to examine how OPEX is successfully managed across departments in an integrated manner. For this purpose, a survey-based study was conducted among OPEX functions in pharmaceutical production. The findings of the survey contributed to the research twofold. At first, outcomes immediately delivered insights on industry's current status of comprehensively managing OPEX involving production and laboratories. Secondly, responses gathered allowed to select production sites for further case study research.

A content-driven qualitative review of production site profiles based on their answers in the different categories of the survey led to the observation of dependencies between the structure and strategy, the level of excellence, and the approaches to address barriers and levers for improvement. Establishments that indicated a consistent level of excellence, thus production sites achieving a high degree of alignment in performance, maturity and compliance between plant areas and laboratories, demonstrated a set of commonalities:

Consistent performance across manufacturing and quality control is associated with maintaining a formalized OPEX roadmap and following an integrated site level strategy. Facilities operating a site level OPEX organization, which owns this strategy, struggle less to spread resources, information, and knowledge across departments than sites relying on corporate departmental OPEX organizations. Furthermore, all sites characterized by alignment in quality, delivery, and cost efficiency performance, actively foster information and knowledge sharing. This also prevents emergence of departmental bottlenecks. Aligned maturity levels between manufacturing and quality control are in particular achieved by the production sites, which started their OPEX initiatives in parallel across departments. In addition to that, these sites indicate a high proportion of cross-trained employees in all areas coming along with a strong mindset for Continuous Improvement embedded into the entire organization.

Answers to free text questions situated in the survey revealed concrete measures the sites take to manage OPEX comprehensively and achieve the level of performance demonstrated. On this basis, successful practices for comprehensive OPEX management were uncovered and determined a selection of three production sites for subsequent case study research. Interviews with representatives from the three pharmaceutical sites were conducted in the following and allowed to individually understand, evaluate, and document case-by-case selected proven successful practices for cross-departmental OPEX management:

Application and adaption of corporate OPEX frameworks, a product centric organization in case of small or variant product portfolios, an integrated idea and suggestion system, and the harmonization of OPEX initiatives with employee qualification programs contribute to achieving excellent performance across manufacturing and quality control at the case study sites. Furthermore, standardizing all departmental and cross-departmental huddle meetings, formalizing feedback processes in between departmental and site level OPEX functions, and systematically conducting Gemba walks tailored to specific aims were identified as powerful routines.

SRQ 4 – How to consolidate uncovered causes for performance differences, identified strategies for cross-departmental alignment, and proven successful practices in a guideline for interdepartmental OPEX management?

Ultimately, all implications derived within the core research phases were consolidated in a guideline for comprehensive OPEX management across manufacturing and quality control. Grounded in the research theories TDC, TOC, and CT, this comprised the combination of conclusions drawn from qualitative empiricism, literature, and quantitative empiricism, while paying special attention on integrating and harmonizing the manifold research findings. Thereby, all recommendations to OPEX management were clustered content-wise according to their subject fields and situated in a newly developed overarching guideline model to simplify application for practitioners.

The guideline is structured along an architecture of three central pillars Directing, Acting and Evaluating, which jointly represent the overarching fields of activity for comprehensively managing Operational Excellence across departments. Within these three pillars, the five modules Strategy, Organizational Set-Up, Procedures, Performance Indicators, and Maturity Attributes are situated to guide the practitioner through the set of recommendations provided. The different modules do not solely advise management step-by-step, but additionally interact with each other. Some modules are informed by the outcome of others or act as feedback loop in accordance with the principal philosophy of Continuous Improvement. All modules are detailed concordantly as content-wise clustered, consolidated, and condensed compilation of recommendations raised to management in an actionable format and complemented with supplementary explanations for practitioners.

After having developed the guideline set-up and detailed its five modules, clear instruction how to make use of the guideline in practice was provided to OPEX management. Moreover, the benefits of employing the guidance were demonstrated based on performance differences between production sites acting accordingly and other sites that do not. Empiricism-backed findings of the previous research phases allowed to clearly exhibit improvements that practitioners can anticipate and provided confidence for a return of efforts invested in implementation.

When following the stated guidance for interdepartmental optimization, managers are encouraged to tailor their acting to the specific situation at hand as stated in the module Strategy and to evaluate adaption of the specific approach to Operational Excellence even beyond the guideline. A special role of an establishment in its network, distinctive cultural barriers for Continuous Improvement, or a unique product portfolio can necessitate to reprioritize or deviate. Furthermore, attention on properly balancing site and network level operations is required.

Outcomes of the research at hand allow to assume increased levels of effectiveness, efficiency, and compliance throughout the organization as a consequence of adopting the developed guideline for comprehensively approaching and aligning OPEX across manufacturing and quality control. Recommendations given within the modules lead to alignment of departmental maturity levels and thereby eliminate bottlenecks along the site internal value chain. Hence, implementing the guideline impacts the supply reliability and delivery performance of pharmaceutical production sites. In addition to safeguarding product quality and ensuring delivery on time, manufacturing's interplay with high performing quality control units can also engender competitive advantages and increase efficiency, since process quality within laboratories is significantly associated with the Just-in-Time performance of plant operations. On top of that, applying the guideline and optimizing departments in conjunction pays off in a higher probability to receive favorable inspection outcomes by regulators.

MRQ – How to improve operational performance across manufacturing & quality control and avoid optimizing silos along the pharmaceutical value chain?

The presented studies aimed to comprehensively research interdepartmental Operational Excellence along the pharmaceutical value chain. Above summarized findings answered the sub research questions and thereby added up to the overarching achievement of this dissertation project: A managerial guideline how to approach Operational Excellence across manufacturing and quality control. This guideline was successively informed by implications drawn from manifold data sources through mixed-methods research along the iterative research procedure. Triangulation of the outcomes allowed not only to finally state and compile recommendations for management, but also revealed detailed insights on how operational

performance levels across pharmaceutical departments interdepend and interact. In conjunction, these findings exposed procedures to optimize production areas, laboratories, and their interplay in an actionable manner.

Aligned excellent performance across manufacturing and quality control is achieved through systematically approaching optimization according to a well-defined and tailored strategy. A suitable organizational set-up substantiates all associated OPEX programs, initiatives, or projects by specifying overarching structures and responsibilities at the concerned production site. On this basis, execution of targeted managerial procedures within and across departments addresses the opportunity gaps, installs improvements, and pays off in higher levels of maturity, effectiveness, efficiency, and compliance throughout the entire organization. Not only emphasizing everlasting optimization but being grounded in the principles of Continuous Improvement itself, the way to achieving interdepartmentally excellence is evolving. Therefore, instituting and regularly evaluating proper performance scores in conjunction with maturity attributes along the site-internal value chain is crucial. These indicators reveal and quantify the current status of operational performance, which provides the needed evidence for active and purposeful OPEX management across manufacturing and quality control.

7.2 Contributions

According to the definitions of Ulrich (1982, p. 6, 1984, p. 168), the presented research is situated in the field of applied social and management science. It strives to develop and design social systems and shall therefore especially deliver impact to practice. However, even if driven by practice, management research must not lack of a theoretical perspective. (Ulrich, 1984, p. 168 f.) Having emphasized these principles along the entire research procedure, the dissertation at hand finally contributes to both theory and practice in various manners. The contributions are outlined and detailed subsequently.

Contributions to Theory

Compiling a guideline for comprehensively approaching Operational Excellence across pharmaceutical manufacturing and quality control forms a new specific use case of applied management science. In that way, the research streams Operational Excellence, Organizational Strategy, and Capability Management are individually enriched and combined in a unique manner that was not priorly exploited by scholars. Consequently, the presented research outcomes do not only contribute to theory by applying and further developing established concepts of Operations Management, but also introduce new perspectives on the interplay of all three research streams to the scientific community.

Addressing the manifoldness of the research problem, this thesis conjointly follows the research theories TOC, CT, and TDC as its conceptual background. Partially

adopting and adapting the theories to the individual needs of the different research phases is proven successful along the research process of the present dissertation. This provides confidence for Gassmann et al. (2016, p. 40) advising scholars to consider multiple theoretical lenses to guide projects in the context of business and management research. Moreover, achieving the initially aspired objectives through prosperously pursuing the developed research procedure informed by the iterative learning process introduced by Baumbach (1998, p. 15) and Gassmann (1999, p. 13) confirms suitability of the adaption made. Hence, scholars are encouraged to supplement iterative execution of core research phases with upstream grounding and downstream conclusion.

Apart of its specific context, this thesis touches on long-lasting research questions in the fields of Operations, Lean, and Quality Management. The comprehensive analyses of multidimensional performance indicators, their dependencies, and the impact of structural context, further informs the academic debate about trade-offs in manufacturing, originally rooted in the work of Skinner (1969, 1986), Hayes and Wheelwright (1984) as well as Ferdows and De Meyer (1990). On top of that, the present research comments on the general perception that higher levels of maturity and the presence of capabilities noticeably improve operational performance. The latter is continuously discussed by scholars since decades, confer opinions voiced by Flynn and Flynn (2004), Peng et al. (2008), Voss et al. (1995) and Zhang et al. (2017).

Referring to the identified theoretical gap, this dissertation is the first scholarly contribution on Operational Excellence across pharmaceutical manufacturing and quality control. Thus, it expands the scientific knowledge basis and complements the arising literature stream discussing Lean Management in laboratories segregated from production areas by now: This research underpins and specifies the role of optimizing laboratories while striving for excellence throughout the production site in an aligned manner. Vice versa, researchers not particularly focusing on Operational Excellence or the domain pharmaceutical production, but concerned with interorganizational collaboration and cross-departmental optimization, also benefit from the outlined findings. The mixed-methods research set-up of quantitatively leveraging the power of benchmarking data, uncovering and adopting knowledge from broader subject fields, and incorporating industry's successful practices through qualitative research, serves as role model for similar studies.

Contributions to Practice

The need to carry out the presented research evolved from practice and has been motivated by initial observations of inconsistent effectiveness levels across manufacturing and quality within pharmaceutical production sites. Moreover, a tremendous industry pull for a comprehensive, cross-departmental approach to Operational Excellence is visible in the perceptions among OPEX executives (cf. appendix

A.1) and underlines the relevance of the thesis at hand. Striving to make an impact in the pharmaceutical industry, implications drawn within the different research phases of this dissertation are finally combined, condensed, and transferred in an actionable format. The overarching outcome, a guideline for OPEX management, provides a ready-to-use benefit to practitioners. Thus, the findings of the doctoral research in their entirety highly contribute to practice.

Above mentioned guideline for comprehensive OPEX management does not only comprise of certain practices to align maturity across manufacturing and quality control. It comes along with advices concerning the underlying strategy, the required organizational set-up, and the evaluations needed to inform and sustain Continuous Improvement along the site-internal value chain. Consequently, practitioners are broadly equipped to improve effectiveness, efficiency, and compliance throughout their organizations by implementing the recommendations. Furthermore, stating clear directions for effectuating the guidance in practice and transparently highlighting pitfalls encourages management to reflect the individual needs of their production sites. In this way management is enabled to prioritize and balance the different components of comprehensively approaching Operational Excellence across manufacturing and quality control accordingly.

In parallel, the present research serves as scientific basis to support practice in understanding the interdependency of pharmaceutical departments in the light of Operational Excellence. While doing so, the practitioners are informed about industry's current status of excellence within and across manufacturing and quality control of pharmaceutical production sites. Based on real-world benchmarking data, the analyses deliver causes for performance differences, uncover drivers for interdepartmental alignment, and specify the levers to comprehensively improve operations along the entire value chain. Even if learning through benchmarking is not new to the pharmaceutical industry, the research project at hand is the first that comprehensively combines and integrates the evaluation of performance indicators gathered across manufacturing and quality control. Legacy benchmarking studies, regardless if driven by academia or consultancies, all show a departmental focus or lack the required depth in assessing laboratories' process quality, while spotlighting the quality of products.

Identifying and exposing approaches for cross-departmental optimization from theory not limited to Operational Excellence nor to the pharmaceutical industry provides practitioners with stimulations far beyond their own specialized area of expertise. Nevertheless, having systematically evaluated all outcomes of the desk research for their applicability and adaptability to pharmaceutical manufacturing and quality control ensures relevance to industry. In addition to that, successful practices within the pharmaceutical industry, uncovered by the survey-based study and detailed in the supplementary case study research, offer a crisp, tangible, and achievable vision to practitioners. Alongside with the aspired improvements in effectiveness, efficiency

and compliance, these inspirations shall motivate management to act on the present research in practice, to tackle the corresponding subject field, and to start approaching Operational Excellence comprehensively.

7.3 Limitations

Transparently stating the limitations of a research project is common courtesy and crucial to raise awareness of existing challenges. Moreover, this allows to comment on existing shortcomings while advising fellow researchers and practitioners how to tackle pitfalls best. (Olufowote, 2017, p. 2) For the dissertation at hand limitations concerning the research methodology, the samples' characteristics and sizes, the exhaustiveness of outcomes, and the generalizability of findings are to be highlighted.

This thesis follows a mixed-method approach of combining quantitative and qualitative research. That is why outcomes of the individual research phases face limitations caused by the underlying methodologies. Quantitative research is often lacking context and in-depth background supplementing the data points gathered. Effective quantitative research usually requires large samples of a well-designed and balanced population (Choy, 2014, p. 102). Furthermore, meaningful conclusions can only be drawn if reliable and validated outcome measures are utilized. The importance placed on statistical significance may not necessarily represent the level of practical relevance of all findings. (Walker, 2005, p. 578) Moreover, qualitative methods also come with limitations to be considered: Findings are limited to the specific cases analyzed, implications are hardly adaptable to wider populations, and do not allow to test for significance. On top of that, the frequency of occurrence and longitudinal development of observed phenomena cannot be taken into account as case study interviews are conducted at a certain point of time. Ambiguities caused by human language may further limit unbiased interpretation and thus impact the comparability of findings. (Ochieng, 2009, p. 17)

Among other reasons, the weaknesses introduced above led to the decision to follow a mixed-method approach that allows to complement quantitative research findings with additional background gathered through qualitative research. This research design also paves the way to confirm single observations and pursue confidence. Velez (2008, p. 9) summarizes the advantages of mixed-method research as not being restrained by epistemological, axiological, and ontological assumptions, which come into play with mono-method research. However, mixed-method research is not able to solve all issues associated with qualitative and quantitative research by simply combining both paradigms. On the contrary, applying mixed methods increases the complexity of studies leading to a time-intensive research process that requires to adapt research steps according to additional needs showing up along the study. (Greene et al., 1989, p. 257) Being well aware of the limitations caused by the methodologies, the present research project strictly followed the

iterative nature of its specified procedure throughout the three core phases. In this fashion risks were mitigated by immediately adapting planned next steps of the research process in case given conditions and prerequisites for analyses changed.

The dissertation builds on quantitative and qualitative empiricism gathered from pharmaceutical production sites. While the research project succeeded in convincing as many manufacturers as possible to engage in the benchmarking programs for manufacturing and quality control, the number of observations is negligibly small compared to the population of pharmaceutical facilities around the world. The sample sizes and characteristics of the data attributes limit the range of applicable methods available for statistical exploration within the quantitative research. Even though the three case studies fulfilled the targeted purpose of detailing individual successful practices and were selected being aware of the limitations, it needs to be underlined that the qualitative research set-up does not allow for a formal cross-case analysis. Beyond that, all empiricism demonstrates a clear focus on Europe. The samples are biased accordingly although the different underlying studies were globally launched and well acknowledged worldwide. Consequently, sample sizes and characteristics do not allow for claiming full representation of the global pharmaceutical industry.

Findings of all research phases are compiled and condensed in the guideline for comprehensively managing Operational Excellence across manufacturing and quality control, which serves as overarching outcome of the doctoral research at hand. The guideline is informed and underpinned by implications drawn from manifold data sources based on mixed-methods research allowing for triangulation of findings. On top of this, it is structured in an actionable manner for the benefit of practitioners and includes advises for tailored application beyond the recommendations themselves. However, the guideline's content is limited to observations made during the research phases of this dissertation and is solely based on the empiricism available. Thus, exhaustiveness of recommendations provided to practice can neither be tested nor confirmed. Whereas all implications included in the guideline are carefully justified by research, this cannot ensure there are further aspects important to consider for comprehensively optimizing pharmaceutical manufacturing and quality control but missed within the present dissertation. Furthermore, the newly compiled guideline in its entirety has not been tested in the field yet. Depending on the maturity and legacy approaches, full implementation of the principles within a pharmaceutical production site requires fundamental changes in organizational set-up and managerial acting. Hence, corresponding time horizons for comprehensive application of the guideline in practice exceed the research schedule of the present thesis by far.

Even if internal validity of the research is ensured by combining different research methods and data sources, the external validity of findings is restricted by the sole focus on the pharmaceutical industry. Applicability and relevance of research outcomes for other industries might be given but need to be proven by future research before taken for granted. Moreover, it is noted that all results are derived from static

and time-centric observations within the individual research phases. No statement about dynamic or reinforcing effects, which are expected to further impact the lasting optimization across manufacturing and quality control over time, can be inferred.

7.4 Future Research

The present research establishes a profound scientific basis for understanding the interdependence of manufacturing and quality control in pharmaceutical production sites. In addition to providing actionable guidance for comprehensive cross-departmental optimization to OPEX management, this dissertation newly introduces the subject field to academia. Consequently, the studies offer manifold opportunities for conducting subsequent research. Promising starting points for future research having emerged within the different research phases are outlined in the following. These possibilities might support scholars in prospectively addressing and tackling the previously stated limitations of the thesis at hand but are not confined to do so. Beyond that, future projects can also broaden the research field.

Both St.Gallen benchmarking programs are in operation and continuously sought by industry. Consequently, the databases are expected to grow with operational indicators from further participating pharmaceutical establishments in the months and years to come. A higher number of combined benchmarking datasets including manufacturing and quality control allows to confirm and expand the quantitative research of this thesis based on more sophisticated statistical methods that presuppose larger data sets. Among others, this can comprise cluster analysis, multi linear regression, ANOVA, or factor analysis. On top of revealing further findings by unleashing advanced analytics, supplying the research with additional benchmarking data is expected to diminish the regional bias of the samples and thereby to increase representativeness of research outcomes.

The survey-based study launched for the purpose of this thesis has established unique access to a highly engaged community of pharmaceutical SMEs beyond the St.Gallen Industrial Research & Exchange Groups. This offers academia golden opportunities to continue and expand the case study research initiated. While the three case studies conducted and documented for the doctoral research at hand have been narrowly focused on the individual successful practices, future research might further detail these case establishments not confined to the practices discussed. Moreover, scholars are enabled to extend the scope and carry out additional qualitative research among the other establishments having participated in the survey-based study. In both ways, complementing case study interviews with in-depth review of firm documents or on-site observations can enrich the results.

Findings of the research at hand are transferred in actionable recommendations and add up to the guideline advising management how to comprehensively approach Operational Excellence throughout manufacturing and quality control. Forthcoming

implementation of the guideline in practice allows to extend the scope of research to a longitudinal study afterwards: Future research shall accompany the application of recommendations in industry and frequently document resulting progress within a period of time. Based on such observations, the improvements in effectiveness, efficiency, and compliance, anticipated by the present research based on its data sources, can either be confirmed or refined. Furthermore, proceeding accordingly allows scholars to judge sustainability of achievements in manufacturing and quality control.

All prospective research opportunities detailed above directly draw on the narrow focus of the present dissertation and similarly target to further improve operational performance across manufacturing and quality control within pharmaceutical production sites. Beyond these options, future projects might extend the scope and incorporate further departments in their studies. Complementary to the interplay of manufacturing and quality control, interfaces to quality assurance, site logistics, or even R&D determine overall performance of a pharmaceutical production site and are worth exploring from the perspective of Operational Excellence. One research step ahead, adopting the outcomes of this dissertation to other industries than pharmaceutical production is principally deemed feasible and comes along with tremendous benefits for practice. However, pursuing this path requires researchers to thoroughly evaluate the overall applicability in the new context first and fundamentally adapt the guideline as appropriate.

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Appendix

A.1 Initial Industry Statements – OPEX across Departments

Table 89 provides an overview on statements from industry with regard to the need and relevance for managing Operational Excellence across manufacturing and qc labs. The author conducted these unstructured interviews regularly as a side activity in meetings with pharmaceutical representatives to initially explore the presumed relevance of the dissertation topic.

All firms behind the statements made by OPEX executives are anonymized to maintain confidentiality. Additionally, it must be noted that the meeting locations are stated for documentation only and do not allow to draw any conclusion on the specific company interviewed. Most interviews took place in parallel to conventions or workshop meetings of the St.Gallen Industrial Research & Exchange Groups. Even if the locations give the impression to uncover specific companies operating production sites at these places, this is not the case as representatives of several organizations have been present.

Table 89: Statements on OPEX across Manufacturing and Quality Control

Date	Meeting Location	Company	Key Statement
July 20, 2018	Washington DC, US	Regulator	<i>We are extremely interested in better understanding the relation between plant and lab performance. Actually, we have been expecting similar levels of maturity within sites.</i>
Sep 25, 2018	Barcelona, Spain	Company A	<i>Our QC lab here in -Location- is one of the lighthouses and was recently lean certified. In QC we see much more diversity across the network and optimization efforts are less standardized than in production. It would be great if our analysts could benefit from the lean knowledge in manufacturing.</i>
Nov 6, 2018	Philadelphia, US	Company B	<i>Production and Labs are still more or less separate worlds in our OTC drug facilities. However, I can imagine it is even worth in Pharma.</i>
May 21, 2019	Leiden, Netherlands	Company C	<i>We launched Smart QC especially to optimize capacity planning in the laboratories. Aligning with the very dynamic production schedule is our biggest challenge. Together with the new system, we introduced a proper visual management that has been inspired by some well-working solutions for visualization in manufacturing.</i>

Date	Meeting Location	Company	Key Statement
June 25, 2019	Waltham, US	Company D	<i>Our company is still new to OPEX. We do not have a corporate organization or global roadmap. When we start now, we want to ensure to follow a systematic approach that covers both production and quality.</i>
Nov 19, 2019	Montpellier, France	Company E	<i>One of the weaknesses of our past continuous improvement programs in both manufacturing and qc was to strictly follow individual targets rather than thinking about consequences and opportunities for the whole system.</i>
Feb 20, 2020	St.Gallen, Switzerland	Company F	<i>This research is definitely needed. Even if our quality colleagues did a lot in the recent past, I still see huge potentials if they would be willing to consequently adapt our lean thinking from manufacturing.</i>
Feb 25, 2020	Aubonne, Switzerland	Company G	<i>After we set a strong focus on transformation and digitalization in the labs during the last years standardization and harmonization along the value chain is the logical next step.</i>
May 06, 2020	Remote Meeting	Company H	<i>It's not entirely surprising that there's not a correlation between manufacturing and qc lab performance and we've had similar observations across our network. Lean and OPEX focus has been on manufacturing over the last few decades which may have had an unintended consequence. Specifically, Lean has embedded the philosophy that manufacturing is the value-added activity and QC and QA as the cost-added activities. Further, the regulatory requirement of the "independence of the Quality Unit" has yielded both the physical and organizational separation of QC and QA activities which has further compartmentalized the Operational Excellence activities and improvement in Quality and Manufacturing. This may also yield two different "cultures" within the same site in labs and operations.</i>

A.2 Statistical Methods – Detailed Explanations

Supplementary details on the methods used in chapter 3 are outlined in the following. This concerns descriptive statistics and linear regressions.

Descriptive Measurements of Frequency, Central Tendency, and Variability

Measurement of frequency describes both count of occurrence and the quantity within categories. It may also provide the percentage share of a sample represented. Evaluating frequency distributions is applicable to discrete data and can be presented in the form of numeric value tables or with the use of graphical techniques, e.g. histograms and bar charts. Depending on the underlying data sets and focus of analyses, frequency distributions are mostly univariate (analyzing one variable only). However, bivariate (analyzing two variables) or multivariate (analyzing more than two variables) measurements of frequency in the form of complex tables exist as well. (Thompson, 2009, p. 57 f.)

Measures of central tendency evaluate the middle position of samples. The mode, describing the value most frequently occurring in a sample, is helpful for level data with a limited set of discrete categories and less insightful for continuous data scales. As a next measure of central tendency, the median indicates the value in the exact middle of the sample. Half of the individual observations lie above the median, half below it. Obviously, the median requires a content-wise order of the data points and is not applicable to nominal level data. Summing the values for all subjects and dividing the result by the total number of subjects leads to the mean of a sample, also called average. It is the most common measure of central tendency but more sensitive to outliers compared to the median. Depending on the phenomena researched and the characteristics of the data set, the median, mean, or both can be especially insightful. All measures of central tendency inform where the middle or majority of data points is located within a sample but do not allow to analyze distributions of different data points. (Thompson, 2009, p. 58)

In addition to frequency and central tendency, analyses of the variability of data sets complete the types of descriptive statistics. Calculating the range as the difference between the lowest and the highest value of a sample can inform how broadly the data points are spread out. Similar to the mean, the range is heavily impacted by outliers, what needs to be considered to avoid misleading interpretation. The variation of the entire sample is reflected by the standard deviation that can be interpreted as average distance from the mean across all individual data points. (Thompson, 2009, p. 59) Quartiles divide the sample into four equally sized groups comprising values in an ascending or descending order. Calculating the interquartile range between the 1st and 3rd quartile of the dataset is an additional measure of variability and statistical dispersion. Accordingly, dividing the sample in 100 equal groups and assessing the position of individual data points by calculating the percentile is established in applying descriptive statistics. (Mishra et al., 2019, p. 69)

Testing Preconditions of Linear Regression

Linearity is judged with the help of a scatter plot. Normal distribution of variables is shown by a Shapiro-Wilk test resulting $p > 0.05$ in combination with graphical interpretation of the Q-Q plot. The Shapiro-Wilk test hypothesizes the variable to be normally distributed. Hence, a not significant test result $p > 0.05$ suggests not to reject the null hypothesis and allows to assume normal distribution. (Brosius, 2013, p. 403 ff.)

Autocorrelation between residuals can be assessed by applying Durbin-Watson statistics and testing the sample accordingly. The test result value d can range between $d = 0$ (indicating highest positive autocorrelation) and $d = 4$ (indicating highest negative autocorrelation). No autocorrelation exists at $d = 2$. Literature describes Durbin-Watson tests results $1.5 < d < 2.5$ as sufficient to assume a non-critical level of autocorrelation for linear regressions. Beyond checking for autocorrelation, the Durbin-Watson test also serves as indicator for homoscedasticity at the same time. D values not highlighting autocorrelation also indicate a non-critical level of heteroscedasticity. However, homoscedasticity needs to be additionally confirmed by analyzing the residual plot and ensuring absence of any heteroscedastic patterns. (Urban & Mayerl, 2018, p. 255 ff.)

A.3 Questionnaire – OPEX Manufacturing Benchmarking



Benchmarking Project OPEX Maturity & Performance in the Pharmaceutical Industry Pharmaceuticals Questionnaire

The project

Based on the well-established, scientifically backed and industry tested St.Gallen Operational Excellence Benchmark, this next generation benchmark is designed to help participants gain new insights into their operational performance relative to their peers. This new development has been created by the Institute of Technology Management at the University of St.Gallen (ITEM-HSG), Switzerland, with input from industry experts and is fully compatible with St.Gallen's existing data, totaling over 350 data points.

Since 2004, ITEM-HSG and the Transfer Center for Technology Management at the University of St.Gallen (TECTEM), Switzerland, have conducted an international research project in the field of Operational Excellence (OPEX) in the Pharmaceutical Industry. This continuous benchmarking project deals with the implementation of Lean Thinking and other basic principles of OPEX. The results provide participating companies with the opportunity to position their production sites against industry peers and show possibilities to improve productivity, quality and reduce lead time by implementing principles of Lean Manufacturing.

This new enhanced benchmark builds on St.Gallen's enabler benchmark to provide a holistic view of site performance around cost/headcount, production, quality & service. Notably, we assess OPEX maturity as well as performance outputs by Technology & Value Chain Step.

The following questionnaire is part of this project and aims to collect data from further pharmaceutical sites worldwide.

Your commitment

Your participation is vital to the success of this unique study. Filling out the questionnaire takes about 60 minutes for each the Corporate Level, Site Level and Enablers sheets and around 45 minutes for technology sheets. The time to collect the data (e.g. performance indicators) differs from company to company.

Your benefits

The questionnaire and corresponding personalized analysis has been developed by ITEM-HSG, in cooperation with leading pharmaceutical companies. This will:

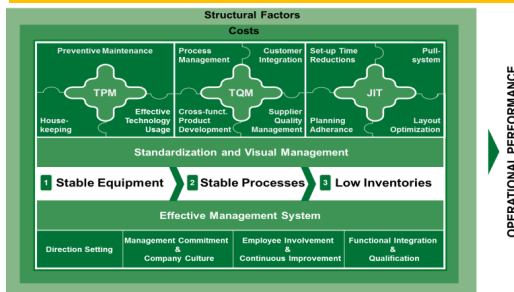
- provide an overview of what is driving the site performance, with deep dive analyses on the level of maturity for quality, production, service and management systems as well as basic production elements
- provide meaningful and understandable comparative data at the technology and line level
- incorporate structural and complexity-related factors to fully contextualize performance and maturity data

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 utmost discretion, and following the tripartite non-disclosure agreement signed at the inception of this assessment

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:

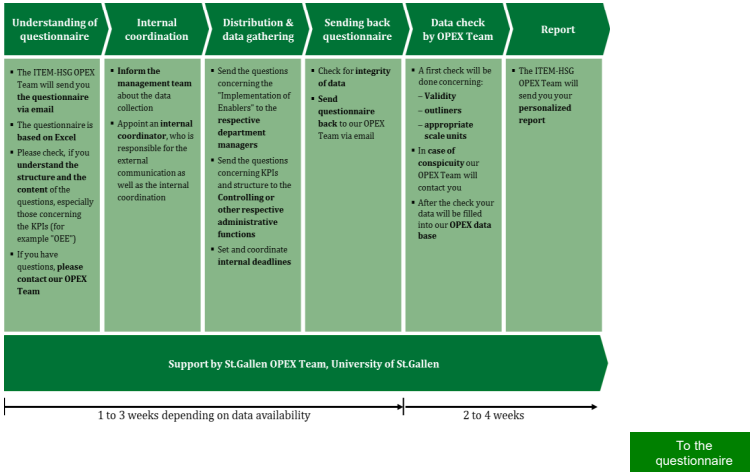
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To the
questionnaire

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. The proposed timeline should help you to coordinate the data gathering process and explain how we plan to support you throughout the assessment.



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General information

	Contact information			
A01	Last name			
A02	First name (s)			
A03	Position or role			
A04	Company name *			
A05	Production site *			
A06	Telephone			
A07	Fax			
A08	E-mail *			
A09	Address			
	Please fill in the year your data is valid for.			Commentary
A10	Year *			
	Please fill in the currency the following answers are based on.			Commentary
A11	Currency *			
	Please select your site location.			Commentary
A12a-b	Country*		If "other" please specify	
proceed				

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* are the mandatory fields

Your company**A. Corporate level**

	How many fully-owned production sites are part of your network?				Commentary
B01	Number				
	In addition, how many external (CMO) production sites does you company manage?				Commentary
B02	Number				
B03	Percentage of manufacturing (by volume) completed by external production sites				
	What was your total company sales in the last year?				Commentary
B04	In millions				
	Please fill in the cost structure of your company as a percentage of sales (approximate figures are sufficient)				Commentary
B05	R&D				
B06	Manufacturing costs				
B07	General & administration costs				
B08	Sales & marketing costs				
B09	Net profit				
	Compared to your competitors, indicate the development of your company on the following dimensions within the last 3 years.				Commentary
		Significantly lower	Average	Significantly higher	
B10	Market share	☐	☐	☐	
B11	Sales growth	☐	☐	☐	
B12	Return on sales	☐	☐	☐	
B13	Launches of new promising products	☐	☐	☐	
B14	Share price	☐	☐	☐	
	Company type				Commentary
	<i>Please indicate your company type (yes/ no). Multiple answers are possible.</i>			<i>Please indicate which one applies most.</i>	
	<i>Please note that detailed product categories are included on the site level sheet.</i>				
B15	Pharmaceutical company with R&D (inc. biotech)	☐ yes ☐ no		☐	
B16	Generics manufacturer (inc. biotech / biosimilars)	☐ yes ☐ no		☐	
B17	Contract manufacturer	☐ yes ☐ no		☐	
B18	OTC / Consumer	☐ yes ☐ no		☐	
B19	Miscellaneous (If the stated types do not reflect your business please provide us the information)			☐	
	What is the structure of your Corporate OPEX Function?				Commentary
	<i>Please indicate describe the structure of your Corporate OPEX function</i>	Units	Measure		
B200	Do you have a Corporate OPEX Function		☐ yes ☐ no		
B201	How old is the function?	Years since establishment			
B202	How large is the function?	FTE			
B203	How large is the OPEX function as a percentage of all corporate staff?	%			
B204	What proportion of the OPEX function is temporary as a percentage of all corporate OPEX staff?	%			

What is the role of your Corporate OPEX Function?							Commentary
Please indicate which roles apply to your Corporate OPEX function							
B205a-f	Coordination	Links top management to line management	Bundles existing initiatives in umbrella programmes	Coordinates OPEX implementation	Supervises OPEX implementation	Controls OPEX aspects of the implementation process	n/a
	☐		☐	☐	☐	☐	☐
B206a-f	Execution	Recommends actions to line management	Makes strategic OPEX decisions	Makes operational OPEX decisions	Implements OPEX methodology (e.g. six sigma)	Directly implements actions	n/a
	☐		☐	☐	☐	☐	☐
B207a-e	Enabler		Streamlines OPEX decision making by increasing responsibilities at lower levels	Provides standard tools and operational methods	Conducts training programmes on OPEX methods	Deploys OPEX champions	n/a
			☐	☐	☐	☐	☐
B208a-e	Communication		Empowers persons in charge of implementation	Transfers knowledge to lower hierarchical levels	Creates common understanding and standard language of OPEX	Clearly communicates activities across all levels	n/a
			☐	☐	☐	☐	☐

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proceed

Your site**B. Type of production site**

History of the plant					Commentary
C01	The plant is an original plant and was founded by the company itself	☐ yes ☐ no			
C02a-c	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			
C190	The site mission has changed during its lifetime	☐ yes ☐ no			
C191	How old is the plant in years?				
C192	What is the size of the site (square feet)?				

Site role					Commentary
<i>If your site is part of a manufacturing network, does the site have a specific role within this network? Multiple answers are possible!</i>					
C03	We have a manufacturing network.	☐ yes ☐ no			
		Not applicable	Average	Highly applicable	
C04	Launch site	☐	☐	☐	
C05	Special technology	☐	☐	☐	
C06	Special capacity size	☐	☐	☐	
C07	High packaging and production flexibility	☐	☐	☐	
C08	Access and entrance to markets	☐	☐	☐	
C09	Close to regional technology clusters	☐	☐	☐	
C10	Follow-the-customer	☐	☐	☐	
C11	Low cost site	☐	☐	☐	
C12	Securing of raw material sources	☐	☐	☐	
C13	Development site	☐	☐	☐	
C14	Back-up site (redundancy/ capacity)	☐	☐	☐	
C15	No special site role	☐ yes ☐ no			

Type of site					Commentary
<i>Please select all that apply.</i>					
Drug Substance					
C16	Chemicals (API)	☒ yes ☐ no			
C17	Biologics	☒ yes ☐ no			
Formulation, Filling and/or Packaging (Primary and Secondary)					
C18	Solids	☒ yes ☐ no			
C19	Creams	☒ yes ☐ no			
C20	Suppositories	☒ yes ☐ no			
C21	Sterile liquids	☒ yes ☐ no			
C22	Non-Sterile liquids	☒ yes ☐ no			
C23	Patches	☒ yes ☐ no			
C24	Inhalers	☒ yes ☐ no			

Appendix

Indicate how your production site is organized.			Commentary
C25	☐ Cost-center ☐ Profit-center		

Profit & Loss Structure			Commentary
<i>Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.</i>			
		Unit	Measure
C26	Gross Sales	thousand	
	COGS (Cost of Goods Sold)	thousand	n/a
C27	Conversion Costs	thousand	n/a
C28	Material costs (inc. cost of API)	thousand	
C29	Labor costs	thousand	
C30	Plant, property and equipment costs	thousand	
C31	Other costs	thousand	
C32	Inventory write-off costs	thousand	
C33			

Headcount Structure			Commentary
<i>Please include all FTEs working at your site independent from being on your payroll.</i>			
C34	Direct labour		n/a
C35	Production labour	Total	n/a
C36		Drug Substance / API production	
C37		Formulation, Filling & Primary Packaging	
C38		Secondary Packaging	
C39	Quality control (Direct)	Total	n/a
C40		QC lab testing	
C41		Incoming inspection (inc. raw material and release of components coming from CMOs/other companies' sites)	
C42		Batch record review	
C43	Indirect labour		n/a
C44	Quality control (Indirect)	Total	n/a
C45		Testing ("taking samples") management	
C46		Laboratories management	
C47		Stability testing	
C48		Environmental Monitoring	
C49	Quality assurance	Total	n/a
C50		Validation	
C51		Quality Administration	
C52		In-process testing	
C53		Equipment maintenance (lab and product and process control)	
C54		Supplier Quality	
C55		Quality systems and documentation	
C56		Investigations (OOS, events, complaints and deviations) and CAPAs	
C57		Audits	
C58	Complaints Management		
C59		Change control	
C60	Maintenance	Total	n/a
C61		Reactive (Fire fighting)	
C62		Basic Care (e.g. lubrication, cleaning)	
C63		Preventive (calendar based exchange of parts)	
C64		Predictive (condition based exchange of parts)	
C65		Other Maintenance	
C193	Supply Chain	Total	n/a
C68		Supply Chain Management (procurement and logistics)	
C194		Other Supply Chain	

C66	Other functions	Total	n/a					
C67		Production Management (Site Leadership Team)						
C69		Manufacturing engineering						
C70		EH&S (environment, health and safety)						
C71		IT Support						
C72		Operational Excellence and continuous improvement						
C73		Human Resources						
C74		Finance						
C75	General Management							
C76	Technical Services							
C77	Overall number of FTEs at the site		n/a					

Employment structure								Commentary
C78	Percentage of FTEs permanently employed by the company							
C79	Percentage of FTEs temporarily employed by the company							
C80	Percentage of FTEs temporarily employed by a temp agency							

Product Structure								Commentary
Product portfolio								
Please select all that apply.								
C81a-f	☐ Rx	☐ Otc	☐ Bx	☐ Biosimilar	☐ OTC	☐ AH		
Indicate the proportion of products manufactured at your plant (% in the last year.								
	Research driven	Generics	Biologics	Biosimilar	Over the Counter	Animal Health		
% value								
C82a-f	Own manufacturing							
C83a-f	Contract manufacturing (share of CMO of total products)							
Sum should add up to 100%					Sum:	0%		
% volume								
C84a-f	Own manufacturing							
C85a-f	Contract manufacturing (share of CMO of total products)							
Sum should add up to 100%					Sum:	0%		

Biotechnological products								Commentary
Please indicate the type of bio-technological product as % volume of total bio-technological products								
C86	Monoclonal antibodies							
C87	Cytokines							
C88	Enzymes							
C89	Hormones							
C90	Clotting factors							
C91	Vaccines							
C92	Cell therapies							
C93	Antisense drugs							
C94	Peptides therapeutics							
C95a-b	Other 1 (Please Specify)	Specify product here						
C96a-b	Other 2 (Please Specify)	Specify product here						
C97a-b	Other 3 (Please Specify)	Specify product here						
					Sum:	0%		

Appendix

Miscellaneous					
Please indicate those of the below that apply to your site:				%-volume	
C08a-b	Clinical trials	☐ yes ☐ no			
C09a-b	High containment products	☐ yes ☐ no			
C100a-f	Drug license approvals	☐ GMP ☐ FDA ☐ EMA ☐ PMDA ☐ CFDA ☐ WHO			
Procurement and Supplier Structure in the last year				Commentary	
Supplier count: number of active suppliers both internal and external					
		API / starting & raw materials	Excipients	Packaging material	Others (e.g. utilities)
C101a-d	Number of active suppliers for...				
C102a-d	Total amount purchased (in millions) of...				
C103	Total				n/a
C104	Percentage of internal suppliers (suppliers within the same manufacturing network)				
C105	Percentage of suppliers that deliver your site frequently				
C106	Frequently means on average every ... days.				
C107	Number of orders placed with your suppliers				
Sourcing by regions (primary the location of production, not the registered office/ in %) in the last year					
		% value	% volume		
C108a-b	West Europe				
C109a-b	North America				
C110a-b	East Europe				
C111a-b	South and Middle America				
C112a-b	Middle East and Africa				
C113a-b	India				
C114a-b	China				
C115a-b	Asia (excl India, China and Japan)				
C116a-b	Japan				
C117a-b	Australia and New Zealand				
Customer Structure				Commentary	
Customer structure in the last year					
C118	Overall number of customers				
	Customer split		% value	% volume	
C119a-b	Internal sites				
C120a-b	Internal warehouses				
C121a-b	External sites				
C122a-b	External warehouses				
C123a-b	Pharmacists				
C124a-b	Whole sale				
C125a-b	Hospitals				

C126	Percentage of customers delivered frequently		
C127	Frequently means on average every ... days.		
C128	Number of orders received from your customers		
Customers by regions (primary the location of delivery, not the registered office/ in % in the last year			
		% value	% volume
C129a-b	West Europe		
C130a-b	North America		
C131a-b	East Europe		
C132a-b	South and Middle America		
C133a-b	Middle East and Africa		
C134a-b	India		
C135a-b	China		
C136a-b	Asia (excl India, China and Japan)		
C137a-b	Japan		
C138a-b	Australia and New Zealand		
Innovation structure			
C141	Number of new drug substance introductions within the last 3 years ("new drug substance" should be understood in the sense of new for the site)		Commentary
C142	Number of launched single dose units (SDU) at the site within the last 3 years (new for the site)		
C143	Number of launched stock keeping units (SKU) at the site within the last 3 years (new for the site)		
C144	Number of inspections at site within the last 3 years from...		
C145	...regulatory body		
C146	...headquarters		
C147	...customer		
Compliance Metrics			
Figures should refer to operations over the course of the last year			
Internal Compliance Metrics			
C148	Number of CAPAs		
C149	Total number of critical CAPAs that went overdue in the last year		
C150	Total number of non-critical CAPAs that went overdue in the last year		
C151	# of observations of a health authority inspection		
C152	# of observations per internal audit		
External Compliance Metrics			
Market actions			
C153	Number of recalls (Class I and II)		
C154	Number of supply stops (e.g. drug shortages)		
C155	Others (e.g. withdrawals)		
Regulatory actions			
C156	Number of Warning Letters		
C157	Number of 483s		
C158	Others (e.g. Field Alert Reports)		
EMS performance			
	Name	Definition	Unit
C159	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
C160	Management span of control	The average number of employees directly reporting to supervisors.	Number

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C160	Management span of control	The average number of employees directly reporting to supervisors.	Number		
C161	Group work	Percentage of production workers that are organized in self directed teams in terms of e.g. holiday planning and team meetings.	%		
C162	Functional integration	Number of production workers that are qualified to work on 3 or more technologies/functional areas as a percentage of all workers.	%		
C163	Suggestions (quantity)	Average number of suggestions per employee in the last year.	Number		
C164	Suggestions (financial impact)	Estimated total savings due to suggestions that were implemented.	thousand		
C165	Employee fluctuation	Employees leaving your site due to terminations, expired work contracts, retirements etc. as a percentage of all employees.	%		
C166	Sick leave	Total time of employees absent (e.g. sick leave) as a percentage of the total working time.	%		
C167	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.	%		
C168	Training	Number of training days per employee (all kinds of training off- and on the job) in the last year.	Days		
C169	Level of qualification	Number of workers with prior work related qualification/education as a percentage of the total number of workers at your site.	%		
C170	Level of safety	Reportable incidents due to accidents and safety on average per month that are internally (on site) reported.	Number per month		

Breakdown of manufacturing supervisor work					Commentary
If there are manufacturing supervisors at your site, please indicate the percentage of time dedicated to...					
		Unit	Measure		
C195	Time working away from the Line	%			
C171	Line Staffing	%			
C172	Problem Solving	%			
C173	Training	%			
C174	Working on the line directly	%			

Planned improvements of the manufacturing strategy at your site						Commentary
Indicate the degree of emphasis which your manufacturing plant places on the following future activities.						
		No activities planned	Activities planned	Key activities		
Increase of flexibility						
C175	Reduce cycle time	☐	☐	☐	☐	
C176	Reduce set-up time and cleaning time	☐	☐	☐	☐	
C177	Increase flexibility to respond to demand changes in volume	☐	☐	☐	☐	
C178	Increase flexibility to respond to market needs for broad product mix (concerning package size, concentrations, flavors etc.)	☐	☐	☐	☐	
C179	Increase flexibility to respond to shorter product lifecycles and higher number of product launches	☐	☐	☐	☐	
C180	Accelerate new product introductions (time to market)	☐	☐	☐	☐	
Increase quality						

[illegible]

Commentary

[illegible]

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Enablers

1: Total Productive Maintenance (TPM)

Preventive Maintenance						Commentary	
	1	2	3	4	5		
1	To what degree is there a formal program for maintaining machines and equipment?	There is no formal maintenance program	Formal program exists but is not widely visible	Formal program exists and is visible but is adhered to unevenly	Formal program is regularly adhered to but not regularly updated	Formal program strictly adhered to and updated regularly	
		☐	☐	☐	☐	☐	
2	To what degree are maintenance jobs documented, and maintenance plans and checklists posted close to machines?	Jobs, plans, and checklists are not documented & posted	Jobs, plans, and checklists are rarely documented & posted	Jobs, plans, and checklists are sometimes documented & posted	Jobs, plans, and checklists are regularly documented & posted	Jobs, plans, and checklists are always documented & posted	
		☐	☐	☐	☐	☐	
3	To what degree is good maintenance emphasised as a strategy for increasing quality and planning for compliance?	We do not communicate maintenance goals	Maintenance goals are communicated but not emphasised	Maintenance is emphasised, but unevenly across the site	Maintenance is emphasised across the whole site, but not core to improvement	Maintenance is core to quality improvement across the whole site	
		☐	☐	☐	☐	☐	
4	To what degree are potential bottleneck machines identified and supplied with additional spare parts?	Bottleneck machines are not identified	Bottleneck machines are identified but not supplied with spare parts	Bottleneck machines are supplied with spares, but unevenly across the site	Bottleneck machines are supplied with spare parts across the site	Bottleneck analysis is regularly refreshed, and machines supplied with spares	
		☐	☐	☐	☐	☐	
5	To what degree is the maintenance program continuously optimized based on a dedicated failure analysis?	Dedicated failure analysis is not carried out	Dedicated failure analysis is carried out but not used to optimise maintenance	Failure analysis is used to optimise maintenance, but unevenly across site	Failure analysis is used to optimise the maintenance program across the site	Regularly-refreshed failure analysis is used to optimise maintenance	
		☐	☐	☐	☐	☐	
6	To what degree does the maintenance department focus on assisting machine operators perform their own preventive maintenance?	Operators receive no assistance relating to preventive maintenance	Operators receive little assistance relating to preventive maintenance	Operators receive some assistance relating to preventive maintenance	Operators receive significant assistance relating to preventive maintenance	Operators receive extensive assistance relating to preventive maintenance	
		☐	☐	☐	☐	☐	
7	To what degree are machine operators actively involved in the decision making process when buying new machines?	Operators are not involved in buying new machines	Operators are rarely consulted when buying new machines	Operators are sometimes consulted when buying new machines	Operators are regularly consulted when buying new machines	Operators are extensively involved in buying new machines	
		☐	☐	☐	☐	☐	
8	To what degree are machines maintained internally vs externally?	<20% of maintenance is conducted internally	20% - 40% of maintenance is conducted internally	40% - 60% of maintenance is conducted internally	60% - 80% of maintenance is conducted internally	>80% of maintenance is conducted internally	
		☐	☐	☐	☐	☐	
Technology assessment and usage						Commentary	
	1	2	3	4	5		
9	To what degree is the site situated at the leading edge of new technology?	We do not seek to use leading edge technology	We rarely incorporate leading edge technology	We sometimes incorporate leading edge technology	We regularly incorporate leading edge technology	We seek to stay at the frontier of leading edge technology	
		☐	☐	☐	☐	☐	
10	To what degree do you screen the market for new production technology and assess new technology concerning its technical and financial benefit?	We do not screen for and assess new technology	We rarely screen for and assess new technology	We sometimes screen for and assess new technology	We regularly screen for and assess new technology	We are always screening for and assessing new technology	
		☐	☐	☐	☐	☐	
11	To what degree is the site effectively using new technology?	We have not introduced new technology in the last 5 years	We are interested in improving technology but do not devote much capex to this	We seek to introduce new technology, and devote some capex to this	We seek to introduce new technology, and devote a significant portion of capex	Our site is used to pilot new technology within our network	
		☐	☐	☐	☐	☐	
12	To what degree does the site rely on vendors for its equipment?	<20% of equipment from vendors	20% - 40% of equipment from vendors	40% - 60% of equipment from vendors	60% - 80% of equipment from vendors	>80% of equipment from vendors	
		☐	☐	☐	☐	☐	
13	What proportion of equipment is proprietary?	<20% of equipment is proprietary	20% - 40% of equipment is proprietary	40% - 60% of equipment is proprietary	60% - 80% of equipment is proprietary	>80% of equipment is proprietary	
		☐	☐	☐	☐	☐	
14	To what degree is proprietary process technology and equipment used to gain a competitive advantage?	We use off-the-shelf process technology and equipment	We buy equipment on the market and use it with minimal modification	We buy equipment on the market, and carry out some modification as needed	We buy equipment on the market, and continuously modify to suit our needs	We build equipment to fit our needs - if it doesn't exist on the market we build it	
		☐	☐	☐	☐	☐	

Housekeeping						Commentary
	1	2	3	4	5	
D15	To what degree do employees strive to keep the site neat and clean?	Housekeeping is not a core part of our site culture	Housekeeping is a small part of our site culture	Housekeeping is a reasonable part of our site culture, and a part of our training program	Housekeeping is a significant part of our site culture and training program	Housekeeping is a core part of our site culture, and we perform regular audits
		☐	☐	☐	☐	
D16	To what degree are plant procedures in place, regarding putting all tools and fixtures in their place?	We do not have formal housekeeping procedures	Formal housekeeping procedures exist but are not widely visible	Formal housekeeping procedures exist and are visible, but are adhered to unevenly	Formal housekeeping procedures are adhered to across the site	Regularly-updated formal housekeeping procedures are adhered to across the site
		☐	☐	☐	☐	
D17	To what degree are housekeeping checklists used to continuously monitor the condition and cleanliness of our machines and equipment?	We do not have housekeeping checklists	Housekeeping checklists exist but are not widely visible	Housekeeping checklists exist and are visible, but are adhered to unevenly	Housekeeping checklists are adhered to across the site	Regularly-updated housekeeping checklists are adhered to across the site
		☐	☐	☐	☐	

2: Total Quality Management (TQM)

Process Management						Commentary
	1	2	3	4	5	
D18	To what degree are direct and indirect processes documented?	Documentation does not exist	Documentation exists but is not widely visible	Documentation exists and is visible but is enforced unevenly	Documentation is regularly enforced but not regularly updated	Documentation is strictly enforced and updated regularly
		☐	☐	☐	☐	
D19	To what degree is process quality continually measured?	Continuous measurement of process quality does not exist	Continuous measurement exists but is not widely used	Continuous measurement exists and is used but is enforced unevenly	Continuous measurement exists and is enforced	Continuous measurement exists and is strictly enforced across the whole site
		☐	☐	☐	☐	
D20	To what degree is process quality continually measured using process metrics (e.g. on-time-in-full delivery rate)?	No clear definition of metrics	Clearly defined metrics, but not standardised across the site	Standardised metrics, but not exhaustive of site performance	Standardised exhaustive metrics	Standardised exhaustive metrics, with leading and lagging indicators
		☐	☐	☐	☐	
D21	To what degree are process measures directly linked to site objectives?	No clear link to site objectives	Some metrics linked to site objectives	Majority of metrics clearly linked to site objectives	Metrics clearly linked to site objectives, and cascaded across site organisation	Metrics clearly linked to specific objectives for each area, and cascaded across site
		☐	☐	☐	☐	
D22	To what degree are dedicated process owners responsible for planning, managing, and improving their processes?	No dedicated process owners	Some ownership of processes	Dedicated process owners, but little responsibility attached	Dedicated process owners responsible for planning & mgmt	Dedicated process owners responsible for planning, mgmt, and improvement
		☐	☐	☐	☐	
D23	What proportion of the equipment on the shop floor is currently under statistical process control (SPC)?	<20% of equipment	20% - 40% of equipment	40% - 60% of equipment	60% - 80% of equipment	>80% of equipment
		☐	☐	☐	☐	
D24	To what degree is statistical process control utilised to reduce variances in processes?	Statistical process control never utilised	Statistical process control rarely utilised	Statistical process control sometimes utilised	Statistical process control often utilised	Statistical process control always utilised
		☐	☐	☐	☐	
D25	To what degree are standardised tools in place for root cause analysis, to get a deeper understanding of the influencing factors (e.g. DMAIC)?	No tools in place	Some tools in place but not standardised	Standardised tools in place, but used unevenly	Standardised tools used regularly	Standardised tools used regularly and a core part of training
		☐	☐	☐	☐	
D26	What proportion of equipment makes use of Process Analytical Technology (PAT), for real-time process monitoring and controlling?	<20% of equipment	20% - 40% of equipment	40% - 60% of equipment	60% - 80% of equipment	>80% of equipment
		☐	☐	☐	☐	

Cross functional product development						Commentary
	1	2	3	4	5	
D27	To what extent are manufacturing engineers (e.g. Industrial engineers) involved in the development of a new drug formulation and the development of the necessary production processes?	Engineers are rarely involved in developing new drugs	Engineers are rarely consulted when developing new drugs	Engineers are sometimes consulted when developing new drugs	Engineers are regularly consulted when developing new drugs	Engineers are extensively involved in developing new drugs
		☐	☐	☐	☐	
D28	To what degree are product and process development linked?	Product and process development are not linked	Product and process development teams rarely work together	Product and process development teams sometimes work together	Product and process development teams regularly work together	Product and process development teams work extensively together
		☐	☐	☐	☐	
D29	To what degree is there close collaboration between the R&D and the manufacturing department, to shorten launch times?	R&D and manufacturing teams do not collaborate	R&D and manufacturing teams collaborate on an ad hoc basis	R&D and manufacturing teams collaborate ~monthly	R&D and manufacturing teams collaborate ~weekly	R&D and manufacturing teams work extensively together
		☐	☐	☐	☐	

Appendix

D30	In the last 2 years, what proportion of product launches have been on time? (launch by planned launch date)	<20% of launches	20% - 40% of launches	40% - 60% of launches	60% - 80% of launches	>80% of launches	
		☐	☐	☐	☐	☐	
D31	To what degree are standardised procedures in place for product and process transfers between different units or sites?	We do not have formal transfer procedures	Transfer procedures exist but are not widely visible	Transfer procedures exist and are visible, but are adhered to unevenly	Transfer procedures are adhered to across the units/site	Regularly-refined transfer procedures are adhered to across units/site	
		☐	☐	☐	☐	☐	
Customer involvement							Commentary
		1	2	3	4	5	
D32	To what degree are you in close contact with your customers (e.g. email, phone, e-room)?	We are not in close contact with our customers	We are rarely in close contact with our customers	We are sometimes in close contact with our customers	We are regularly in close contact with our customers	We are very frequently in close contact with our customers	
		☐	☐	☐	☐	☐	
D33	To what degree do your customers give you feedback on quality and delivery performance?	We do not receive feedback from our customers	We rarely receive feedback from our customers	We sometimes receive feedback from our customers	We regularly receive feedback from our customers	We very frequently receive feedback from our customers	
		☐	☐	☐	☐	☐	
D34	To what degree do you survey your customer's requirements?	We do not survey our customers' requirements	We rarely survey our customers' requirements	We sometimes survey our customers' requirements	We regularly survey our customers' requirements	We very frequently survey our customers' requirements	
		☐	☐	☐	☐	☐	
D35	To what degree do you conduct customer satisfaction surveys?	We do not survey our customers' satisfaction	We rarely survey our customers' satisfaction	We sometimes survey our customers' satisfaction	We regularly survey our customers' satisfaction	We very frequently survey our customers' satisfaction	
		☐	☐	☐	☐	☐	
D36	To what degree is on time delivery part of your philosophy?	On time delivery is not a core part of our site culture	On time delivery is a small part of our site culture	On time delivery is a reasonable part of our site culture	On time delivery is a significant part of our site culture	On time delivery is a core part of our site culture	
		☐	☐	☐	☐	☐	
D37	To what degree do you use joint improvement programs with your customers to increase your performance?	We do not use joint improvement programs	We rarely use joint improvement programs	We sometimes use joint improvement programs	We regularly use joint improvement programs	We very frequently use joint improvement programs	
		☐	☐	☐	☐	☐	
Supplier quality management							Commentary
		1	2	3	4	5	
D38	To what degree is supplier selection oriented around quality?	Selection is entirely oriented around other factors	Selection is mainly oriented around other factors	Selection is partly oriented around other factors and partly quality oriented	Selection is mainly quality oriented	Selection is entirely quality oriented	
		☐	☐	☐	☐	☐	
D39	To what degree do you conduct supplier qualifications and audits in order to rank your suppliers?	We do not conduct supplier audits or rank our suppliers	We conduct some audits but do not rank our suppliers	We conduct some audits and loosely rank our suppliers	We conduct rigorous audits and rank our suppliers	We regularly refresh our supplier audits and update rankings	
		☐	☐	☐	☐	☐	
D40	What proportion of your suppliers have you validated?	<20% of suppliers	20% - 40% of suppliers	40% - 60% of suppliers	60% - 80% of suppliers	>80% of suppliers	
		☐	☐	☐	☐	☐	
D41	For what proportion of your suppliers do you perform inspections of the incoming parts/ materials?	<20% of suppliers	20% - 40% of suppliers	40% - 60% of suppliers	60% - 80% of suppliers	>80% of suppliers	
		☐	☐	☐	☐	☐	
D42	To what degree are inspections of incoming materials usually performed in proportion to the past quality performance or type of supplier?	Inspections are unrelated to past supplier performance or type	Inspections are mainly related to other factors	Inspections are partly related to other factors and partly to supplier factors	Inspections are mainly related to past supplier performance or type	Inspections are entirely based on past supplier performance or type	
		☐	☐	☐	☐	☐	
D43	What proportion of incoming shipments do you inspect?	<20% of shipments	20% - 40% of shipments	40% - 60% of shipments	60% - 80% of shipments	>80% of shipments	
		☐	☐	☐	☐	☐	
D44	To what degree do you use joint improvement programs with your suppliers to increase your performance?	We do not use joint improvement programs	We rarely use joint improvement programs	We sometimes use joint improvement programs	We regularly use joint improvement programs	We very frequently use joint improvement programs	
		☐	☐	☐	☐	☐	
D128	To what extent do you employ a holistic supplier management process incorporating Lean / OpEx tools (e.g. map/visualise supplier relationships & performance metrics)?	We do not employ Lean / OpEx tools in our supplier mgmt process	We rarely employ Lean / OpEx tools in our supplier mgmt process	We sometimes employ Lean / OpEx tools in our supplier mgmt process	We regularly employ Lean / OpEx tools in our supplier mgmt process	We extensively employ Lean / OpEx tools in our supplier mgmt process	
		☐	☐	☐	☐	☐	

3: Just In Time (JIT)

Setup time reduction						Commentary	
	1	2	3	4	5		
D45	To what degree do you continuously work to lower set-up and cleaning times in your plant?	We do not seek to continuously improve set-up and cleaning times ☐	Continuously improving times is a small part of our site culture ☐	Continuously improving times is a reasonable part of our site culture ☐	Continuously improving times is a significant part of our site culture ☐	Continuously improving times is a core part of our site culture ☐	
D46	To what degree does the production department focus on assisting machine operators to lowering set-up and cleaning times?	Operators receive no assistance relating to set-up and cleaning time reduction ☐	Operators receive little assistance relating to set-up and cleaning time reduction ☐	Operators receive some assistance relating to set-up and cleaning time reduction ☐	Operators receive significant assistance relating to set-up and cleaning time reduction ☐	Operators receive extensive assistance relating to set-up and cleaning time reduction ☐	
D47	To what degree do crews practice set-ups to reduce the time required?	Operators do not practice set-ups ☐	Operators rarely practice set-ups ☐	Operators sometimes practice set-ups ☐	Operators regularly practice set-ups ☐	Operators practice set-ups extensively ☐	
D48	To what degree do you put a high priority on optimizing batch sizes in your site?	We do not seek to optimize batch sizes ☐	For a small number of products, we seek to optimize batch sizes ☐	For some products, we seek to optimize batch sizes ☐	For most products we seek to optimize batch sizes linked to the production strategy ☐	For all products we seek to optimize batch sizes linked to the production strategy ☐	
D49	What proportion of set-ups are scheduled so that the regular up-time of our machines is not affected?	<20% of set-ups ☐	20% - 40% of set-ups ☐	40% - 60% of set-ups ☐	60% - 80% of set-ups ☐	>80% of set-ups ☐	
D50	To what degree are optimized set-up and cleaning procedures documented as best-practices and rolled-out throughout the whole site?	Best practices are not documented ☐	Best practices are documented but not rolled-out ☐	Best practices are documented and rolled-out unevenly across the site ☐	Best practices are shared across the whole site, but not regularly ☐	Best practices are shared across the whole site regularly ☐	
Pull Production						Commentary	
	1	2	3	4	5		
D51	To what degree is the production schedule designed to allow for catching up, due to production stoppings because of problems (e.g. quality problems)?	Production schedule is explicitly designed to allow for catch-up production ☐	Schedule design makes significant allowance for catch-up design ☐	Schedule design makes some allowance for catch-up production ☐	Schedule design makes little allowance for catch-up production ☐	Schedule design does not consider catch-up production ☐	
D52	To what degree is production control driven by a 'Pull' system (kanban squares, containers, or signals)?	System is entirely 'Push' oriented ☐	System is mainly 'Push' oriented ☐	System is partly 'Push' and partly 'Pull' oriented ☐	System is mainly 'Pull' oriented ☐	System is entirely 'Pull' oriented ☐	
D53	To what degree is your production aligned with S&OP planning?	We do not seek to align production with S&OP planning ☐	We rarely align production with S&OP planning ☐	We sometimes align production with S&OP planning ☐	We regularly align production with S&OP planning ☐	We always align production with S&OP planning ☐	
D54	To what degree are suppliers integrated and to what degree do vendors fill kanban containers, rather than filling purchasing orders?	No integration or use of kanban ☐	Little integration and little use of kanban ☐	Little integration but regular use of kanban ☐	Some integration and regular use of kanban ☐	Full integration and regular use of kanban ☐	
D55	What proportion of supplier associations are long-term (>3 years)?	<20% of suppliers are long-term ☐	20% - 40% of suppliers are long-term ☐	40% - 60% of suppliers are long-term ☐	60% - 80% of suppliers are long-term ☐	>80% of suppliers are long-term ☐	
D56	To what degree do you enforce your suppliers to deliver on time (>70% of deliveries on time)?	We do not enforce our suppliers to deliver on time ☐	We rarely enforce our suppliers to deliver on time ☐	We regularly, but unevenly enforce our suppliers to deliver on time ☐	We regularly enforce most of our suppliers to deliver on time ☐	We always enforce all our suppliers to deliver on time ☐	
D57	What is your manufacturing approach (make-to-order vs. make-to-stock)?	We produce to stock ☐	We mainly hold stock, and produce little to order ☐	We sometimes produce to stock and sometimes to order ☐	We mainly produce to order, and hold little stock ☐	We only produce to order ☐	

Appendix

Layout optimization						Commentary	
	1	2	3	4	5		
D58	To what degree are your processes located close together so that material handling and part storage are minimized?	Related processes are not located close together	Related processes are located close together in one or two parts of the site	Related processes are located close together in some parts of the site	Related processes are located close together in most parts of the site	Related processes are located close together across the site	
		☐	☐	☐	☐	☐	
D59	What proportion of products are classified into groups with similar processing requirements to reduce set-up times?	<20% of products	20% - 40% of products	40% - 60% of products	60% - 80% of products	>80% of products	
		☐	☐	☐	☐	☐	
D60	What proportion of products are classified into groups with similar routing requirements to reduce transportation time?	<20% of products	20% - 40% of products	40% - 60% of products	60% - 80% of products	>80% of products	
		☐	☐	☐	☐	☐	
D61	To what degree does the layout of the shop floor facilitate low inventories and fast throughput?	Shopfloor layout is not optimised for inventories and throughput	Shopfloor layout is optimised in one or two parts of the site	Shopfloor layout is optimised in some parts of the site	Shopfloor layout is optimised in most parts of the site	Shopfloor layout is optimised across the site	
		☐	☐	☐	☐	☐	
D62	To what degree can your shop floor layout be characterized as separated into "mini-plants", if products have been classified based on their specific requirements?	Shopfloor layout does not resemble mini-plants	Shopfloor layout resembles mini-plants in one or two parts of the site	Shopfloor layout resembles mini-plants in some parts of the site	Shopfloor layout resembles mini-plants in most parts of the site	Shopfloor layout resembles mini-plants across the site	
		☐	☐	☐	☐	☐	
D63	If applicable, to what degree are manufacturing processes synchronized over all steps (e.g. within 1 task)?	<20% of related manufacturing processes are synchronized	20% - 40% of related manufacturing processes are synchronized	40% - 60% of related manufacturing processes are synchronized	60% - 80% of related manufacturing processes are synchronized	>80% of related manufacturing processes are synchronized	
		☐	☐	☐	☐	☐	
D64	To what degree can your current manufacturing process be described as a full continuous flow, involving almost no interruptions?	The process is almost entirely 'batch' steps	There are multiple 'batch' steps in the process	There are a few 'batch' steps in the process	The process is mostly continuous or semi-continuous	The full process could be described as continuous flow	
		☐	☐	☐	☐	☐	
D65	To what degree are you working to reach the status of a full continuous flow?	Continuous flow is not a core part of our site aims	Continuous flow is a small part of our site aims	Continuous flow is a reasonable part of our site aims	Continuous flow is a significant part of our site aims	Continuous flow is a core part of our site aims	
		☐	☐	☐	☐	☐	
D66	To what degree do you use "Value Stream Mapping" as a methodology to visualize and optimize processes.	VSM is not used	VSM is rarely used	VSM is sometimes used	VSM is regularly used	VSM is extensively used	
		☐	☐	☐	☐	☐	

Planning adherence						Commentary	
	1	2	3	4	5		
D67	To what degree do you meet your daily production plans?	<20% of days	20% - 40% of days	40% - 60% of days	60% - 80% of days	>80% of days	
		☐	☐	☐	☐	☐	
D68	To what degree do you know the root causes of variance in your production schedule and continuously try to eliminate them?	We do not have a clear view of root causes of variation	We have some view of the root causes, but do not work on eliminating them	We have a good view of the root causes, but unevenly work on eliminating them	We have a good view of the root causes and regularly work on eliminating them	We have a clear view of the root causes and continuously work on eliminating them	
		☐	☐	☐	☐	☐	
D69	To what degree do you share data with customers and suppliers based on a rolling production plan, to increase planning adherence?	We do not share data with customers or suppliers	We share data with one of customers or suppliers	We share some data with both customers and suppliers	We share most relevant data with both customers and suppliers	We share almost all relevant data with both customers and suppliers	
		☐	☐	☐	☐	☐	
D70	To what degree do you work on achieving smoothly leveled production capacity throughout the whole production process?	We do not work on achieving smoothed production capacity	We rarely work on achieving smoothed production capacity	We regularly, but unevenly work on achieving smoothed production capacity	We regularly work on achieving smoothed production capacity	We continuously work on achieving smoothed production capacity	
		☐	☐	☐	☐	☐	
D71	To what degree does your site have flexible working shift models in order to easily adjust production capacity according to current demand changes?	We do not have flexible shift models	We have flexible shift models in one or two areas of the site	We have flexible shift models in some areas of the site	We have flexible shift models in most areas of the site	We have flexible shift models throughout the whole site	
		☐	☐	☐	☐	☐	
D72	To what degree do you prefer a smoothly leveled production schedule to a high level of capacity utilization of single machines?	We value capacity utilisation over smoothed production	We value both, but capacity utilisation is more important	We value both equally	We value both, but smoothed production is more important	We value smoothed production over capacity utilisation	
		☐	☐	☐	☐	☐	

4: Effective Management System (EMS)

Direction setting						Commentary
	1	2	3	4	5	
D73	To what degree is your site's strategy and vision clear and linked to your corporate mission statement?	Site level strategy unclear	Site level strategy is relatively clear	Site level strategy is clear	Site level strategy is clear and somewhat linked to corporate mission statement	Clear links between site strategy & vision, and corporate mission statement
	☐	☐	☐	☐	☐	
D74	To what degree is your vision, mission and strategy communicated to employees?	Vision, mission, and strategy are not communicated to the shop floor	Strategy is only communicated to employees -annually	Strategy is communicated broadly to employees	Vision, mission, and strategy are broadly communicated and lived by employees	Vision, mission, and strategy are broadly communicated and lived by employees
	☐	☐	☐	☐	☐	
D75	To what degree are the focus, goals and objectives of your site's manufacturing unit closely linked to and consistent with corporate objectives?	The site's focus is not clear	The site's focus is relatively clear and some goals are set at site level	The site's focus is clear and extensive site goals are set	The site's focus is clear and site goals are linked to its network role	The site's network role is clear and goals are linked to corporate objectives
	☐	☐	☐	☐	☒	
D76	To what degree are the overall objectives of the site closely linked to the team or personal objectives of your shop-floor teams and employees?	Site objectives are not linked to shop floor objectives	Site objectives are mostly independent from the shop floor objectives	Site objectives are linked to shop floor objectives	Site objectives are closely linked to shop floor team objectives	Site objectives are closely linked to shop floor employee objectives
	☐	☐	☐	☐	☐	
D77	To what degree do manufacturing managers (head of manufacturing, site leader etc.) have a good understanding of how the corporate divisional strategy is formed?	It is not clear how corporate or divisional strategy is formed	Manufacturing managers have an incomplete view of strategy formation	Manufacturing managers have a clear view of division strategy formation	Manufacturing managers have a clear view of corp. strategy formation	Manufacturing managers are actively consulted when forming corp. strategy
	☐	☐	☐	☐	☐	
D78	To what degree do manufacturing managers know the most important criteria for manufacturing jobs (i.e. low costs, delivery, quality, etc.)?	Manufacturing managers are not clear on the most important criteria	Manufacturing managers are clear on important criteria for one or two areas	Manufacturing managers are clear on important criteria for some areas	Manufacturing managers are clear on important criteria for most areas	Manufacturing managers are clear on important criteria across the whole site
	☐	☐	☐	☐	☐	
D129	To what extent are maturity standards set and assessed by an external party (e.g. central team, peers) vs. by the site?	Standards are set and monitored by the site only	Standards are set and monitored mostly by the site	Standards are set with equal involvement from the site and external parties	Standards are set and monitored mostly by external parties	Standards are set and monitored solely by external parties
	☐	☐	☐	☐	☐	
Management commitment and company culture						Commentary
	1	2	3	4	5	
D79	To what degree does Leadership promote and develop the necessary behaviours and standards required for operational excellence at your site?	No presence of the leadership at the Gemba; leaders do not coach or involve teams in problem solving; leaders are fire fighting	Leaders go to the Gemba sometimes; some evidence of team problem solving but the team doesn't own the process or process improvement	Leaders joins the Gemba weekly, coach and support their team in problem solving but the team does not own the process or process improvement	Leaders joins the Gemba daily, and routinely coach their team in problem solving & team begins to own process & process improvement	Leaders regularly attend the Gemba, responding promptly to problems; teams own problem solving, process & process improvement
	☐	☐	☐	☐	☐	
D80	To what degree is site management (committee) is personally involved in improvement projects?	Site mgmt are not involved in improvement projects	Site mgmt are involved in setting objectives for improvement, but no further	Site mgmt are sometimes personally involved in improvement projects	Site mgmt are regularly personally involved in improvement projects	Site mgmt are personally involved in virtually all improvement projects
	☐	☐	☐	☐	☐	
D81	To what degree do you align your approach to departmental interaction with your wider management goals (e.g. encouraging competition/cooperation)?	We do not seek to encourage dept. interaction in line with wider mgmt goals	We rarely encourage dept. interaction in line with wider mgmt goals	We sometimes encourage dept. interaction in line with wider mgmt goals	We regularly encourage dept. interaction in line with wider mgmt goals	We always encourage dept. interaction in line with wider mgmt goals
	☐	☐	☐	☐	☐	
D82	To what degree is communication made via official channels?	Communication is not made via official channels	A little communication is made via official channels	Some communication is made via official channels	Most communication is made via official channels	All communication is made via official channels
	☐	☐	☐	☐	☐	
D83	To what degree does your site have an open communication culture, encourage the flow of information between the departments and the different management levels?	We have trouble with communication across the site	We have trouble with communication across most of the site	We have a good flow of info across parts of the site	We have an open comms culture, with a good flow of info across most of the site	We have a very open comms culture, with a good flow of info across the whole site
	☐	☐	☐	☐	☐	
D84	To what degree are you informed early enough about innovations (e.g. new products, new SKUs, new technologies)?	We are never informed early enough	We are rarely informed early enough	We are sometimes informed early enough	We are informed early enough about most innovations	We are always informed early enough about all innovations
	☐	☐	☐	☐	☐	
D85	To what degree are problems (e.g. complaints, etc.) traced back to their origin to identify root causes?	We do not trace problems of this type to their origin	We rarely trace problems to their origin	We trace problems to their root cause if they repeat	We trace most problems to their root cause	We rigorously examine all problems, and identify root causes
	☐	☐	☐	☐	☐	

Appendix

D66	To what degree do you align your approach to quality standards with your wider mgmt goals (e.g. shared responsibility or primarily the task of QA/QC)?	We do not seek to align quality approach with wider mgmt goals	We rarely align quality approach with wider mgmt goals	We sometimes align quality approach with wider mgmt goals	We regularly align quality approach with wider mgmt goals	We always align quality approach with wider mgmt goals	
		☐	☐	☐	☐	☐	
D67	To what degree do your employees continuously strive to reduce waste in processes (e.g. waste of time, waste of production space, etc.)?	Waste reduction is not a core activity	Waste reduction is a focus for specialised employees only	Shop floor employees strive to reduce process waste in some of the plant	Shop floor employees strive to reduce process waste in most of the plant	Shop floor employees strive to reduce all kinds of waste in every process	
		☐	☐	☐	☐	☐	
D68	To what degree do you have a clear leadership approach (command and control vs open culture)?	We have a clear command and control leadership approach	Command and control is spread across more departments than open culture	Both approaches are spread evenly across different departments	Open culture is spread across more departments than command and control	We have a clear open culture leadership approach	
		☐	☐	☐	☐	☐	
D130	To what extent do shop floor leaders seek to implement a 'change culture' built on Lean / OpEx principles?	Shop floor leaders do not actively seek to implement a 'change culture'	One or two shop floor leaders actively seek to implement a 'change culture'	Some shop floor leaders actively seek to implement a 'change culture'	Most shop floor leaders actively seek to implement a 'change culture'	Seeking to implement a 'change culture' is core to our leaders' agendas	
		☐	☐	☐	☐	☐	

Employee involvement and continuous improvement		1	2	3	4	5	Commentary
To what degree have you implemented tools and methods to display a continuous improvement process?	We do not have a continuous improvement program	Continuous improvement processes are not supported by tools	We have some tools and methods to support continuous improvement	We have multiple tools to support continuous improvement	Comprehensive tools and training in place to support continuous improvement		
To what degree are your employees involved in writing policies and procedures (concerning <i>Value Vision</i> down to <i>Standard Operating Procedures</i>)?	Employees are not involved in developing policies	Employees are rarely consulted when developing policies	Employees are sometimes consulted when developing policies	Employees are regularly consulted when developing policies	Employees are extensively involved in developing policies		
To what degree do shop-floor employees actively drive suggestion programs?	Employees do not actively drive suggestion programs	Employee engagement with suggestion programs is limited	Employees are engaged in suggestion programs in some depts.	Employees are actively engaged in suggestion programs in the site of most	Employees are extensively involved in driving suggestion programs		
To what degree do you align your work team responsibility with wider management goals (e.g. work teams taking autonomous action, or requiring mgmt approval)?	We do not seek to align work team responsibility with wider mgmt goals	We rarely align work team responsibility with wider mgmt goals	We sometimes align work team responsibility with wider mgmt goals	We regularly align work team responsibility with wider mgmt goals	We always align work team responsibility with wider mgmt goals		
To what degree do your employees have the authority to correct problems when they occur?	Problem solving is not carried out by shop floor employees	Very few shop floor employees have the authority to correct problems	Some shop floor employees have the authority to correct problems	Most shop floor employees have the authority to correct problems	Shop floor employees have the authority to actively correct problems		
To what degree do you align supervisor problem solving responsibility with wider management goals (e.g. problems always solved by supervisors, or solved by teams)?	We do not seek to align supervisor responsibility with wider mgmt goals	We rarely align supervisor responsibility with wider mgmt goals	We sometimes align supervisor responsibility with wider mgmt goals	We regularly align supervisor responsibility with wider mgmt goals	We always align supervisor responsibility with wider mgmt goals		
To what degree do supervisors focus on assisting employees to perform their own problem solving?	Employees receive no assistance relating to problem solving	Employees receive little assistance relating to problem solving	Employees receive some assistance relating to problem solving	Employees receive significant assistance relating to problem solving	Employees receive extensive assistance relating to problem solving		
To what degree does your plant form cross-functional project teams to solve problems?	Our plant does not utilize cross functional teams	Our plant rarely utilizes cross functional teams	Our plant sometimes utilizes cross functional teams	Our plant regularly utilizes cross functional teams	Our plant makes extensive use of cross functional teams		
To what degree does the company take care of the employees?	Our company emphasises other priorities	Our company takes reasonable care of its employees	Our company takes good care of its employees	Our company considers employee welfare one of its top priorities	Employee welfare is extremely important to our company - top priority		
Please indicate which of the following statements are true for your work teams							
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					
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		1	2	3	4	5	Commentary
D100	What proportion of your production employees are cross-trained?	<20% of production employees ☐	20% - 40% of production employees ☐	40% - 60% of production employees ☐	60% - 80% of production employees ☐	>80% of production employees ☐	
D101	To what degree has your plant implemented a formal program to increase the flexibility of your production workers?	We do not seek to increase cross-trained employees ☐	We support employees who seek to cross-train on their own initiative ☐	We have ad hoc training for some employees to become cross-trained ☐	We have a formal program to cross-train employees ☐	In addition to training, employees rotate to maintain their qualification. ☐	
D102	How frequently does your company hold open feedback meetings?	We do not have open feedback meetings ☐	We have annual open feedback meetings ☐	We have 6-monthly open feedback meetings ☐	We have quarterly open feedback meetings ☐	We have monthly open feedback meetings ☐	
D103	To what degree is the information from these official feedback meetings used in further training?	The information is not used ☐	The information is used, but not in any broad program ☐	Some of the information is used in further trainings ☐	Most of the information is used in further trainings ☐	The information is used systematically in further training ☐	
D104	To what degree does your site invest in the training and qualification of your employees?	We do not invest in the training and qualification of our employees ☐	We invest a little in training, but do not offer qualifications ☐	We have some trainings and offer one or two qualifications ☐	We have a dedicated development and qualification program for our workers ☐	We continuously seek to improve our dedicated training and qualification program ☐	
D131	To what degree are Lean / OpEx trainings rolled out in a structured programme tied to business needs?	We do not have a programme of Lean / OpEx trainings ☐	We run some Lean / OpEx trainings ☐	We run a structured programme of Lean / OpEx trainings ☐	We run a structured programme of Lean / OpEx trainings tied to business needs ☐	We have extensive Lean / OpEx trainings tied to business needs ☐	
D132	To what degree do shop floor leaders participate in and facilitate Lean / OpEx trainings?	Shop floor leaders do not participate in Lean / OpEx trainings ☐	Shop floor leaders rarely participate in Lean / OpEx trainings ☐	Shop floor leaders sometimes participate in Lean / OpEx trainings ☐	Shop floor leaders regularly participate in Lean / OpEx trainings ☐	Shop floor leaders regularly lead the Lean / OpEx trainings ☐	

5: Basic Elements

Standardisation and Simplification							Commentary
	1	2	3	4	5		
To what degree is standardization emphasised as a strategy for continuously improving processes, machines and products?	We do not communicate standardisation goals	Standardisation is communicated but not emphasised	Standardisation is emphasised, but unevenly across the site	Standardisation is emphasised across the whole site, but not core to improvement	Standardisation is core to continuous improvement programme		
(Closely relates to JIT segment)	☐	☐	☐	☐	☐		
To what degree are documented operating procedures used to standardize processes (e.g. set-ups)?	Documentation does not exist	Documentation exists but is not used to drive adherence	Documentation exists and is visible but is not adhered to unevenly	Documentation is regularly adhered to but not regularly updated	Documentation strictly adhered to and updated regularly		
(Closely relates to JIT segment)	☐	☐	☐	☐	☐		
To what degree are optimized operating procedures (e.g. shortened set-up) documented as best-practice processes and rolled-out throughout the whole site?	Best practice is not documented	Best practice is documented but not rolled-out	Best practice is documented and rolled-out unevenly across the site	Best practice is shared across the whole site, but not regularly	Best practice is shared across the whole site regularly		
(Closely relates to JIT segment)	☐	☐	☐	☐	☐		
To what degree are standardized functional descriptions used to reduce the period of vocational training for new employees?	Standardised functional descriptions do not exist	Standardised functional descriptions exist but are not used in training	Standard functional descriptions inform training but do not reduce the period	Standard functional descriptions inform training and reduce the period a little	Standard functional descriptions inform training and reduce the period significantly		
(Closely relates to EMS segment)	☐	☐	☐	☐	☐		
To what degree are standardized machines and equipment (e.g. machine design, spare parts etc.) used to achieve a high up time of our machines?	Equipment is not standardised	Equipment is standardised in one or two areas	Equipment is standardised in some areas	Equipment is standardised in most of the site	Equipment is standardised throughout the site		
(Closely relates to TPM segment)	☐	☐	☐	☐	☐		
To what degree are standardized machines and fixtures used to lower material costs for spare parts?	Equipment is not standardised	Some standardisation of equipment exists, but effect on material costs is not measured	Standardised equipment exists but does not reduce material costs	Use of standardised equipment reduces costs a little	Use of standardised equipment reduces costs significantly		
(Closely relates to TPM segment)	☐	☐	☐	☐	☐		

Appendix

Visual management						Commentary
	1	2	3	4	5	
D111	To what degree do you utilise performance charts to show objectives across production processes on the shop floor?	We do not utilise performance charts on the shop floor	Performance charts are used in some cases to show objectives	Performance charts across most processes show objectives	Performance charts across all key processes show objectives	Regularly-updated charts across all key processes show objectives
		☐	☐	☐	☐	☐
D112	To what degree are technical documents (e.g. maintenance documents) and workplace information (e.g. standardized inspection procedures, team structures) visible on the shop floor?	Information is not posted on the shop floor	Some information is posted on the shop floor in some parts of the plant	Technical and workplace information is posted on the shop floor in some areas	Technical and workplace information is posted on the shop floor in most areas	Info is posted on the shop floor, easily accessible and visible for all workers
		☐	☐	☐	☐	☐
D113	To what degree do you utilise charts showing the current performance status (e.g. current scrap-rates, current up-times etc.) on the shop floor?	We do not utilise performance charts on the shop floor	Performance charts are used in some cases to show current KPIs	Performance charts across most processes show current KPIs	Performance charts across all key processes show current KPIs	Regularly-updated charts across all key processes show current KPIs
		☐	☐	☐	☐	☐
D114	To what degree do you utilise charts showing current takt times and schedule compliance (e.g. Andon boards) on the shop floor?	We do not utilise performance charts on the shop floor	Performance charts are used in some cases to show takt times	Performance charts across most processes show takt times	Performance charts across all key processes show takt times	Regularly-updated charts across all key processes show takt times
		☐	☐	☐	☐	☐
D133	To what extent do you make use of real-time data collection and visualisation?	We do not employ real-time data collection and visualisation	We rarely employ real-time data collection on one or two lines	We employ real-time data collection across some of the site	We employ real-time data across most of the site, and mostly use the dashboards not PPTs	We extensively employ real-time data, and solely use the dashboards
		☐	☐	☐	☐	☐
Problem Solving						
		1	2	3	4	5
D134	To what degree do you ensure performance gaps are clear? (e.g. make conditions visible to identify non-standard performance)	We do not review the degree to which performance gaps are made clear	We rarely review the degree to which performance gaps are made clear	We sometimes review the degree to which performance gaps are made clear	We regularly review the degree to which performance gaps are made clear	We extensively review the degree to which performance gaps are made clear
		☐	☐	☐	☐	☐
D135	To what degree do you ensure that, where necessary, actions are underway to close performance gaps? (e.g. monitor timelines and ensure responsibility for actions underway)	We do not monitor actions underway	We monitor actions underway in one or two parts of the site	We monitor actions underway in some parts of the site	We monitor actions underway in most of the site, including timelines and responsible parties	We monitor actions underway across the whole site, including timelines and responsible parties
		☐	☐	☐	☐	☐
D136	To what extent do you have a structured approach to escalating problems? (e.g. identifying critical escalation points, clarity on how to escalate well)	We do not have a structured approach to escalating problems	A structured approach to escalation exists but is not widely visible	A structured approach to escalation exists and is visible, but is adhered to unevenly	A structured approach to escalation is adhered to across most of the site	Escalating well is embedded in our site culture
		☐	☐	☐	☐	☐
Reasons for launching Operational Excellence initiatives						
		1	2	3	4	5
D115	To meet FDA regulations	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch
		☐	☐	☐	☐	☐
D116	To implement Process Analytical Technology (PAT)	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch
		☐	☐	☐	☐	☐
D117	To change from functional organization to process organization	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch
		☐	☐	☐	☐	☐
D118	To increase cost awareness	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch
		☐	☐	☐	☐	☐

D120	To increase employee empowerment	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D121	To reduce lead times and inventory	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D122	To change the quality focus from final product to process quality	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D123	To initiate a cultural change for continuous improvement	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D124	To introduce standardized methodologies for problem solving	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D125	To launch a broader cost cutting program	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D126	To improve final product quality	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	
D127	To fulfill site targets between corporate and plant management	We do not launch initiatives for this reason	We rarely launch initiatives for this reason	We sometimes launch initiatives for this reason	We regularly launch initiatives for this reason	This reason is core to most initiatives that we launch	
		☐	☐	☐	☐	☐	

proceed

Appendix

ICH Q10 Maturity Assessment:

The St. Gallen enabler assessment has recently been made fully compatible with the ICH Q10 Guideline to assesses maturity in Q10 categories. For this purpose, the present sheet shows assigned legacy enabler questions as well as newly derived questions that address the Q10 categories. **Please note:** Light grey questions with UIDs "DMP" have already been answered as part of the overall enabler section and cannot be answered again. **Please only answer the new questions with UID "NMP".**

☐ Please answer the additional question by ticking the appropriate box.

☐ This question is a legacy enabler question and has already been answered by you as part of the overall enabler section. The "x" indicates your answer from the enabler section and cannot be edited.

Management Responsibilities							Commentary
		1	2	3	4	5	
N01	To what degree does your site management participate in the design, implementation, monitoring and maintenance of an effective pharmaceutical quality system?	Management does not participate in these activities	Management rarely participates in these activities	Management sometimes participates in these activities	Management regularly participates in these activities	Management always participates in these activities	
		☐	☐	☐	☐	☐	
N02	To what degree does your quality policy facilitate continual improvement of the PQS?	Quality policy represents a major barrier for continual improvement of PQS	Quality policy sometimes represents a barrier for continual improvement of PQS	Quality policy does not represent a barrier for continual improvement of PQS	Quality policy in part facilitates continual improvement of PQS	Quality policy is designed to facilitate continual improvement of PQS	
		☐	☐	☐	☐	☐	
N03	To what degree does your site management determine and provide adequate and appropriate resources (e.g. human, financial) to implement and maintain the PQS and to continually improve its effectiveness?	Site management does not determine and provide adequate and appropriate resources	Site management rarely determines and provides adequate and appropriate resources	Site management sometimes determines and provides adequate and appropriate resources	Site management regularly determines and provides adequate and appropriate resources	Site management always determines and provides adequate and appropriate resources	
		☐	☐	☐	☐	☐	
N04	To what degree are performance indicators, which measure progress against quality objectives, established, monitored, communicated regularly and acted upon?	No such performance indicators are established	Performance indicators are established, but not monitored, communicated or acted upon	Performance indicators are established and monitored, but not communicated and acted upon	Performance indicators are established, monitored, communicated, but not acted upon	Performance indicators are established, monitored, communicated and acted upon	
		☐	☐	☐	☐	☐	
N05	To what degree has your management established and trained all employees in a quality policy, that describes the overall quality related intentions and direction of your company?	Management has not established such a quality policy	Management has established, but has not clearly communicated such a quality policy to site employees	Management has established and communicated such a quality policy to site employees, but has not yet trained the employees	Management has established and communicated such a quality policy to site employees and has started to train the employees	Management has established such a quality policy, has communicated it to all site employees and has trained all employees	
		☐	☐	☐	☐	☐	
N06	To what degree does your management conduct reviews of process performance and product quality on a regular basis?	Management does not conduct reviews of process performance and product quality	Management rarely conducts reviews of process performance and product quality	Management sometimes conducts reviews of process performance and product quality	Management regularly conducts reviews of process performance and product quality	Management always conducts reviews of process performance and product quality	
		☐	☐	☐	☐	☐	
D75	To what degree are the focus, goals and objectives of your site's manufacturing unit closely linked to and consistent with corporate objectives?	The site's focus is not clear	The site's focus is relatively clear and some goals are set at site level	The site's focus is clear and extensive site goals are set	The site's focus is clear and site goals are linked to its network role	The site's network role is clear and goals are linked to corporate objectives	
		☐	☐	☐	☐	☐	
D76	To what degree are the overall objectives of the site closely linked to the team or personal objectives of your shop-floor teams and employees?	Site objectives are not linked to shop floor objectives	Site objectives are mostly independent from the shop floor objectives	Site objectives are linked to shop floor objectives	Site objectives are closely linked to shop floor team objectives	Site objectives are closely linked to shop floor employee objectives	
		☐	☐	☐	☐	☐	
D79	To what degree does Leadership promote and develop the necessary behaviors and standards required for operational excellence at your site?	No presence of the leadership at the Gemba; leaders do not coach or involve teams in problem solving; leaders are fire fighting	Leaders go to the Gemba sometimes; some evidence of team problem solving but the team does not own the process or process improvement	Leaders join the Gemba weekly, coach and support their team in problem solving but the team does not own the process or process improvement	Leaders join the Gemba daily, and routinely coach their team in problem solving & team begins to own process & process improvement	Leaders regularly attend the Gemba, responding promptly to problems; teams own problem solving, process & process improvement	
		☐	☐	☐	☐	☐	
D80	To what degree is site management (committee) personally involved in improvement projects?	Site mgmt are not involved in improvement projects	Site mgmt are involved in setting objectives for improvement, but no further	Site mgmt are sometimes personally involved in improvement projects	Site mgmt are regularly personally involved in improvement projects	Site mgmt are personally involved in virtually all improvement projects	
		☐	☐	☐	☐	☐	
D83	To what degree does your site have an open communication culture, encourage the flow of information between the departments and the different management levels?	We have trouble with communication across the site	We have trouble with communication across most of the site	We have a good flow of info across parts of the site	We have an open comms culture, with a good flow of info across most of the site	We have a very open comms culture, with a good flow of info across the whole site	
		☐	☐	☐	☐	☐	
D86	To what degree do you align your approach to quality standards with your wider mgmt goals (e.g. shared responsibility or primarily the task of QA/QC)?	We do not seek to align quality approach with wider mgmt goals	We rarely align quality approach with wider mgmt goals	We sometimes align quality approach with wider mgmt goals	We regularly align quality approach with wider mgmt goals	We always align quality approach with wider mgmt goals	
		☐	☐	☐	☐	☐	
D90	To what degree are your employees involved in writing policies and procedures (concerning Site Vision down to Standard Operating Procedures)?	Employees are not involved in developing policies	Employees are rarely consulted when developing policies	Employees are sometimes consulted when developing policies	Employees are regularly consulted when developing policies	Employees are extensively involved in developing policies	
		☐	☐	☐	☐	☐	

[illegible]

Appendix

Capa System						Commentary
	1	2	3	4	5	
Do you have a process to ensure that information regarding nonconforming product, quality problems and appropriate CAPAs properly disseminated, including dissemination for management review?	There is no process to disseminate this information	There is a process to disseminate this information. It is not used in practice.	There is a process to disseminate this information. It is rarely used in practice.	There is a process to disseminate this information. It is used in practice.	There is a process to disseminate this information. It is used in practice and continuously reviewed.	
	☐	☐	☐	☐	☐	
Please describe your current CAPA documentation process.	No formal process for documenting CAPA	Formal process for documenting CAPA exists	Process for documenting CAPA is applied, however may have inconsistencies in execution from record to record	Process for documenting CAPA is executed consistently from record to record	Process for documenting CAPA results in being robust documentation of all CAPA records	
	☐	☐	☐	☐	☐	
To what degree do you distinguish corrections, corrective actions & preventive actions?	There is no SOP and/or training that outlines the differences between corrections, corrective & preventive actions	Introducing SOP/ training outlining the differences is planned	SOP/ training outlining the differences is in place	SOP/ training outlining is in place & mandatory for operators	SOP/ training outlining is in place, mandatory for operators & frequently updated	
	☐	☐	☐	☐	☐	
Do you use metrics to measure CAPA effectiveness?	There are no measures in place to identify the overall effectiveness / health of the CAPA Quality System	We have minimal measures in place & targets are defined partly	We have defined measures in place & targets are defined	We have defined measures in place, targets are defined & data is available	We have defined measures in place, targets are defined, data is available & proactively reviewed by management	
	☐	☐	☐	☐	☐	
Do you ensure that corrective and preventive actions were verified or validated prior to implementation?	CAPAs are not verified or validated prior to implementation.	Critical CAPAs are sometimes verified or validated prior to implementation.	Critical CAPAs are always verified or validated prior to implementation.	All CAPAs are verified or validated prior to implementation.	All CAPAs are verified or validated prior to implementation. There is a standard how verification/validation has to be performed.	
	☐	☐	☐	☐	☐	
Do you follow a formal SOP on how to implement a new CAPA process and are your employees trained on this process?	There is no formal SOP on how to implement a new CAPA process.	There is a formal SOP on how to implement a new CAPA process. It is rarely applied in practice.	There is a formal SOP on how to implement a new CAPA process. It is applied to new CAPAs with special attention.	There is a formal SOP on how to implement a new CAPA process. It is applied to all new CAPAs.	There is a formal SOP on how to implement a new CAPA process. The SOP is applied to all new CAPAs and continuously reviewed.	
	☐	☐	☐	☐	☐	
Quality Risk Management						Commentary
	1	2	3	4	5	
Do you operate cross-functional teams dedicated to analyse risks with qualified experts of the following departments? Site Management, Quality, Business Development, Engineering, Regulatory Affairs, Operations & Legal	No cross-functional teams	At least two of the departments involved	At least three of the departments involved	At least four of the departments involved	All five departments involved	
	☐	☐	☐	☐	☐	
Are you aware of existing risks, review existing risks on a regular base, prioritize & communicate them proactively?	We do not document existing risks	We document existing risks if we come across	We follow a structured approach to identify & document risks	We follow a structured approach to identify risks, document them and communicate them	We follow a structured approach to identify risks, document them and communicate them across the organization. All documented risks are reviewed periodically.	
	☐	☐	☐	☐	☐	
Is your quality risk management process integrated with the overall Quality System and do you assess the effectiveness of the QRM?	We do not have a formal QRM process.	The QRM process is not integrated with the overall Quality Management System. We do not measure its effectiveness.	The QRM process is not integrated with the overall Quality Management System or its effectiveness is not measured.	The QRM process is integrated with the overall Quality Management System and its effectiveness is measured.	The QRM process is integrated with the overall QMS. Its effectiveness is measured, the interaction with QMS is continuously reviewed.	
	☐	☐	☐	☐	☐	
Do you use a set of methods & tools dedicated to access & manage risks? (e.g. Fault Tree Analysis, Hazard Operability Analysis, etc.) If so, is there a systematic & logical approach to select the methods & tools?	We do not use tools dedicated to access & manage risks	We use one tool to access & manage all types of risks	We use a set of tools to access & manage different types of risks	We use a set of tools to access & manage different types of risks. There is a structured approach to summarize and harmonize all tool's outcomes.	We use a set of tools to access & manage different types of risks. All tool's outcomes are summarized. We strive to develop further tools on our own.	
	☐	☐	☐	☐	☐	
Do you have a SOP to conduct risk assessment and are your employees trained on this SOP? Are risk management procedures for each area of application clearly defined?	We do not have a SOP to conduct Risk assessment	We have an appropriate SOP. However, procedures are not defined for each area and employees are not trained dedicatedly.	We have an appropriate SOP. However, procedures are not defined for each area and employees are not trained dedicatedly.	We have a SOP to conduct Risk assessment. Procedures are defined for each area and employees are trained dedicatedly to the SOP.	We continuously review our SOP to conduct Risk assessment. Procedures are defined for each area and employees are trained dedicatedly.	
	☐	☐	☐	☐	☐	

[illegible]

Appendix

Process Perf. & Product Quality Monitoring System							Commentary
	1	2	3	4	5		
To what degree do you analyse parameters and attributes identified in the control strategy to verify continued operation within a state of control?	We do not analyse these parameters and attributes to verify state of control	We rarely analyse these parameters and attributes to verify state of control	We sometimes analyse these parameters and attributes to verify state of control	We regularly analyse these parameters and attributes to verify state of control	We continuously analyse these parameters and attributes to verify state of control		
	○	○	○	○	○		
To what degree do you identify sources of variation affecting process performance and product quality?	We do not identify these sources of variation	We rarely identify these sources of variation	We sometimes identify these sources of variation	We regularly identify these sources of variation	We continuously identify these sources of variation		
	○	○	○	○	○		
To what degree does your process performance and product quality monitoring system include feedback on product quality from both internal and external sources?	Our monitoring system does neither include feedback on product quality from internal nor from external sources	Our monitoring system does include feedback on product quality from internal but not from external sources	Our monitoring system does include feedback on product quality from internal and in rare instances from external sources	Our monitoring system does include feedback on product quality from internal and sometimes from external sources	Our monitoring system always includes feedback on product quality from both internal and frequently sources		
	○	○	○	○	○		
To what degree does your process performance and product quality monitoring system provide knowledge to enhance process understanding?	Our monitoring system does not provide knowledge to enhance process understanding	Our monitoring system rarely provides knowledge to enhance process understanding	Our monitoring system sometimes provides knowledge to enhance process understanding	Our monitoring system regularly provides knowledge to enhance process understanding	Our monitoring system continuously provide knowledge to enhance process understanding		
	○	○	○	○	○		
To what degree does your process performance and product quality monitoring system ensure a state of control is maintained and areas for continual improvement are identified?	Our monitoring system is neither suited to ensure a state of control nor to identify areas for continual improvement	Our monitoring system is mostly suited to ensure a state of control but not to identify areas for continual improvement	Our monitoring system is suited to ensure a state of control but not to identify areas for continual improvement	Our monitoring system is suited to ensure a state of control and to some degree to identify areas for continual improvement	Our monitoring system is suited to ensure a state of control and to degree to identify areas for continual improvement in real time		
	○	○	○	○	○		
To what degree do you monitor, measure and control process quality of outsourcing activities?	We do not monitor, measure and control process quality of outsourcing activities	We rarely monitor, measure and control process quality of outsourcing activities	We sometimes monitor, measure and control process quality of outsourcing activities	We regularly monitor, measure and control process quality of outsourcing activities	We continuously monitor, measure and control process quality of outsourcing activities		
	○	○	○	○	○		
To what degree is process quality continually measured?	Continuous measurement of process quality does not exist	Continuous measurement exists but is not widely used	Continuous measurement exists and is used but is enforced unevenly	Continuous measurement exists and is enforced	Continuous measurement exists and is strictly enforced across the whole site		
To what degree is process quality continually measured using process metrics (e.g. on-time-in-full delivery rate)?	No clear definition of metrics	Clearly defined metrics, but not standardised across the site	Standardised metrics but not exhaustive of site performance	Standardised exhaustive metrics	Standardised exhaustive metrics, with leading and lagging indicators		
What proportion of the equipment on the shop floor is currently under statistical process control (SPC)?	<20% of equipment	20% - 40% of equipment	40% - 60% of equipment	60% - 80% of equipment	>80% of equipment		
To what degree is statistical process control utilised to reduce variances in processes?	Statistical process control never utilised	Statistical process control rarely utilised	Statistical process control sometimes utilised	Statistical process control often utilised	Statistical process control always utilised		
To what degree are standardised tools in place for root cause analysis, to get a deeper understanding of the influencing factors (e.g. DMAIC)?	No tools in place	Some tools in place but not standardised	Standardised tools in place, but used unevenly	Standardised tools used regularly	Standardised tools used regularly and a core part of training		
What proportion of equipment makes use of Process Analytical Technology (PAT), for real-time process monitoring and controlling?	<20% of equipment	20% - 40% of equipment	40% - 60% of equipment	60% - 80% of equipment	>80% of equipment		
To what degree do your customers give you feedback on quality and delivery performance?	We do not receive feedback from our customers	We rarely receive feedback from our customers	We sometimes receive feedback from our customers	We regularly receive feedback from our customers	We very frequently receive feedback from our customers		
To what extent do you make use of real-time data collection and visualisation?	We do not employ real-time data collection and visualisation	We rarely employ real-time data collection on one or two lines	We employ real-time data collection across some of the site	We employ real-time data across most of the site, and mostly use live dashboards not PPTs	We extensively employ real-time data, and solely use live dashboards		
To what degree do you ensure performance gaps are clear (e.g. make conditions visible to identify non-standard performance)	We do not review the degree to which performance gaps are made clear	We rarely review the degree to which performance gaps are made clear	We sometimes review the degree to which performance gaps are made clear	We regularly review the degree to which performance gaps are made clear	We extensively review the degree to which performance gaps are made clear		

Change Management System						Commentary
	1	2	3	4	5	
To what degree do you utilize quality risk management to evaluate proposed changes?	We do not utilize quality risk management to evaluate proposed changes	We utilize quality risk management, but not with an appropriate level of effort and formality to evaluate proposed changes	We sometimes utilize quality risk management with an appropriate level of effort and formality to evaluate proposed changes	We regularly utilize quality risk management with an appropriate level of effort and formality to evaluate proposed changes	We always utilize quality risk management with an appropriate level of effort and formality to evaluate proposed changes	
	☐	☐	☐	☐	☐	
To what degree are proposed changes evaluated by expert teams from relevant areas (e.g. Pharmaceutical Development, Manufacturing, Quality, Regulatory Affairs and Medical), to ensure the change is technically justified?	Proposed changes are not evaluated by expert teams that ensure the change is technically justified	Proposed changes are rarely evaluated by expert teams that ensure the change is technically justified	Proposed changes are sometimes evaluated by expert teams that ensure the change is technically justified	Proposed changes are regularly evaluated by expert teams that ensure the change is technically justified	Proposed changes are always evaluated by expert teams that ensure the change is technically justified	
	☐	☐	☐	☐	☐	
To what degree does Management evaluate whether the change objectives were achieved?	We do not evaluate whether the change objectives were achieved	We rarely evaluate whether the change objectives were achieved	We sometimes evaluate whether the change objectives were achieved	We regularly evaluate whether the change objectives were achieved	We always evaluate whether the change objectives were achieved	
	☐	☐	☐	☐	☐	
To what degree do you evaluate that there was no deleterious impact on quality across the entire product lifecycle, after implementation of changes?	We do not evaluate the impact of changes on product quality	We do evaluate the impact of changes on product quality, but do not have a formalized and risk-based change management system in place	We evaluate the impact of changes based on a formalized, but not risk-based change management system	We evaluate the impact of changes based on a formalized change management system that includes product quality risks	We evaluate the impact of changes based on a formalized change management system that includes all product and process related risks	
	☐	☐	☐	☐	☐	
Do you have a SOP for proposing, evaluating, approving, reviewing and managing change control and are your employees trained in this SOP?	We do not have any of these SOPs	We do have some of these SOPs, but only few of the involved employees are trained on it	We do have some of these SOPs, but not all of the involved employees are trained on it	We do have all of these SOPs, but not all involved employees are trained on it	We do have all of these SOPs and all involved employees are trained on it	
	☐	☐	☐	☐	☐	
How often is quality department actively involved in the change management process?	Quality department is not actively involved in the change management process	Quality department is rarely actively involved in the change management process	Quality department is sometimes actively involved in the change management process	Quality department is usually actively involved in the change management process	Quality department is always actively involved in the change management process	
	☐	☐	☐	☐	☐	
To what degree have you implemented tools and methods to deploy a continuous improvement process?	We do not have a continuous improvement program	Continuous improvement processes are not supported by tools	We have some tools and methods to support continuous improvement	We have multiple tools and methods to support continuous improvement	Comprehensive tools and training in place to support continuous improvement	
	☐	☐	☐	☐	☐	
Management Review						Commentary
	1	2	3	4	5	
To what degree does management measure effectiveness of pharmaceutical quality system (PQS) objectives (including process performance and product quality) at your site?	Management does not measure the achievements of PQS objectives	Management rarely measures the achievements of PQS objectives	Management sometimes measures the achievements of PQS objectives	Management regularly measures the achievements of PQS objectives	Management continuously measures the achievements of PQS objectives	
	☐	☐	☐	☐	☐	
To what degree does Management Review at your site include a timely and effective communication and escalation process to relate appropriate quality issues to senior levels of management for review?	It does not include a structured approach for timely and effective communication and escalating problems	It includes a structured approach for timely and effective communication and escalation, but it is not widely visible	It includes a structured approach for timely and effective communication and escalation, which is visible, but is not adhered to universally	It includes a structured approach for timely and effective communication and escalation, which is visible and adhered to across most of the site	It includes a structured approach for timely and effective communication and escalation, which is visible and adhered to all across the site	
	☐	☐	☐	☐	☐	
To what degree does your site management review the results of regulatory inspections and findings, audits and other assessments, and commitments made to regulatory authorities?	Site management does not review the results of such inspections	Site management rarely reviews the results of such inspections	Site management sometimes reviews the results of such inspections	Site management regularly reviews the results of such inspections	Site management continuously reviews the results of such inspections	
	☐	☐	☐	☐	☐	
To what degree does your site management perform periodic reviews, that include measures of customer satisfaction such as product quality complaints and recalls?	Periodic reviews do not include measures of customer satisfaction	Periodic reviews rarely include measures of customer satisfaction	Periodic reviews sometimes include measures of customer satisfaction	Periodic reviews usually include measures of customer satisfaction	Periodic reviews always include measures of customer satisfaction	
	☐	☐	☐	☐	☐	
To what degree does your site management perform periodic reviews, that include conclusions of process performance and product quality monitoring?	Periodic reviews do not include conclusions of process performance and product quality	Periodic reviews rarely include conclusions of process performance and product quality	Periodic reviews sometimes include conclusions of process performance and product quality	Periodic reviews usually include conclusions of process performance and product quality	Periodic reviews always include conclusions of process performance and product quality	
	☐	☐	☐	☐	☐	

Appendix

N46	To what degree is quality policy at your site reviewed periodically for continuing effectiveness?	Quality policy at our site has not been reviewed in the last 5 years for continuing effectiveness	Quality policy has been reviewed within the last 5 years and is since rarely reviewed	Quality policy has been reviewed within the last 5 years and is since sometimes reviewed	Quality policy has been reviewed within the last 5 years and is since regularly reviewed	Quality policy has been reviewed within the last 5 years and is since continuously reviewed
		○	○	○	○	○
N47	To what degree does your Management Review process support identification of gaps in training, resources and knowledge dissemination and recommendations of appropriate actions to close these gaps?	It does not support identification of gaps and recommendation of appropriate actions to close these gaps	It rarely supports identification of gaps and recommendation of appropriate actions to close these gaps	It sometimes supports identification of gaps and recommendation of appropriate actions to close these gaps	It usually supports identification of gaps and recommendation of appropriate actions to close these gaps	It well supports identification of gaps and recommendation of appropriate actions to close these gaps
		○	○	○	○	○
N48	To what degree does management review of your pharmaceutical quality system include monitoring of internal and external factors, including resource allocation, training, emerging regulations, changes to quality policy and quality objectives?	Management Review does not include monitoring of such internal or external factors	Management Review does include monitoring of some of these internal factors but none of these external factors	Management Review does include monitoring of some of these internal factors and some of these external factors	Management Review does include monitoring of all of these internal factors and some of these external factors	Management Review does include monitoring of all of these internal and external factors
		○	○	○	○	○
D85	To what degree are problems (e.g. complaints, etc.) traced back to their origin to identify root causes?	We do not trace problems of this type to their origin	We rarely trace problems to their origin	We trace problems to their root cause if they repeat	We trace most problems to their root cause	We rigorously examine all problems, and identify root causes
		○	○	○	○	○

proceed to
Technology Level

Technology: Drug Substance - Chemical

Please select the process steps and sub-steps/descriptors that you carry out at your site:

	Reaction level	Separation level	Dryer level	Milling & grinding level
E-1-01a-d	☐ Weighing	☐ Extraction	☐ Drying	☐ Milling/sieving
E-1-01a.1-3	☐ Reaction	☐ Distillation	☐ Lyophilization	
E-1-01b.1-6	☐ Mixing	☐ Evaporation		
E-1-01c.1-2		☐ Chromatography		
E-1-01d.1		☐ Purification		
		☐ Crystallisation		

Commentary**1: Cost and Structural KPIs**

Production structure		Unit	Measure
E-1-02	Amount of drug substance produced at your site in the last year	KG	
E-1-03	Percentage of drug substance produced at your site that was processed for own production	%	
E-1-04	Percentage of drug substance produced in the last year protected by patent	%	

Commentary

Complexity Comments	
Please highlight here the key drivers of complexity in your operation (comments will be reported without editing)	
E-1-151	

Batch & campaign structure in the last year			
E-1-17	Number of batches produced in the last year		
E-1-18	Number of campaigns in the last year		
E-1-162	Number of machine hours operated in the last year		
		Min	Median
E-1-19a-c	Batch size range (in KG)		Max

Commentary

Age of production technology in the last year		Unit	Measure
E-1-22	Total number of machines	Number	
E-1-23	Percentage of machines which are less than 3 years old	%	
E-1-24	Percentage of machines that are between 3 and 5 years old	%	
E-1-25	Percentage of machines that are between 6 and 10 years old	%	
E-1-26	Percentage of machines that are between 11 and 15 years old	%	
E-1-27	Percentage of machines that are older than 15 years	%	

Commentary

Level of automation in the last year		Unit	Measure
E-1-28	Percentage of machines that are manually operated	%	
E-1-29	Percentage of machines that are operated with IT-support	%	
E-1-30	Percentage of machines that are fully automated (without supervision/ from a control room)	%	

Commentary

Number of products in the last year		Unit	Measure
E-1-31	Number of different drug substances produced at your plant	Number	
E-1-32	Number of different SDUs produced at your plant	Number	
E-1-33	Number of different SKUs produced at your plant	Number	

Commentary

Cost structure in the last year		Unit	Measure
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.			
E-1-34	COGS (Cost of Goods Sold) Conversion and Material costs 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.	thousand	n/a
E-1-35	Conversion Costs Labor + plant, property + equipment, write-offs, other	thousand	n/a
E-1-36	Material costs (inc. cost of API) Direct material costs	thousand	
E-1-37	Indirect material costs	thousand	
E-1-38	Labor costs Direct labor costs	thousand	
E-1-39	thereof overtime costs	thousand	
E-1-153	thereof contractor spend	thousand	
E-1-40	Indirect labor costs	thousand	

Commentary

Appendix

E-1-40	Indirect labor costs	thousand	
E-1-41	thereof overtime costs	thousand	
E-1-154	thereof contractor spend	thousand	
	Plant, property and equipment costs	thousand	
E-1-43	Costs for machines & tools	thousand	
E-1-44	thereof depreciation, amortisation (CAPEX)	thousand	
E-1-45	Costs for property and plant	thousand	
E-1-46	thereof depreciation, amortisation (CAPEX)	thousand	
E-1-47	Capex Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)	thousand	
	Other costs	thousand	
E-1-48	Corporate allocations	thousand	
E-1-49	Other costs	thousand	
	Inventory write-off costs	thousand	
E-1-50	Write-off costs due to shelf-life expiry	thousand	
E-1-51	Write-off costs due to handling damages/losses	thousand	
E-1-52	Write-off costs due to poor quality/out of spec	thousand	
E-1-53	Write-off costs due to other reasons	thousand	

Specific Cost Items

Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.

		Unit	Measure
E-1-54	Maintenance costs	thousand	
E-1-55	Thereof preventive maintenance cost (Planned and condition-based activities)	thousand	
E-1-56	QA and QC cost	thousand	
E-1-57	Percentage of quality cost due to outsourced quality activities	%	
E-1-58	Rework cost	thousand	
E-1-59	Destruction cost (excl. write-offs)	thousand	

Headcount structure

Please include all FTEs working at your plant on this technology independent from being on your payroll

		Measure
E-1-60	Direct labor	n/a
E-1-61	FTE in Production	
E-1-62	FTE in Quality Control (e.g. QC lab testing, in-process testing)	
E-1-63	Indirect labor	n/a
E-1-64	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)	
E-1-65	FTE in Quality Assurance	
E-1-66	FTE in Maintenance	
E-1-67	FTE in Supply Chain	
E-1-68	FTE in other functions	
E-1-69	Overall number of FTEs working on this technology	n/a

2: Technology Level Performance KPIs

TPM performance						
	Name	Definition	Unit		Average	Median
E-1-70a-b	Setup and Cleaning	The total time spent for setup and cleaning as a percentage of total scheduled time	%			
E-1-71a-b	Dedicated equipment	The percentage of your equipment that is dedicated to one product	%			
E-1-72a-b	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance works	%			
				Mon - Fri	Sat	Sun
E-1-75a-c	Shift-model	Number of shifts per day				
E-1-76a-c	Shift length	Average length of one shift in hours	Hours			
E-1-77a-c	Line staffing	FTEs per shift				
	OEE					
	Definition see figure of this page		Unit	Average		
E-1-78	Loading = Scheduled Time / Calendar Time		%			
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours					
E-1-79	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%			
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime					

E-1-80	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%			
	<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime				
E-1-81	(OEE) Quality = (Input - Defects) / Input	%			
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)				
E-1-82	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a	

Calendar time				
Unscheduled time	Scheduled time			
	Down time	Available time		
		Speed losses	Net run time	
			Amount produced x cycle time	
			Quality losses	Value added net operating time
Losses included	Losses included	Losses included		
• Preventive Maintenance	• Minor stops	• Startup losses		
• Routine validation	• Material and product jams	• Defective product yield losses		
• Meetings / Plant breaks	• Ramp up			
• Setup, cleaning	• Reduced Speeds			
• Goning				
• Breakdowns				
• Waiting material / labour				
Leading	(OEE) - Availability	(OEE) - Performance	(OEE) - Quality	

TQM performance								
Name	Definition	Unit	Min	Average	Median	Max	SD	
E-1-83a-e	Yield	Real achieved output in pharmaceutical production (input minus material losses, weighting, sediments etc.)	%					
E-1-84a-e	Release time	Average time from sampling to release of finished products including all waiting times.	Working days					
E-1-85a-e	Deviations	Number of deviations per month that arise from raw materials purchased, production components (equipment) and product/ process specifications.	Number per month					
E-1-86a-e	Deviation closure time	Average deviation closure time in days.	Working days					
Name	Definition	Unit	Min	Average	Median	Max	SD	
E-1-155a-b	Recurring Deviations	A deviation which, during the defined review period, on at least one other occasion the same event has occurred with the same root cause within the same process and/or work area. If redundant/duplicative processes or equipment exist, consider deviation events common to the grouping/work centre as recurring.	%					
E-1-156a-b	CPKs	Average CPK score across the top 5 products	Number					
E-1-87a-b	Complaint rate (customer)	Number of justified complaints as a percentage of all customer orders delivered.	%					
E-1-88a-b	Complaint rate (supplier)	Number of complaints as a percentage of all deliveries received (from your supplier).	%					
E-1-89a-b	RFT	Total number of batches produced without document errors or exception reports as a percentage of the total number of batches produced.	%					
E-1-90a-b	Rejected batches	Number of rejected batches as a percentage of all batches produced.	%					
E-1-91a-b	Mean time between failure	Average time between breakdowns	Hours					
E-1-93a-b	Number of tests	Number of quality tests per month	Number per month					
E-1-157	CTQ	Is 'Critical to Quality' analysis utilised? (Yes/No)	Yes/No					

JIT Performance								
Name	Definition	Unit	Min	Average	Median	Max	SD	
E-1-94a-e	Order lead time	Time between a customer placing an order and receiving delivery.	Working days					
E-1-95a-e	Production lead time	Time in days from start of production (SOP) to release of finished products	Working days	n/a	n/a	n/a	n/a	n/a
E-1-96a-e	... thereof Waiting time	Sum of waiting times, for example during set-up, or before and after QA/QC.	Working days					
E-1-97a-e	... thereof Production time	Value adding time of the production process not including set-up time or waiting time in between two process	Working days					

Appendix

E-1-108a-e	...thereof QA/QC	Time for release testing of finished goods. If different release tests have to be performed it also includes waiting in	Working days						
E-1-090a-e	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						
	Name	Definition	Unit		Average	Median			
E-1-100a-b	Days on hand (DOH)	Average inventory less write downs x 365 divided by the 'Cost of Goods Sold (COGS)	Days						
E-1-101a-b	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.	%						
E-1-102a-b	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.	%						
E-1-103a-b	Forecast accuracy	Actual orders received compared to the annual sales forecast.	%						
E-1-104a-b	Production schedule adherence	Number of orders finished in the correct week and vol (+/- 10%) / Total Number of orders planned for completion that week.	%						
E-1-105a-b	Priority orders	Number of priority orders as a percentage of all orders produced.	%						
E-1-106a-b	Production freeze period	Freezing period in which you do not allow any changes of your production schedule	Working days						
E-1-107a-b	Number of stockouts	Number of out-of-stock events per month	Number per month						
E-1-108a-b									
E-1-109a-b	Cycle time	Cycle time 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 15-30 days > 30 days						
E-1-110a-b									
E-1-111a-b	Raw material turns	Annual cost of raw materials purchased divided by the average raw material inventory.	Number						
E-1-112a-b	WIP turns	Annual cost of raw materials purchased plus annual cost of conversion divided by the average work in process inventory.	Number						
E-1-113a-b	Finished goods turns	Annual cost of goods sold divided by the average finished goods inventory.	Number						
	Changeovers								
	Name	Definition	Unit	Min	Average	Median	Max	SD	
E-1-114a-e	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes						
E-1-118a-e	Number of Changeovers	Average number of changeovers performed per month including changing lots and changing formats.	Number						

3: Line Level Performance KPIs

Add a Line	Remove a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Commentary
E-1-122-L1	Line Number (auto-generated)	1					
E-1-123-L1	Line Description						
TPM performance							
OEE							
Definition see figure of this page (Tech-level performance segment)		Unit			Average		
E-1-124-L1	Loading = Scheduled Time / Calendar Time	%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours							
E-1-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%					
E-1-126-L1	<i>Downtime</i> : of which <i>setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime							
E-1-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%					
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime							

E-1-128-L1	(OEE) Quality = (Input - Defects) / Input		%						
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)								
E-1-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				
JIT Performance									Commentary
Changeovers									
E-1-130a-e-L1	Changeover time	Time in minutes spent between different products for setting up and clearing the equipment.	Minutes						
TQM performance									Commentary
E-1-140a-e-L1	Yield	Real achieved output in pharmaceutical production (input minus material losses, weighting, sediments etc.)	%						

proceed

Technology: Drug Substance - Biologics

Please select the process steps and sub-steps/descriptors that you carry out at your site:

Upstream		Downstream		
Media prep	Fermentation	Capture	Purification	Polishing
☐ Steel ¹	☐ Disposable ¹	☐ In-Cell (Centrifuge & cell disruption)	☐ Low pH incubation ☐ Filtration ☐ Chromatography	☐ UF/DF filtration ☐ Chromatography
☐ Outside-Cell (Chromatography)				

¹ Refers to technology used in final step of fermentation

Commentary

1: Cost and Structural KPIs

Production structure					
	Unit	Measure			
E-2-02	Amount of drug substance produced at your site in the last year	KG			
E-2-03	Percentage of drug substance produced at your site that was processed for own production	%			
E-2-05	Percentage of drug substance produced at your site that was protected by patent	%			
E-2-05	Total fermentation capacity for biologics drug substance production	Litres			
E-2-06	Number of bioreactor trains	Number			
E-2-07	Number of downstream / purification trains	Number			
Types of fermentation (mark in the matrix all those that take place at your site)					
		Batch	Fed-Batch	Perfusion	Other
E-2-08a-d	Mammalian	☐	☐	☐	☐
E-2-09a-d	Microbial	☐	☐	☐	☐
E-2-10a-d	Yeast	☐	☐	☐	☐
E-2-11a-d	Insect	☐	☐	☐	☐

Commentary

Complexity Comments	
Please highlight here the key drivers of complexity in your operation (comments will be reported without editing)	
E-2-151	

Batch & campaign structure in the last year					
	Unit	Measure			
E-2-17	Number of batches produced in the last year				
E-2-18	Number of campaigns in the last year				
E-2-152	Number of machine hours operated in the last year				
E-2-19a-c	Formulation batch size range (in Litres)	Min	Median	Max	

Commentary

Age of production technology in the last year		
	Unit	Measure
E-2-22	Total number of machines	Number
E-2-23	Percentage of machines which are less than 3 years old	%
E-2-24	Percentage of machines that are between 3 and 5 years old	%
E-2-25	Percentage of machines that are between 6 and 10 years old	%
E-2-26	Percentage of machines that are between 11 and 15 years old	%
E-2-27	Percentage of machines that are older than 15 years	%

Commentary

Level of automation in the last year		
	Unit	Measure
E-2-28	Percentage of machines that are manually operated	%
E-2-29	Percentage of machines that are operated with IT-support	%
E-2-30	Percentage of machines that are fully automated (without supervision/ from a control room)	%

Commentary

Number of products in the last year		
	Unit	Measure
E-2-31	Number of different drug substances produced at your plant	Number
E-2-32	Number of different SKUs produced at your plant	Number
E-2-33	Number of different SKUs produced at your plant	Number

Commentary

Cost structure in the last year		
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General information sheet.		
	Unit	Measure
E-2-34	COGS (Cost of Goods Sold)	n/a
E-2-35	Conversion Costs (Labor + plant, property + equipment, write-offs, other)	n/a
E-2-36	Material costs (inc. cost of APs)	
E-2-37	Direct material costs	
	Indirect material costs	

Commentary

	Labor costs	thousand	
E-2-38	Direct labor costs	thousand	
E-2-39	thereof overtime costs	thousand	
E-2-153	thereof contractor spend	thousand	
E-2-40	Indirect labor costs	thousand	
E-2-41	thereof overtime costs	thousand	
E-2-154	thereof contractor spend	thousand	
	Plant, property and equipment costs		
E-2-43	Costs for machines & tools	thousand	
E-2-44	thereof depreciation, amortisation (CAPEX)	thousand	
E-2-45	Costs for property and plant	thousand	
E-2-46	thereof depreciation, amortisation (CAPEX)	thousand	
E-2-47	Capex <i>Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)</i>	thousand	
	Other costs	thousand	
E-2-48	Corporate allocations	thousand	
E-2-49	Other costs	thousand	
	Inventory write-off costs	thousand	
E-2-50	Write-off costs due to shelf-life expiry	thousand	
E-2-51	Write-off costs due to handling damages/losses	thousand	
E-2-52	Write-off costs due to poor quality/out of spec	thousand	
E-2-53	Write-off costs due to other reasons	thousand	

	Specific Cost Items	Unit	Measure	Commentary
	<i>Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.</i>			
	Specific cost items	Unit	Measure	
E-2-54	Maintenance costs	thousand		
E-2-55	Thereof preventive maintenance cost (Planned and condition-based activities)	thousand		
E-2-56	QA and QC cost	thousand		
E-2-57	Percentage of quality cost due to outsourced quality activities	%		
E-2-58	Rework cost	thousand		
E-2-59	Destruction cost (excl. write-offs)	thousand		

	Headcount structure	Measure	Commentary
	<i>Please include all FTEs working at your plant on this technology independent from being on your payroll</i>		
	Direct labor	n/a	
E-2-60	FTE in Production		
E-2-61	FTE in Quality Control (e.g. QC lab testing, in-process testing)		
	Indirect labor	n/a	
E-2-62	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)		
E-2-63	FTE in Quality Assurance		
E-2-64	FTE in Maintenance		
E-2-65	FTE in Supply Chain		
E-2-66	FTE in other functions		
E-2-67	Overall number of FTEs working on this technology	n/a	

2: Technology Level Performance KPIs

	TPM performance			Average	Median	Commentary
	Name	Definition	Unit			
E-2-70a-b	Setup and Cleaning	The total time spent for setup and cleaning as a percentage of total scheduled time	%			
E-2-71a-b	Dedicated equipment	The percentage of your equipment that is dedicated to one product	%			
E-2-72a-b	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance works	%			
				Mon - Fri	Sat	Sun
E-2-75a-c	Shift-model	Number of shifts per day	Number			
E-2-76a-c	Shift length	Average length of one shift in hours	Hours			
E-2-77a-c	Line staffing	FTEs per shift	Number			
	OEE			Average		
	Definition see figure of this page		Unit			
E-2-78	Loading = Scheduled Time / Calendar Time		%			
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed					
	<i>Calendar Time</i> - usually 365 days, 8760 hours					

Appendix

E-2-79	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-2-80	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
	<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-2-81	(OEE) Quality = (Input - Defects) / Input		%					
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-2-82	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			
Calendar time Unscheduled time Scheduled time Down time Available time Losses included: - Preventive Maintenance - Routine validation - Meetings / Paid breaks - Setup, clearing - Gowning - Breakdowns - Waiting material / labour Speed losses Net run time Amount produced x cycle time Losses included: - Minor stops - Material and product jams - Ramp Up - Reduced Speeds Quality losses Value added net operating time Losses included: - Startup losses - Defective product - Yield losses Loading (OEE) - Availability (OEE) - Performance (OEE) - Quality								

JIT Performance								Commentary
Name	Definition	Unit	Min	Average	Median	Max	SD	
E-2-94a-e	Order lead time	Time between a customer placing an order and receiving delivery.	Working days					
E-2-95a-e	Production lead time	Time in days from start of production (SOP) to release of finished products.	Working days	n/a	n/a	n/a	n/a	Indicate here, if Production lead time is not sum of cells below.
E-2-96a-e	... thereof Waiting time	Sum of waiting times, for example during set-up, or before and after QA/QC.	Working days					
E-2-97a-e	... thereof Production time	Value adding time of the production process not including set-up time or waiting time in between two process	Working days					
E-2-98a-e	... thereof QA/QC	Time for release testing of finished goods. If different release tests have to be performed it also includes waiting in	Working days					
E-2-99a-e	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					
E-2-100a-b	Name	Definition	Unit		Median			
	Days on hand (DOH)	Average Inventory less write downs x 365 divided by the 'Cost of Goods Sold (COGS)	Days					
E-2-101a-b	Service level - delivery (OTF)	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 .	%					
E-2-102a-b	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 .	%					
E-2-103a-b	Forecast accuracy	Actual orders received compared to the annual sales forecast.	%					
E-2-104a-b	Production schedule adherence	Number of orders finished in the correct week and vd (+/- 10%) / Total Number of orders planned for completion that week	%					
E-2-105a-b	Priority orders	Number of priority orders as a percentage of all orders produced.	%					
E-2-106a-b	Production freeze period	Freezing period in which you do not allow any changes of your production schedule	Working days					
E-2-107a-b	Number of stockouts	Number of out-of-stock events per month	Number per month					
E-2-108a-b	Cycle time	Cycle time 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					
E-2-109a-b			15-30 days					
E-2-110a-b			> 30 days					
E-2-111a-b	Raw material turns	Annual cost of raw materials purchased divided by the average raw material inventory.	Number					
E-2-112a-b	WIP turns	Annual cost of raw materials purchased plus annual cost of conversion divided by the average work in process inventory.	Number					
E-2-113a-b	Finished goods turns	Annual cost of goods sold divided by the average finished goods inventory.	Number					
Changeovers								
E-2-114a-e	Name	Definition	Unit	Min	Average	Median	Max	SD
	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-2-115a-e	Number of Changeovers	Average number of changeovers performed per month including changing lots and changing formats.	Number					

3: Line Level Performance KPIs

Add a Line

Remove a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics		
E-2-122-L1	Line Number (auto-generated)	1
E-2-123-L1	Line Description	

TPM performance						Commentary	
OEE		Unit		Average			
Definition see figure of this page (Tech-level performance segment)							
E-2-124-L-I	Loading = Scheduled Time / Calendar Time	%					
<i>Scheduled Time</i> - time during which the equipment was <i>scheduled</i> or <i>expected to operate</i> during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-2-125-L-I	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%					
E-2-126-L-I	<i>Downtime of which setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> - time during which the equipment was <i>scheduled</i> or <i>expected to operate</i> during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-2-127-L-I	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%					
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran - scheduled time - downtime							
E-2-128-L-I	(OEE) Quality = (Input - Defects) / Input	%					
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-2-129-L-I	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a			

JIT Performance								Commentary	
Changeovers		Unit	Min	Average	Median	Max	SD		
E-2-130a-e-L-I	Changeover time Time in minutes spent between different products for setting up and cleaning the equipment.	Minutes							

TQM performance							Commentary		
		Unit	Min	Average	Median	Max	SD		
E-2-140a-e-L-I	Yield Real achieved output in pharmaceutical production (input minus material losses, weighing, sediments etc.)	%							

proceed

Technology: Drug Product - Solids

Please select the process steps and sub-steps/descriptors that you carry out at your site:

	Weighting / Mixing	Granulation	Sieving	Drying	Pelletisation	Compression / Encapsulation	Coating	Printing	Primary Packaging	Secondary Packaging
E-3-01a										
E-3-01b-1-2	☐ Wet	☐ Wet				☐ None	☐ Sugar		☐ Bottles	
E-3-01c-1-2	☐ Dry	☐ Dry				☐ Powder	☐ Film		☐ Blisters	
E-3-01f-1-4						☐ Tablet			☐ Bags	
E-3-01g-1-2						☐ Capsule				
E-3-01i-1-3										

Note: Primary Packaging refers to packing into bottles, blisters, bags etc.
Note: Secondary Packaging refers to packing those bottles, blisters etc. into boxes with leaflets

F Formulation
 PP Primary Packaging
 SP Secondary Packaging

Commentary

1: Cost and Structural KPIs

Production structure			Unit	Measure
Indicate the <u>total volume of bulk goods that was produced at your site in the last year:</u>				
E-3-05	Solid forms (tablets, capsules etc.)		Million Pieces	
E-3-06	- thereof tablets		Million Pieces	
E-3-07	- thereof capsules		Million Pieces	
Indicate the <u>total volume of bulk goods that was packed (Primary Packing) at your site in the last year:</u>				
E-3-08	Solid form packs (blisters, bottles, bags)		Million Units	
E-3-09	- thereof blisters		Million Units	
E-3-10	- thereof bottles		Million Units	
E-3-11	- thereof bags		Million Units	
Indicate the <u>total volume of bulk goods that was packed (Secondary Packing) at your site in the last year:</u>				
E-3-12	Packages / boxes		Million Packs	
E-3-13	Average pieces per packed blister (Primary Packaging)		Pieces	
E-3-14	Average pieces per packed bottle (Primary Packaging)		Pieces	
E-3-15	Average pieces per packed bag (Primary Packaging)		Pieces	
E-3-16	Average units per packed boxes (Secondary Packaging)		Units	

Commentary

Complexity Comments

Please highlight here the key drivers of complexity in your operation, in your opinion (comments will be reported without editing)

E-3-151

Batch & campaign structure in the last year			Formulation	PP	SP
E-3-17a-c	Number of batches / lots produced in the last year				
E-3-18	Number of campaigns in the last year				
E-3-152a-c	Number of machine hours operated in the last year				
E-3-19a-c	Formulation batch size range (in KG)		Min	Median	Max
E-3-20a-c	Primary Packaging lot size range (in pieces)				
E-3-21a-c	Secondary Packaging lot size range (in units)				

Commentary

Age of production technology in the last year			Unit	Formulation	PP	SP
E-3-22a-c	Total number of machines		Number			
E-3-23a-c	Percentage of machines which are less than 3 years old		%			
E-3-24a-c	Percentage of machines that are between 3 and 5 years old		%			
E-3-25a-c	Percentage of machines that are between 6 and 10 years old		%			
E-3-26a-c	Percentage of machines that are between 11 and 15 years old		%			
E-3-27a-c	Percentage of machines that are older than 15 years		%			

Commentary

Level of automation in the last year			Unit	Formulation	PP	SP
E-3-28a-c	Percentage of machines that are manually operated		%			
E-3-29a-c	Percentage of machines that are operated with IT-support		%			
E-3-30a-c	Percentage of machines that are fully automated (without supervision/ from a control room)		%			

Commentary

Number of products in the last year			Unit	Formulation	PP	SP
E-3-31a-c	Number of different drug substances / bulks / blends produced at your plant		Number			
E-3-32a-c	Number of different SDUs produced at your plant		Number			
E-3-33a-c	Number of different SKUs produced at your plant		Number			

Commentary

Appendix

Cost structure in the last year					Commentary	
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.						
		Unit	Formulation	PP	SP	
E-3-34a-c	COGS Conversion and Material costs 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.	thousand	n/a	n/a	n/a	
E-3-35a-c	Conversion Costs Labor + plant, property + equipment, write-offs, other	thousand	n/a	n/a	n/a	
E-3-36a-c	Material costs (inc. cost of API)	thousand				
E-3-37a-c	Direct material costs	thousand				
E-3-38a-c	Indirect material costs	thousand				
E-3-39a-c	Labor costs	thousand				
E-3-153a-c	Direct labor costs	thousand				
E-3-40a-c	thereof overtime costs	thousand				
E-3-41a-c	thereof contractor spend	thousand				
E-3-154a-c	Indirect labor costs	thousand				
E-3-42a-c	thereof overtime costs	thousand				
E-3-43a-c	thereof contractor spend	thousand				
E-3-44a-c	Plant, property and equipment costs	thousand				
E-3-45a-c	Costs for machines & tools	thousand				
E-3-46a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-3-47a-c	Costs for property and plant	thousand				
E-3-48a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-3-49a-c	Capex investment	thousand				
E-3-50a-c	Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)	thousand				
E-3-51a-c	Other costs	thousand				
E-3-52a-c	Corporate allocations	thousand				
E-3-53a-c	Other costs	thousand				
E-3-54a-c	Inventory write-off costs	thousand				
E-3-55a-c	Write-off costs due to shelf-life expiry	thousand				
E-3-56a-c	Write-off costs due to handling damages/losses	thousand				
E-3-57a-c	Write-off costs due to poor quality/out of spec	thousand				
E-3-58a-c	Write-off costs due to other reasons	thousand				

Specific Cost Items					Commentary	
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.						
		Unit	Formulation	PP	SP	
E-3-54a-c	Specific cost items					
E-3-55a-c	Maintenance costs	thousand				
E-3-56a-c	Thereof preventive maintenance (Planned & condition-based activities)	thousand				
E-3-57a-c	QA and QC cost	thousand				
E-3-58a-c	Percentage of quality cost due to outsourced quality activities	%				
E-3-59a-c	Rework cost	thousand				
E-3-60a-c	Destruction cost (excl. write-offs)	thousand				

Headcount structure					Commentary	
Please include all FTEs working at your plant on this technology independent from being on your payroll						
		Formulation	PP	SP	TOTAL	
E-3-60a-d	Direct labor	n/a	n/a	n/a	n/a	
E-3-61a-d	FTE in Production				n/a	
E-3-62a-d	FTE in Quality Control (e.g. QC lab testing, in-process testing)				n/a	
E-3-63a-d	Indirect labor	n/a	n/a	n/a	n/a	
E-3-64a-d	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)				n/a	
E-3-65a-d	FTE in Quality Assurance				n/a	
E-3-66a-d	FTE in Maintenance				n/a	
E-3-67a-d	FTE in Supply Chain				n/a	
E-3-68a-d	FTE in other functions				n/a	
E-3-69a-d	Overall number of FTEs working on this technology	n/a	n/a	n/a	n/a	

2: Technology Level Performance KPIs

TLM performance				Performance				Primary Parameters				Secondary Parameters				Comments
Name	Definition	Unit	Average	Median				Average	Median			Average	Median			
E-3-70a	Setup and Cleaning	The total time spent for setup and cleaning as a percentage of total scheduled time	%													
E-3-71a	Dedicated equipment	The percentage of your equipment that is dedicated to one product	%													
E-3-72a	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance work	%													
E-3-73a	Uptime	Definition	Unit	Mon - Fri	Sat	Sun		Mon - Fri	Sat	Sun		Mon - Fri	Sat	Sun		
E-3-74a	Overhead	Number of shifts per day	Number													
E-3-75a	Shift length	Average length of one shift in hours	Hours													
E-3-76a	Line staffing	FTEs per shift	Number													
E-3-77a	OTL	Definition and Range of Data range	Unit													
E-3-78a	Leadtime	Leadtime = Scheduled Time - Collection Time	%													
E-3-79a	OTL Availability	OTL Availability = (Scheduled Time - Downtime) / Scheduled Time	%													
E-3-80a	OTL Performance	OTL Performance = (Percent Produced x Ideal Cycle Time) / Available time	%													
E-3-81a	OTL Quality	OTL Quality = (Input - Defects) / Input	%													
E-3-82a	Overall Equipment Effectiveness (OEE) Availability x OEE Performance x OEE Quality	%														

Calculator time			
Unscheduled time	Scheduled time		
Down time	Available time		
- Losses included: - Production - Maintenance - Quality improvement - Changeover / Pre-Change - Changeover / Setup - Changeover / Breakdown - Changeover / Repair - Changeover / Material	- Losses included: - Material and waste product - Setup - Repair - Changeover / Breakdown - Changeover / Repair - Changeover / Material	Material produced x Cycle time	Material produced x Cycle time
Lossing	OTL Availability	OTL Performance	OTL Quality

LXXXII

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics						Commentary	
E-3-122-L1	Line Number (auto-generated)	1					
E-3-123-L1	Line Description						
TPM performance							
OEE							
Definition see figure of this page (Tech-level performance segment)		Unit		Average			
E-3-124-L1	Loading = Scheduled Time / Calendar Time	%					
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-3-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%					
E-3-126-L1	<u>Downtime of which setup and cleaning</u> The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-3-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%					
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-3-128-L1	(OEE) Quality = (Input - Defects) / Input	%					
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-3-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a			
JIT Performance							
Changeovers		Unit	Min	Average	Median	Max	SD
E-3-130a-e-L1	Changeover time Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove Primary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics						Commentary
E-3-131-L1	Line Number (auto-generated)	1				
E-3-132-L1	Line Description					
TPM performance						
OEE						
Definition see figure of this page (Tech-level performance segment)		Unit		Average		
E-3-133-L1	Loading = Scheduled Time / Calendar Time	%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours						
E-3-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%				
E-3-135-L1	<u>Downtime of which setup and cleaning</u> The time spent for setup and cleaning as a percentage of the scheduled time	%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime						
E-3-136-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%				
<u>Amount Produced</u> - the number of units produced during the time period <u>Ideal Cycle Time</u> - the designed or optimum cycle time <u>Available Time</u> - the time the machine actually ran: scheduled time - downtime						
E-3-137-L1	(OEE) Quality = (Input - Defects) / Input	%				
<u>Input</u> - the number of units that were started through the process <u>Defects</u> - the number of defective units (even if they were subsequently salvaged)						
E-3-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-3-139a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-3-158-a-e-L1		Country change	Minutes					
E-3-159-a-e-L1		Format change	Minutes					
E-3-160-a-e-L1		Product change	Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line	Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Commentary
E-3-140-L1	Line Number (auto-generated)		1				
E-3-141-L1	Line Description						
TPM performance							
OEE							
Definition see figure of this page (Tech-level performance segment)							
E-3-142-L1	Loading = Scheduled Time / Calendar Time		%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-3-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%				
E-3-144-L1	<u>Downtime, of which, changeovers.</u> The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time		%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-3-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%				
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-3-146-L1	(OEE) Quality = (Input - Defects) / Input		%				
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-3-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-3-148a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-3-149a-e-L1		Country change	Minutes					
E-3-150a-e-L1		Format change	Minutes					
		Product change	Minutes					

proceed

Please select the process steps and sub-steps/descriptors that you carry out at your site:

Commentary

[illegible][illegible][illegible]

Commentary

Commentary

Appendix

Cost structure in the last year						Commentary	
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.							
		Unit	Formulation	PP	SP		
E-4-34a-c	COGS (Cost of Goods Sold)	Conversion and Material costs 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.	thousand	n/a	n/a	n/a	
E-4-35a-c	Conversion Costs	Labor + plant, property + equipment, write-offs, other	thousand	n/a	n/a	n/a	
	Material costs (inc. cost of API)		thousand				
E-4-36a-c	Direct material costs		thousand				
E-4-37a-c	Indirect material costs		thousand				
	Labor costs		thousand				
E-4-38a-c	Direct labor costs		thousand				
E-4-39a-c	thereof overtime costs		thousand				
E-4-153a-c	thereof contractor spend		thousand				
E-4-40a-c	Indirect labor costs		thousand				
E-4-41a-c	thereof overtime costs		thousand				
E-4-154a-c	thereof contractor spend		thousand				
	Plant, property and equipment costs		thousand				
E-4-43a-c	Costs for machines & tools		thousand				
E-4-44a-c	thereof depreciation, amortisation (CAPEX)		thousand				
E-4-45a-c	Costs for property and plant		thousand				
E-4-46a-c	thereof depreciation, amortisation (CAPEX)		thousand				
E-4-47a-c	Capex Investment	Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)	thousand				
	Other costs		thousand				
E-4-48a-c	Corporate allocations		thousand				
E-4-49a-c	Other costs		thousand				
	Inventory write-off costs		thousand				
E-4-50a-c	Write-off costs due to shelf-life expiry		thousand				
E-4-51a-c	Write-off costs due to handling damages/losses		thousand				
E-4-52a-c	Write-off costs due to poor quality/out of spec		thousand				
E-4-53a-c	Write-off costs due to other reasons		thousand				

Specific Cost Items						Commentary	
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.							
		Unit	Formulation	PP	SP		
E-4-54a-c	Specific cost items						
	Maintenance costs		thousand				
E-4-55a-c	Thereof preventive maintenance (Planned & condition-based activities)		thousand				
E-4-56a-c	QA and QC cost		thousand				
E-4-57a-c	Percentage of quality cost due to outsourced quality activities		%				
E-4-58a-c	Rework cost		thousand				
E-4-59a-c	Destruction cost (excl. write-offs)		thousand				

Headcount structure						Commentary
Please include all FTEs working at your plant on this technology independent from being on your payroll						
		Formulation	PP	SP	TOTAL	
E-4-60a-d	Direct labor	n/a	n/a	n/a	n/a	
E-4-61a-d	FTE in Production				n/a	
E-4-62a-d	FTE in Quality Control (e.g. QC lab testing, in-process testing)				n/a	
E-4-63a-d	Indirect labor	n/a	n/a	n/a	n/a	
E-4-64a-d	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)				n/a	
E-4-65a-d	FTE in Quality Assurance				n/a	
E-4-66a-d	FTE in Maintenance				n/a	
E-4-67a-d	FTE in Supply Chain				n/a	
E-4-68a-d	FTE in other functions				n/a	
E-4-69a-d	Overall number of FTEs working on this technology	n/a	n/a	n/a	n/a	

2: Technology Level Performance KPIs

TLM performance				Performance			Primary Parameters						Comments
	Name	Definition	Unit	Average	Median		Average	Median		Average	Median		
E-4.76a	Setup and Dismantling	The total time spent for setup and dismantling as a percentage of total scheduled time	%										
E-4.77a	Dedicated equipment	The percentage of any equipment that is dedicated to one product	%										
E-4.72a	Unplanned maintenance	Proportion of unplanned maintenance work as a percentage of the total time spent for maintenance work	%										
E-4.73a	Turnover	Units	Units	Min + P5	50th	50th	Min + P5	50th	50th	Min + P5	50th	50th	
E-4.77b	Shift model	Number of shifts per day	Number										
E-4.77c	Shift length	Average length of one shift in hours	Hours										
E-4.77d	Line staffing	FTEs per shift	Number										
OEE				Definition line spans of this page			Average			Average			
E-4.78a	Leading = Scheduled Time / Calendar Time	%											
Schedule Time: time during which the equipment was scheduled to operate for operation during the time period being analyzed Calendar Time: usually 240 days, 8760 hours													
E-4.78b	OEE Availability = (Scheduled Time - Downtime) / Scheduled Time	%											
Schedule Time: time during which the equipment was scheduled to operate during the time period being analyzed Downtime = breakdowns + unplanned downtime + setup downtime													
E-4.80a	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													
E-4.81a	OEE Quality = (Input - Defects) / Input	%											
Input: the number of units that were shipped through the process Defects: the number of defective units found if they were automatically scrapped													
E-4.82a	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%	N/A				N/A						

Calendar time			
Unscheduled time		Scheduled time	
Down time		Availability time	
• Locks involved • Production • Breakdown • Material transport • Setup change • Breakdown • Waiting material • Minor		• Locks involved • Production • Breakdown • Material and product • Setup change • Breakdown • Waiting material • Minor	
• Locks involved • Production • Breakdown • Material and product • Setup change • Breakdown • Waiting material • Minor		• Locks involved • Production • Breakdown • Material and product • Setup change • Breakdown • Waiting material • Minor	
Leading	(OEE) Availability	(OEE) Performance	(OEE) Quality

LXXXVIII

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics						Commentary	
E-4-122-L1	Line Number (auto-generated)	1					
E-4-123-L1	Line Description						
TPM performance							Commentary
OEE							
Definition see figure of this page (Tech-level performance segment)		Unit		Average			
E-4-124-L1	Loading = Scheduled Time / Calendar Time	%		10%			
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-4-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%		10%			
E-4-126-L1	<u>Downtime of which setup and cleaning</u> The time spent for setup and cleaning as a percentage of the scheduled time	%		10%			
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-4-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%		10%			
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-4-128-L1	(OEE) Quality = (Input - Defects) / Input	%		10%			
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-4-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		0%			
JIT Performance							Commentary
Changeovers		Unit	Min	Average	Median	Max	
E-4-130a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes		1		

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove Primary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics						Commentary
E-4-131-L1	Line Number (auto-generated)	1				
E-4-132-L1	Line Description					
TPM performance						
OEE						
Definition see figure of this page (Tech-level performance segment)		Unit		Average		
E-4-133-L1	Loading = Scheduled Time / Calendar Time	%		10%		
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours						
E-4-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Schedules' Time	%		10%		
E-4-135-L1	<u>Downtime of which setup and cleaning</u> The time spent for setup and cleaning as a percentage of the scheduled time	%		10%		
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime						
E-4-136-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%		10%		
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime						
E-4-137-L1	(OEE) Quality = (Input - Defects) / Input	%		10%		
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)						
E-4-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		0%		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-4-139a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-4-158-a-e-L1		Country change	Minutes					
E-4-159-a-e-L1		Format change	Minutes					
E-4-160-a-e-L1		Product change	Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line	Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics						Commentary
E-4-140-L1	Line Number (auto-generated)			1		
E-4-141-L1	Line Description					
TPM performance						
OEE						
Definition see figure of this page (Tech-level performance segment)		Unit		Average		
E-4-142-L1	Loading = Scheduled Time / Calendar Time	%				
<i>Scheduled Time</i> - time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours						
E-4-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%				
E-4-144-L1	<i>Downtime of which changeovers</i> The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time	%				
<i>Scheduled Time</i> - time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime						
E-4-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%				
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime						
E-4-146-L1	(OEE) Quality = (Input - Defects) / Input	%				
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)						
E-4-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-4-148a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-4-149a-e-L1		Country change	Minutes					
E-4-150a-e-L1		Format change	Minutes					
		Product change	Minutes					

proceed

Technology: Drug Product - Suppositories

Please select the process steps and sub-steps/descriptors that you carry out at your site:

E-5-01a-d
E-5-01a.1-3
E-5-01b.1-2

Commentary

1: Cost and Structural KPIs

E-5-02

E-5-03

E-5-04

E-5-05

E-5-12

E-5-13-1

E-5-13-2

E-5-06

[illegible]F-5-151

E-5-17a-c
E-5-18
E-5-152a-c

E-5-19a-c
E-5-20a-c
E-5-21a-c

[illegible]

E-5-22a-c
E-5-23a-c
E-5-24a-c
E-5-25a-c
E-5-26a-c
E-5-27a-c

[illegible]

E-5-28a-c
E-5-29a-c
E-5-30a-c

Commentary

Appendix

Number of products in the last year						Commentary
		Unit	Formulation	PP	SP	
E-5-31a-c	Number of different drug substances / bulks / blends produced at your plant	Number				
E-5-32a-c	Number of different SDUs produced at your plant	Number				
E-5-33a-c	Number of different SKUs produced at your plant	Number				

Cost structure in the last year						Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.						
		Unit	Formulation	PP	SP	
E-5-34a-c	COGS (Cost of Goods Sold) <i>Conversion and Material costs } 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.</i>	thousand	n/a	n/a	n/a	
E-5-35a-c	Conversion Costs <i>Labor + plant, property + equipment, write-offs, other</i>	thousand	n/a	n/a	n/a	
	Material costs (inc. cost of API)	thousand				
E-5-36a-c	Direct material costs	thousand				
E-5-37a-c	Indirect material costs	thousand				
	Labor costs	thousand				
E-5-38a-c	Direct labor costs	thousand				
E-5-39a-c	thereof overtime costs	thousand				
E-5-153a-c	thereof contractor spend	thousand				
E-5-40a-c	Indirect labor costs	thousand				
E-5-41a-c	thereof overtime costs	thousand				
E-5-154a-c	thereof contractor spend	thousand				
	Plant, property and equipment costs	thousand				
E-5-43a-c	Costs for machines & tools	thousand				
E-5-44a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-5-45a-c	Costs for property and plant	thousand				
E-5-46a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-5-47a-c	Capex <i>Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)</i>	thousand				
	Other costs	thousand				
E-5-48a-c	Corporate allocations	thousand				
E-5-49a-c	Other costs	thousand				
	Inventory write-off costs	thousand				
E-5-50a-c	Write-off costs due to shelf-life expiry	thousand				
E-5-51a-c	Write-off costs due to handling damages/losses	thousand				
E-5-52a-c	Write-off costs due to poor quality/out of spec	thousand				
E-5-53a-c	Write-off costs due to other reasons	thousand				

Specific Cost Items						Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.						
		Unit	Formulation	PP	SP	
E-5-54a-c	Maintenance costs	thousand				
E-5-55a-c	Thereof preventive maintenance (Planned & condition-based activities)	thousand				
E-5-56a-c	QA and QC cost	thousand				
E-5-57a-c	Percentage of quality cost due to outsourced quality activities	%				
E-5-58a-c	Rework cost	thousand				
E-5-59a-c	Destruction cost (excl. write-offs)	thousand				

Headcount structure						Commentary
Please include all FTEs working at your plant on this technology independent from being on your payroll						
		Formulation	PP	SP	TOTAL	
E-5-60a-d	Direct labor	0	0	0	0	
E-5-61a-d	FTE in Production					
E-5-62a-d	FTE in Quality Control (e.g. QC lab testing, in-process testing)					
E-5-63a-d	Indirect labor	0	0	0	0	
E-5-64a-d	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)					
E-5-65a-d	FTE in Quality Assurance					
E-5-66a-d	FTE in Maintenance					
E-5-67a-d	FTE in Supply Chain					
E-5-68a-d	FTE in other functions					
E-5-69a-d	Overall number of FTEs working on this technology	0	0	0	0	

2: Technology Level Performance KPIs

TLM performance														Summary
Performance			Throughput				Product Packaging							
Name	Definition	Unit	Average		Median		Average		Median		Average		Median	
E-6-75a	The total time spent for setup and cleaning as a percentage of total scheduled time	%												
E-6-75b	The percentage of your equipment that is dedicated to one product	%												
E-6-75c	Proportion of unplanned maintenance work as a percentage of the overall time spent by production units	%												
E-6-75d	Number of shifts per day	Unit	Mon - Fri	Sat	Sun		Mon - Fri	Sat	Sun		Mon - Fri	Sat	Sun	
E-6-75e	Average length of one shift in hours	Hours												
E-6-75f	FTEs per shift	Number												
OEE														
Definition and Scope of this page			Unit	Average				Average				Average		
Leading = Scheduled Time / Calendar Time														
Availability: The ratio of time during which the equipment was scheduled to operate during the time period during which it was supposed to operate														
E-6-75a-c	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%												
Performance: The ratio of units produced during the time period that equipment is available to operate during the time period during which it was supposed to operate														
E-6-80a-c	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available Time	%												
Quality: The number of units produced during the time period that equipment is available to operate during the time period during which it was supposed to operate														
E-6-81a-c	(OEE) Quality = (Good - Defects) / (Good + Defects)	%												
Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality														
E-6-82a-c		%												

Calendar time									
Unscheduled time					Scheduled time				
Down time					Available time				
Losses included: • Power outage • Maintenance • Changeover • Setup, reconfiguration • Material change • Changeover • Breakdowns • Shipping material / Manual	Speed losses				Not run time				
	Losses included: • Minor stoppage • Changeover • Setup • Breakdowns • Reduced capacity				Amount produced / Cycle time				
	Quality losses				Value added operating time				
	Losses included: • Defective pieces • Defective production								
Leading	(OEE) Availability	(OEE) Performance	(OEE) Quality						

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site

Line characteristics							Commentary	
E-5-122-L1	Line Number (auto-generated)	1						
E-5-123-L1	Line Description							
TPM performance								
OEE								
Definition see figure of this page (Tech-level performance segment)		Unit		Average				
E-5-124-L1	Loading = Scheduled Time / Calendar Time	%		10%				
<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours								
E-5-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%		10%				
E-5-126-L1	<i>Downtime</i> , of which <i>setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time	%		10%				
<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtime) + setup downtime								
E-5-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%		10%				
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime								
E-5-128-L1	(OEE) Quality = (Input - Defects) / Input	%		10%				
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)								
E-5-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		0%				
JIT Performance								
Changeovers								
E-5-130a-e-L1	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes	1		Median	Max	SD	
Line characteristics								
E-5-122-L2	Line Number (auto-generated)	2						Commentary
E-5-123-L2	Line Description							
TPM performance								
OEE								
Definition see figure of this page (Tech-level performance segment)		Unit		Average				
E-5-124-L2	Loading = Scheduled Time / Calendar Time	%						
<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours								
E-5-125-L2	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%						
E-5-126-L2	<i>Downtime</i> , of which <i>setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time	%						
<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtime) + setup downtime								
E-5-127-L2	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%						
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime								
E-5-128-L2	(OEE) Quality = (Input - Defects) / Input	%						
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)								
E-5-129-L2	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a				

Appendix

JIT Performance								Commentary
Changeovers			Unit	Min	Average	Median	Max	
E-5-130a-e-L2	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					

Line characteristics	
E-5-122-L3	Line Number (auto-generated)
E-5-123-L3	Line Description

TPM performance						Commentary
OEE						
Definition see figure of this page (Tech-level performance segment)			Unit		Average	
E-5-124-L3	Loading = Scheduled Time / Calendar Time		%			
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> , usually 365 days, 8760 hours						
E-5-125-L3	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%			
E-5-126-L3	Downtime, of which setup, and cleaning The time spent for setup and cleaning as a percentage of the scheduled time		%			
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> , breakdowns (unplanned downtimes) + setup downtime						
E-5-127-L3	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%			
<i>Amount Produced</i> , the number of units produced during the time period <i>Ideal Cycle Time</i> , the designed or optimum cycle time <i>Available Time</i> , the time the machine actually ran: scheduled time - downtime						
E-5-128-L3	(OEE) Quality = (Input - Defects) / Input		%			
<i>Input</i> , the number of units that were started through the process <i>Defects</i> , the number of defective units (even if they were subsequently salvaged)						
E-5-129-L3	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%	n/a		

JIT Performance								Commentary
Changeovers			Unit	Min	Average	Median	Max	
E-5-130a-e-L3	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					

Line characteristics	
E-5-122-L4	Line Number (auto-generated)
E-5-123-L4	Line Description

TPM performance						Commentary
OEE						
Definition see figure of this page (Tech-level performance segment)			Unit	Average		
E-5-124-L4	Loading = Scheduled Time / Calendar Time		%			
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> , usually 365 days, 8760 hours						
E-5-125-L4	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%			
E-5-126-L4	<i>Downtime</i> , of which setup, and cleaning The time spent for setup and cleaning as a percentage of the scheduled time		%			
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> , breakdowns (unplanned downtimes) + setup downtime						
E-5-127-L4	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%			
<i>Amount Produced</i> , the number of units produced during the time period <i>Ideal Cycle Time</i> , the designed or optimum cycle time <i>Available Time</i> , the time the machine actually ran: scheduled time - downtime						
E-5-128-L4	(OEE) Quality = (Input - Defects) / Input		%			
<i>Input</i> , the number of units that were started through the process <i>Defects</i> , the number of defective units (even if they were subsequently salvaged)						
E-5-129-L4	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%	n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-5-130a-e-L4	Changeover time	Time in <i>minutes</i> spent between different SKUs for setting up and cleaning the equipment.	Minutes					
Line characteristics								Commentary
E-5-122-L5	Line Number (auto-generated)		5					
E-5-123-L5	Line Description							
TPM performance								Commentary
OEE								
E-5-124-L5	Definition see figure of this page (Tech-level performance segment)		Unit		Average			
E-5-124-L5	Loading = Scheduled Time / Calendar Time		%					
E-5-125-L5	<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours							
E-5-125-L5	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-5-126-L5	<i>Downtime</i> , of which <i>setup</i> , and <i>cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time		%					
E-5-127-L5	<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime							
E-5-127-L5	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
E-5-128-L5	<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime							
E-5-128-L5	(OEE) Quality = (Input - Defects) / Input		%					
E-5-129-L5	<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)							
E-5-129-L5	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			
JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-5-130a-e-L5	Changeover time	Time in <i>minutes</i> spent between different SKUs for setting up and cleaning the equipment.	Minutes					

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove Primary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics					Commentary
E-5-131-L1	Line Number (auto-generated)		1		
E-5-132-L1	Line Description				
TPM performance					Commentary
OEE					
Definition see figure of this page (Tech-level performance segment)		Unit		Average	
E-5-133-L1	Loading = Scheduled Time / Calendar Time		%	10%	
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours					
E-5-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%	10%	
E-5-135-L1	<i>Downtime</i> , of which <i>setup</i> , and <i>cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time		%	10%	
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime					
E-5-136-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%	10%	
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime					
E-5-137-L1	(OEE) Quality = (Input - Defects) / Input		%	10%	
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)					
E-5-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%	0%	

Appendix

JIT Performance								Commentary	
Changeovers		Unit	Min	Average	Median	Max	SD		
E-5-139a-e-L3	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes						
E-5-158-a-e-L3		Country change	Minutes						
E-5-159-a-e-L3		Format change	Minutes						
E-5-160-a-e-L3		Product change	Minutes						
Line characteristics								Commentary	
E-5-131-L4	Line Number (auto-generated)		4						
E-5-132-L4	Line Description								
TPM performance								Commentary	
OEE		Unit		Average					
Definition see figure of this page (Tech-level performance segment)									
E-5-133-L4	Loading = Scheduled Time / Calendar Time		%						
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours									
E-5-134-L4	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-5-135-L4	<i>Downtime of which setup and cleaning</i> : The time spent for setup and cleaning as a percentage of the scheduled time		%						
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : (breakdowns (unplanned downtime) + setup downtime)									
E-5-136-L4	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%						
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime									
E-5-137-L4	(OEE) Quality = (Input - Defects) / Input		%						
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)									
E-5-138-L4	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				
JIT Performance								Commentary	
Changeovers		Unit	Min	Average	Median	Max	SD		
E-5-139a-e-L4	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes						
E-5-158-a-e-L4		Country change	Minutes						
E-5-159-a-e-L4		Format change	Minutes						
E-5-160-a-e-L4		Product change	Minutes						
Line characteristics								Commentary	
E-5-131-L5	Line Number (auto-generated)		5						
E-5-132-L5	Line Description								
TPM performance								Commentary	
OEE		Unit		Average					
Definition see figure of this page (Tech-level performance segment)									
E-5-133-L5	Loading = Scheduled Time / Calendar Time		%						
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours									
E-5-134-L5	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-5-135-L5	<i>Downtime of which setup and cleaning</i> : The time spent for setup and cleaning as a percentage of the scheduled time		%						
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : (breakdowns (unplanned downtime) + setup downtime)									
E-5-136-L5	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%						
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime									
E-5-137-L5	(OEE) Quality = (Input - Defects) / Input		%						
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)									
E-5-138-L5	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-5-139a-e-L5	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-5-158-a-e-L5	Country change		Minutes					
E-5-159-a-e-L5	Format change		Minutes					
E-5-160-a-e-L5	Product change		Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

[Add a Secondary Packaging Line](#)[Remove Secondary Packaging a Line](#)

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics					Commentary
E-5-140-L1	Line Number (auto-generated)	1			
E-5-141-L1	Line Description				
TPM performance					
OEE		Unit	Average		
Definition see figure of this page (Tech-level performance segment)					
E-5-142-L1	Loading = Scheduled Time / Calendar Time	%	10%		
	<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours				
E-5-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%	10%		
E-5-144-L1	Downtime of which, changeovers The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time	%	10%		
	<i>Scheduled Time</i> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> = breakdowns (unplanned downtimes) + setup downtime				
E-5-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%	10%		
	<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime				
E-5-146-L1	(OEE) Quality = (Input - Defects) / Input	%	10%		
	<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)				
E-5-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%	0%		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-5-148a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-5-149a-e-L1	Country change		Minutes					
E-5-150a-e-L1	Format change		Minutes					
	Product change		Minutes					

[proceed](#)

Technology: Drug Product - Sterile Liquids

Please select the process steps and sub-steps/descriptors that you carry out at your site:

Formulation	Filtering / Sterilization	Filling & Capping	Lyophilization	Terminal Sterilization	Visual Inspection	Secondary Packaging
☐ Liquid	☐ Filtering ☐ Thermal ☐ Radiation ☐ Other	☐ Large vials ☐ Small vials ☐ Syringes ☐ Pre-filled syringes ☐ Amps ☐ Pens ☐ Bags	☐ Freeze-drying ☐ None	☐ Thermal ☐ Radiation ☐ Other	☐ Automated ☐ Manual	
Note: Primary Packing refers to packing into vials, syringes, amps etc. Note: Secondary Packing refers to packing those vials, syringes etc. into boxes with leaflets						

F Formulation

PP Primary Packaging

SP Secondary Packaging

1: Cost and Structural KPIs

Production structure			Unit	Measure
Indicate the total volume of bulk goods that was produced at your site in the last year.				
E-6-02	Total		Litres	
Indicate the total volume of bulk goods packed (Primary Packaging) at your site in the last year.				
E-6-03	Total		Million Units	
E-6-04	-- thereof packed in syringes / pre-filled syringes		Million Units	
E-6-05	-- thereof packed in vials		Million Units	
E-6-06	-- thereof packed in amps		Million Units	
E-6-07	-- thereof packed in pens, auto-injectors & cartridges		Million Units	
E-6-08	-- thereof packed in bags		Million Units	
Indicate the total volume of bulk goods packed (Secondary Packaging) at your site in the last year.				
E-6-12	Total		Million Packs	
Average packaging size				
E-6-13-1	Average millilitres per packed syringe / pre-filled syringe (Primary Packaging)		Millilitres	
E-6-13-2	Average millilitres per packed vial (Primary Packaging)		Millilitres	
E-6-13-3	Average millilitres per packed amp (Primary Packaging)		Millilitres	
E-6-13-4	Average millilitres per packed pen / auto-injector / cartridge (Primary Packaging)		Millilitres	
E-6-13-5	Average millilitres per packed bag (Primary Packaging)		Millilitres	
E-6-09	Average units per packed boxes (Secondary Packaging)		Units	

Complexity Comments

Please highlight here the key drivers of complexity in your operation. In your opinion (comments will be reported without editing)

E-6-151	

Batch & campaign structure in the last year				
	Formulation	PP	SP	
E-6-17a-c	Number of batches / lots produced in the last year			
E-6-18	Number of campaigns in the last year			
E-6-152a-c	Number of machine hours operated in the last year			
	Min	Median	Max	
E-6-19a-c	Formulation batch size range (in litres)			
E-6-20a-c	Primary Packaging lot size range (in units)			
E-6-21a-c	Secondary Packaging lot size range (in units)			

Age of production technology in the last year				
	Unit	Formulation	PP	SP
E-6-22a-c	Total number of machines	Number		
E-6-23a-c	Percentage of machines which are less than 3 years old	%		
E-6-24a-c	Percentage of machines that are between 3 and 5 years old	%		
E-6-25a-c	Percentage of machines that are between 6 and 10 years old	%		
E-6-26a-c	Percentage of machines that are between 11 and 15 years old	%		
E-6-27a-c	Percentage of machines that are older than 15 years	%		

Level of automation in the last year				
	Unit	Formulation	PP	SP
E-6-28a-c	Percentage of machines that are manually operated	%		
E-6-29a-c	Percentage of machines that are operated with IT-support	%		
E-6-30a-c	Percentage of machines that are fully automated (without supervision/ from a control room)	%		

Number of products in the last year				
	Unit	Formulation	PP	SP
E-6-31a-c	Number of different drug substances / bulks / blends produced at your plant	Number		
E-6-32a-c	Number of different SDUs produced at your plant	Number		
E-6-33a-c	Number of different SKUs produced at your plant	Number		

Cost structure in the last year					Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.					
	Unit	Formulation	PP	SP	
E-6-34a-c	thousand	n/a	n/a	n/a	
E-6-35a-c	thousand	n/a	n/a	n/a	
E-6-36a-c	thousand				
E-6-37a-c	thousand				
E-6-38a-c	thousand				
E-6-39a-c	thousand				
E-6-153a-c	thousand				
E-6-40a-c	thousand				
E-6-41a-c	thousand				
E-6-154a-c	thousand				
E-6-43a-c	thousand				
E-6-44a-c	thousand				
E-6-45a-c	thousand				
E-6-46a-c	thousand				
E-6-47a-c	thousand				
E-6-48a-c	thousand				
E-6-49a-c	thousand				
E-6-50a-c	thousand				
E-6-51a-c	thousand				
E-6-52a-c	thousand				
E-6-53a-c	thousand				

Specific Cost Items					Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.					
	Unit	Formulation	PP	SP	
E-6-54a-c	thousand				
E-6-55a-c	thousand				
E-6-56a-c	thousand				
E-6-57a-c	%				
E-6-58a-c	thousand				
E-6-59a-c	thousand				

Headcount structure					Commentary
Please include all FTEs working at your plant on this technology independent from being on your payroll					
	Formulation	PP	SP	TOTAL	
E-6-60a-d	n/a	n/a	n/a	n/a	
E-6-61a-d					
E-6-62a-d					
E-6-63a-d	n/a	n/a	n/a	n/a	
E-6-64a-d					
E-6-65a-d					
E-6-66a-d					
E-6-67a-d					
E-6-68a-d					
E-6-69a-d	n/a	n/a	n/a	n/a	

2: Technology Level Performance KPIs

TPM performance										Comments									
Metric				Performance				Primary Packaging				Secondary Packaging				Tertiary Packaging			
Item	Definition	Unit		Average	Median			Average	Median			Average	Median						
E-6-70a	Setup and Cleaning	The total time spent for setup and cleaning as a percentage of total scheduled time	%																
E-6-71a	Dedicated equipment	The percentage of total equipment that is dedicated to one product	%																
E-6-72a	Equipment maintenance	Proportion of equipment maintenance work as a percentage of the overall time spent by maintenance teams	%																
E-6-73a	Shifts/week	Number of shifts per day	Number	Mon-Fri	Sat	Sun		Mon-Fri	Sat	Sun		Mon-Fri	Sat	Sun					
E-6-74a	Shift length	Average length of one shift in hours	Hours																
E-6-75a	Line staffing	FTEs per shift	Number																
OEE				Definition and Scope of this topic				Average				Average				Average			
E-6-76a-c	Loading = Scheduled Time / Calendar Time	%																	
Availability = Time during which the equipment was scheduled or available (not under repair) / Calendar Time				Availability = (Availability - (Scheduled Time - Downtime)) / Scheduled Time															
E-6-76a-d	Availability = (Availability - (Scheduled Time - Downtime)) / Scheduled Time	%																	
Performance = (Amount Produced x Ideal Cycle Time) / Available time				Performance = (Amount Produced x Ideal Cycle Time) / Available time															
E-6-80a	Performance = (Amount Produced x Ideal Cycle Time) / Available time	%																	
Quality = (Input - Defects) / Input				Quality = (Input - Defects) / Input															
E-6-81a-c	Quality = (Input - Defects) / Input	%																	
Overall Equipment Effectiveness = (OEE) / Availability x (OEE) / Performance x (OEE) / Quality				Overall Equipment Effectiveness = (OEE) / Availability x (OEE) / Performance x (OEE) / Quality															
E-6-82a	Overall Equipment Effectiveness = (OEE) / Availability x (OEE) / Performance x (OEE) / Quality	%																	

Calendar time									
Unscheduled time		Scheduled time							
Downtime		Available time							
Lost time		Total lost time							
Lost time		Average (Scheduled) x Capacity factor							
Lost time		Quality factor							
Lost time		Value added cost							
Lost time		Operating cost							
Loading		OEE	Availability	OEE	Performance	OEE	Quality		

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Comments		
E-6-122-L1	Line Number (auto-generated)	1							
E-6-123-L1	Line Description								
TPM performance								Comments	
OEE									
Definition see figure of this page (Tech-level performance segment)			Unit		Average				
E-6-124-L1	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									
E-6-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-6-126-L1	Downtime, of which setup and cleaning The time spent for setup and cleaning as a percentage of the scheduled time		%						
Scheduled Time - time during which the equipment was scheduled or expected to operate during the time period being analyzed Downtime - the machine unplanned downtime + setup downtime									
E-6-127-L1	(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									
E-6-128-L1	(OEE) Quality = (Input - Defects) / Input		%						
Input - the number of units that were started through the process Defects - the number of defective units given if they were subsequently salvaged									
E-6-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				
JIT Performance								Comments	
Changeovers			Unit	Min	Average	Median	Max		SD
E-6-130a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes	1			1		

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove Primary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics									
E-6-131-L1	Line Number (auto-generated)		1						
E-6-132-L1	Line Description								
TPM performance									
OEE									
Definition see figure of this page (Tech-level performance segment)			Unit		Average				Comments
E-6-133-L1	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									
E-6-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-6-135-L1	Downtime, of which setup and cleaning The time spent for setup and cleaning as a percentage of the scheduled time		%						
Scheduled Time - time during which the equipment was scheduled or expected to operate during the time period being analyzed Downtime - the sum of unplanned downtime + setup downtime									
E-6-136-L1	(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									
E-6-137-L1	(OEE) Quality = (Input - Defects) / Input		%						
Input - the number of units that were started through the process Defects - the number of defective units given if they were subsequently salvaged									
E-6-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L1		Country change	Minutes					
E-6-159-a-e-L1		Format change	Minutes					
E-6-160-a-e-L1		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L2	Line Number (auto-generated)		2					
E-6-132-L2	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
Definition see figure of this page (Tech-level performance segment)								
E-6-133-L2	Loading = Scheduled Time / Calendar Time		%					
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> , usually 365 days, 8760 hours								
E-6-134-L2	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L2	<i>Downtime of which setup, and cleaning</i>	The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> , breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L2	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<i>Amount Produced</i> , the number of units produced during the time period <i>Ideal Cycle Time</i> , the designed or optimum cycle time <i>Available Time</i> , the time the machine actually ran: scheduled time - downtime								
E-6-137-L2	(OEE) Quality = (Input - Defects) / Input		%					
<i>Input</i> , the number of units that were started through the process <i>Defects</i> , the number of defective units (even if they were subsequently salvaged)								
E-6-138-L2	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			
JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L2	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L2		Country change	Minutes					
E-6-159-a-e-L2		Format change	Minutes					
E-6-160-a-e-L2		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L3	Line Number (auto-generated)		3					
E-6-132-L3	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
Definition see figure of this page (Tech-level performance segment)								
E-6-133-L3	Loading = Scheduled Time / Calendar Time		%					
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> , usually 365 days, 8760 hours								
E-6-134-L3	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L3	<i>Downtime of which setup, and cleaning</i>	The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> , time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> , breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L3	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<i>Amount Produced</i> , the number of units produced during the time period <i>Ideal Cycle Time</i> , the designed or optimum cycle time <i>Available Time</i> , the time the machine actually ran: scheduled time - downtime								
E-6-137-L3	(OEE) Quality = (Input - Defects) / Input		%					
<i>Input</i> , the number of units that were started through the process <i>Defects</i> , the number of defective units (even if they were subsequently salvaged)								
E-6-138-L3	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			

Appendix

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L1		Country change	Minutes					
E-6-159-a-e-L1		Format change	Minutes					
E-6-160-a-e-L1		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L2	Line Number (auto-generated)		2					
E-6-132-L2	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
E-6-133-L2	Definition see figure of this page (Tech-level performance segment)							
E-6-133-L2	Loading = Scheduled Time / Calendar Time		%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours								
E-6-134-L2	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L2	<i>Downtime of which setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time		%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L2	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime								
E-6-137-L2	(OEE) Quality = (Input - Defects) / Input		%					
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)								
E-6-138-L2	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			
JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L2	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L2		Country change	Minutes					
E-6-159-a-e-L2		Format change	Minutes					
E-6-160-a-e-L2		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L3	Line Number (auto-generated)		3					
E-6-132-L3	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
E-6-133-L3	Definition see figure of this page (Tech-level performance segment)							
E-6-133-L3	Loading = Scheduled Time / Calendar Time		%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours								
E-6-134-L3	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L3	<i>Downtime of which setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time		%					
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L3	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime								
E-6-137-L3	(OEE) Quality = (Input - Defects) / Input		%					
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)								
E-6-138-L3	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L3	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L3		Country change	Minutes					
E-6-159-a-e-L3		Format change	Minutes					
E-6-160-a-e-L3		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L4	Line Number (auto-generated)			4				
E-6-132-L4	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
Definition see figure of this page (Tech-level performance segment)								
E-6-133-L4	Loading = Scheduled Time / Calendar Time		%					
<u>Scheduled Time</u> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Calendar Time</u> : usually 365 days, 8760 hours								
E-6-134-L4	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L4	<u>Downtime, of which setup and cleaning</u>	The time spent for setup and cleaning as a percentage of the scheduled time	%					
<u>Scheduled Time</u> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Downtime</u> : breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L4	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<u>Amount Produced</u> : the number of units produced during the time period <u>Ideal Cycle Time</u> : the designed or optimum cycle time <u>Available Time</u> : the time the machine actually ran: scheduled time - downtime								
E-6-137-L4	(OEE) Quality = (Input - Defects) / Input		%					
<u>Input</u> : the number of units that were started through the process <u>Defects</u> : the number of defective units (even if they were subsequently salvaged)								
E-6-138-L4	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			
JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L4	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L4		Country change	Minutes					
E-6-159-a-e-L4		Format change	Minutes					
E-6-160-a-e-L4		Product change	Minutes					
Line characteristics								Commentary
E-6-131-L5	Line Number (auto-generated)			5				
E-6-132-L5	Line Description							
TPM performance								Commentary
OEE		Unit		Average				
Definition see figure of this page (Tech-level performance segment)								
E-6-133-L5	Loading = Scheduled Time / Calendar Time		%					
<u>Scheduled Time</u> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Calendar Time</u> : usually 365 days, 8760 hours								
E-6-134-L5	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%					
E-6-135-L5	<u>Downtime, of which setup and cleaning</u>	The time spent for setup and cleaning as a percentage of the scheduled time	%					
<u>Scheduled Time</u> : time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Downtime</u> : breakdowns (unplanned downtimes) + setup downtime								
E-6-136-L5	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%					
<u>Amount Produced</u> : the number of units produced during the time period <u>Ideal Cycle Time</u> : the designed or optimum cycle time <u>Available Time</u> : the time the machine actually ran: scheduled time - downtime								
E-6-137-L5	(OEE) Quality = (Input - Defects) / Input		%					
<u>Input</u> : the number of units that were started through the process <u>Defects</u> : the number of defective units (even if they were subsequently salvaged)								
E-6-138-L5	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a			

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-139a-e-L5	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-158-a-e-L5		Country change	Minutes					
E-6-159-a-e-L5		Format change	Minutes					
E-6-160-a-e-L5		Product change	Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line

Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics					Commentary
E-6-140-L1	Line Number (auto-generated)	1			
E-6-141-L1	Line Description				
TPM performance					
OEE					
Definition see figure of this page (Tech-level performance segment)		Unit		Average	
E-6-142-L1	Loading = Scheduled Time / Calendar Time	%			
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Calendar Time</i> : usually 365 days, 8760 hours					
E-6-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%			
E-6-144-L1	<u>Downtime of which changeovers</u> The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time	%			
<i>Scheduled Time</i> : time during which the equipment was <i>scheduled or expected to operate</i> during the time period being analyzed <i>Downtime</i> : breakdowns (unplanned downtimes) + setup downtime					
E-6-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%			
<i>Amount Produced</i> : the number of units produced during the time period <i>Ideal Cycle Time</i> : the designed or optimum cycle time <i>Available Time</i> : the time the machine actually ran: scheduled time - downtime					
E-6-146-L1	(OEE) Quality = (Input - Defects) / Input	%			
<i>Input</i> : the number of units that were started through the process <i>Defects</i> : the number of defective units (even if they were subsequently salvaged)					
E-6-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%	n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-6-148a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-6-149a-e-L1		Country change	Minutes					
E-6-150a-e-L1		Format change	Minutes					
		Product change	Minutes					

proceed

Technology: Drug Product - Non-Sterile Liquids

Please select the process steps and sub-steps/descriptors that you carry out at your site.

Note: Primary Packing refers to packing into vials, syringes, amps etc.
Note: Secondary Packing refers to packing those vials, syringes etc. into boxes with leaflets

Commentary

1: Cost and Structural KPIs

E-7-13-4[illegible]E 7.151E 7.21a.e[illegible]E-7-26a-c
E-7-27

Commentary

Appendix

Level of automation in the last year					Commentary
	Unit	Formulation	PP	SP	
E-7-28a-c	Percentage of machines that are manually operated	%			
E-7-29a-c	Percentage of machines that are operated with IT-support	%			
E-7-30a-c	Percentage of machines that are fully automated (without supervision/ from a control room)	%			
Number of products in the last year					Commentary
	Unit	Formulation	PP	SP	
E-7-31a-c	Number of different drug substances / bulks / blends produced at your plant	Number			
E-7-32a-c	Number of different SDUs produced at your plant	Number			
E-7-33a-c	Number of different SKUs produced at your plant	Number			
Cost structure in the last year					Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.					
	Unit	Formulation	PP	SP	
E-7-34a-c	Conversion and Material costs 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. (Cost of Goods Sold)	thousand	n/a	n/a	n/a
E-7-35a-c	Conversion Costs Labor + plant, property + equipment, write-offs, other	thousand	n/a	n/a	n/a
	Material costs (inc. cost of API)	thousand			
E-7-36a-c	Direct material costs	thousand			
E-7-37a-c	Indirect material costs	thousand			
	Labor costs	thousand			
E-7-38a-c	Direct labor costs	thousand			
E-7-39a-c	thereof overtime costs	thousand			
E-7-153a-c	thereof contractor spend	thousand			
E-7-40a-c	Indirect labor costs	thousand			
E-7-41a-c	thereof overtime costs	thousand			
E-7-154a-c	thereof contractor spend	thousand			
	Plant, property and equipment costs	thousand			
E-7-43a-c	Costs for machines & tools	thousand			
E-7-44a-c	thereof depreciation, amortisation (CAPEX)	thousand			
E-7-45a-c	Costs for property and plant	thousand			
E-7-46a-c	thereof depreciation, amortisation (CAPEX)	thousand			
E-7-47a-c	Capex Investment Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)	thousand			
	Other costs	thousand			
E-7-48a-c	Corporate allocations	thousand			
E-7-49a-c	Other costs	thousand			
	Inventory write-off costs	thousand			
E-7-50a-c	Write-off costs due to shelf-life expiry	thousand			
E-7-51a-c	Write-off costs due to handling damages/losses	thousand			
E-7-52a-c	Write-off costs due to poor quality/out of spec	thousand			
E-7-53a-c	Write-off costs due to other reasons	thousand			
Specific Cost Items					Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.					
	Unit	Formulation	PP	SP	
E-7-54a-c	Maintenance costs	thousand			
E-7-55a-c	Thereof preventive maintenance (Planned & condition-based activities)	thousand			
E-7-56a-c	QA and QC cost	thousand			
E-7-57a-c	Percentage of quality cost due to outsourced quality activities	%			
E-7-58a-c	Rework cost	thousand			
E-7-59a-c	Destruction cost (excl. write-offs)	thousand			
Headcount structure					Commentary
Please include all FTEs working at your plant on this technology independent from being on your payroll					
	Formulation	PP	SP	TOTAL	
E-7-60a-d	Direct labor	n/a	n/a	n/a	n/a
E-7-61a-d	FTE in Production				n/a
E-7-62a-d	FTE in Quality Control (e.g. QC lab testing, in-process testing)				n/a
E-7-63a-d	Indirect labor	n/a	n/a	n/a	n/a
E-7-64a-d	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)				n/a
E-7-65a-d	FTE in Quality Assurance				n/a
E-7-66a-d	FTE in Maintenance				n/a
E-7-67a-d	FTE in Supply Chain				n/a
E-7-68a-d	FTE in other functions				n/a
E-7-69a-d	Overall number of FTEs working on this technology	n/a	n/a	n/a	n/a

Customer time									
Unstructured time		Structured time							
		Diverse time		Available time					
- Preparation - Management - Marketing (PR & Social) - Client support - Business development - Bookkeeping - Other overhead		Spaced issues		Not on time					
				Personal/professional/leisure time					
		- Urgent issues - Urgent project projects - Urgent issues - Urgent issues - Urgent issues - Urgent issues - Urgent issues		Quality issues		Value added and working time			
Loading		(G01) Availability	(G02) Performance	(G03) Quality					

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics									
E-7-122-L1	Line Number (auto-generated)		1						
E-7-123-L1	Line Description								
TPM performance									
OEE									
	Definition see figure of this page (Tech-level performance segment)		Unit		Average				
E-7-124-L1	Loading = Scheduled Time / Calendar Time		%						
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours								
E-7-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-7-126-L1	<i>Downtime of which setup and cleaning</i> - The time spent for setup and cleaning as a percentage of the scheduled time		%						
	<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime								
E-7-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%						
	<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime								
E-7-128-L1	(OEE) Quality = (Input - Defects) / Input		%						
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)								
E-7-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				
JIT Performance									
Changeovers			Unit	Min	Average	Median	Max	SD	Commentary
-7-130a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes						

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove Primary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics					
E-7-131-L1	Line Number (auto-generated)		1		
E-7-132-L1	Line Description				
TPM performance					
OEE					
	Definition see figure of this page (Tech-level performance segment)	Unit		Average	
E-7-133-L1	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				
E-7-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%			
E-7-135-L1	Downtime of which setup and cleaning	%			
	The time spent for setup and cleaning as a percentage of the 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				
E-7-136-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%			

	<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime					
E-7-137-L1	(OEE) Quality = (Input - Defects) / Input	%				
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)					
E-7-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-7-139a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-7-158-a-e-L1		Country change	Minutes					
E-7-159-a-e-L1		Format change	Minutes					
E-7-160-a-e-L1		Product change	Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line	Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Commentary
E-7-140-L1	Line Number (auto-generated)		1				
E-7-141-L1	Line Description						
TPM performance							
OEE							
Definition see figure of this page (Tech-level performance segment)			Unit		Average		
E-7-142-L1	Loading = Scheduled Time / Calendar Time		%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-7-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%				
E-7-144-L1	<u>Downtime of which changeovers.</u> The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time		%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-7-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%				
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-7-146-L1	(OEE) Quality = (Input - Defects) / Input		%				
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-7-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-7-148a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-7-149a-e-L1		Country change	Minutes					
E-7-150a-e-L1		Format change	Minutes					
		Product change	Minutes					

proceed

Technology: Drug Product - Patches

Please select the process steps and sub-steps/descriptors that you carry out at your site:

The diagram illustrates the packaging process flow and options. The process flow is shown as a sequence of five steps in a green bar: **Formulation**, **Coating**, **Drying**, **Lamination**, and **Converting**. These steps lead to the final stage, **Secondary Packaging**, which is shown in an orange bar. Below the process flow, a table lists the options for each step:

Option	Formulation	Coating	Drying	Lamination	Converting	Secondary Packaging
☐ Liquid	☐ Reservoir					
☐ Semi-solid	☐ Matrix					
	☐ DIA ¹					
	☐ Multi-laminate DIA					

Note: Secondary Packaging refers to packing patches into boxes with leaflets

Commentary

1: Cost and Structural KPIs

Production structure		
	Unit	Measure
E-0-02	Indicate the total volume of bulk goods that was produced at your site in the last year.	
	Total	Pieces
E-0-03	Indicate the total volume of bulk goods packed (Secondary Packing) at your site in the last year.	
	Total	Million Packs
F-0-04	Average packing size	
	Average inside packed boxes (Secondary Packaging)	Pieces

Commentary

Complexity Comments	
Please highlight here the key drivers of complexity in your operation, in your opinion (comments will be reported without editing)	
E-8-151	

Batch & campaign structure in the last year				
			Formulation	SP
E-8-17a-b	Number of batches / lots produced in the last year			
E-8-18	Number of campaigns in the last year			
E-8-152a-b	Number of machine hours operated in the last year			
		Min	Median	Max
E-8-19a-c	Formulation batch size range (in pieces)			
E-8-20a-c	Packaging lot size range (g/gm/pt)			

[illegible]

Age of production technology in the last year				
		Unit	Formulation	SP
E-5-22a-b	Total number of machines	Number		
E-5-23a-b	Percentage of machines which are less than 3 years old	%		
E-5-24a-b	Percentage of machines that are between 3 and 5 years old	%		
E-5-25a-b	Percentage of machines that are between 6 and 10 years old	%		
E-5-26a-b	Percentage of machines that are between 11 and 15 years old	%		
E-5-27a-b	Percentage of machines that are older than 15 years	%		

[illegible]

Level of automation in the last year		Unit	Formulation	SP
E-8-28a-b	Percentage of machines that are manually operated	%		
E-8-29a-b	Percentage of machines that are operated with IT-support	%		
E-8-30a-b	Percentage of machines that are fully automated (without supervision/ from a control room)	%		

Commentary

Number of products in the last year				
		Unit	Formulation	SP
E-8-31a-b	Number of different drug substances / bulks / blends produced at your plant	Number		
E-8-32a-b	Number of different SDUs produced at your plant	Number		
E-8-33a-b	Number of different SKUs produced at your plant	Number		

Commentary

Appendix

Cost structure in the last year				Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.				
	Unit	Formulation	SP	
E-8-34a-b	thousand	n/a	n/a	
COGS (Cost of Goods Sold) Conversion and Material costs 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.				
E-8-35a-b	thousand	n/a	n/a	
Conversion Costs Labor + plant, property + equipment, write-offs, other				
Material costs (inc. cost of API)				
E-8-36a-b	thousand			
E-8-37a-b	thousand			
Labor costs				
E-8-38a-b	thousand			
E-8-39a-b	thousand			
E-8-153a-c	thousand			
E-8-40a-b	thousand			
E-8-41a-b	thousand			
E-8-154a-c	thousand			
Plant, property and equipment costs				
E-8-43a-b	thousand			
E-8-44a-b	thousand			
E-8-45a-b	thousand			
E-8-46a-b	thousand			
E-8-47a-b	thousand			
Capex Investment Total capex investment in the last financial year (note that this will double-count with the depreciation figures above)				
Other costs				
E-8-48a-b	thousand			
E-8-49a-b	thousand			
Inventory write-off costs				
E-8-50a-b	thousand			
E-8-51a-b	thousand			
E-8-52a-b	thousand			
E-8-53a-b	thousand			

Specific Cost Items				Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.				
	Unit	Formulation	SP	
E-8-54a-b	thousand			
E-8-55a-b	thousand			
E-8-56a-b	thousand			
E-8-57a-b	%			
E-8-58a-b	thousand			
E-8-59a-b	thousand			

Headcount structure				Commentary
Please include				
	Formulation	SP	TOTAL	
E-8-60a-c	n/a	n/a	n/a	
E-8-61a-c			n/a	
E-8-62a-c			n/a	
E-8-63a-c	n/a	n/a	n/a	
E-8-64a-c			n/a	
E-8-65a-c			n/a	
E-8-66a-c			n/a	
E-8-67a-c			n/a	
E-8-68a-c			n/a	
E-8-69a-c	n/a	n/a	n/a	

2: Technology Level Performance KPIs

TPM performance				Performance								Commentary
Name	Definition	Unit		Average	Median			Average	Median			
E-6-70a-4	Setup and Changeover The total time spent for setup and changing as a percentage of total scheduled time	%										
E-6-71a-4	Dedicated equipment The percentage of your equipment that is dedicated to one product	%										
E-6-72a-4	Unplanned maintenance Proportion of unplanned maintenance work as a percentage of the overall time spent for maintenance works	%										
E-6-75a-4	Shifts Number of shifts per day	Unit	Mon - Fri	Sat	Sun			Mon - Fri	Sat	Sun		
E-6-76a-4	Shift length Average length of one shift in hours	Hours										
E-6-77a-4	Line staffing FTEs per shift	Number										
OEE			Definition see figure of this page		Unit	Average		Average				
E-6-78a-4	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 24x7 days, 8760 hours												
E-6-79a-4	(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 = downtime (unplanned downtime) + setup downtime												
E-6-80a-4	(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 design or optimum cycle time Available Time = the time the machine actually ran: scheduled time - downtime												
E-6-81a-4	(OEE) Quality = (Input - Defects) / Input	%										
Good = the number of units that were shipped through the process Defects = the number of defect or units (even if they were reworked) scrapped												
E-6-82a-4	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%			n/a				n/a			
Calendar time												
Unscheduled time												
Scheduled time												
Downtime				Available time								
Losses included: • Prevention • Maintenance • Realign / Post breaks • Setup, changing • Downtime • Breakdowns • Changeover / Material				Speed losses Not run time Amount produced / cycle time								
Losses included: • Minor defects • Scrap and production • Rework • Defective product • Total losses				Quality losses Value added net operating time								
Loading				(OEE) Availability	(OEE) Performance	(OEE) Quality						

Appendix

TQM performance										Inventory management										Commentary
Name		Definition	Unit	Min	Average	Median	Max	SD							Min	Average	Median	Max	SD	
E-8-83a	Yield	Real achieved output in pharmaceutical production (input minus material losses, weighing, sediments etc.)	%																	
E-8-84a	Release time	Average time from sampling to release of finished products including all waiting times	Working days																	
E-8-85a	Deviations	Number of deviations per month that arise from new materials purchased, production components (equipment) and product process specifications	Number per month																	
E-8-86a	Deviation closure time	Average deviation closure time in days	Working days																	
Name <th>Definition</th> <th>Unit</th> <th colspan="5">Formulation</th> <th colspan="5">Inventory management</th> <th colspan="5">Inventory management</th>		Definition	Unit	Formulation					Inventory management					Inventory management						
Recurring Deviations		Percentage of deviations per month that were more than once (i.e. repeating/recurring deviations)	%											Average	Median					
E-8-105a	CPQs	Average CPQ score across the top 5 products	Number																	
E-8-87a	Complaint rate (customer)	Number of justified complaints as a percentage of all customer orders delivered	%																	
E-8-88a	Complaint rate (supplier)	Number of complaints as a percentage of all deliveries received (from your supplier)	%																	
E-8-89a	RFT	Total number of batches produced without document errors or exception reports as a percentage of the total number of batches produced	%																	
E-8-90a	Rejected batches	Number of rejected batches as a percentage of all batches produced	%																	
E-8-91a	Mean time between failure	Average time between breakdowns	Hours																	
E-8-92a	Scrap rate	Average difference between 100% and real achieved output in packaging operations	%																	
E-8-93a	Number of tests	Number of quality tests per month	Number per month																	
E-8-107a	CTQ	Is "Critical to Quality" analysis utilized? (Yes/No)	Yes/No																	

OT Performance										Inventory management										Commentary
Name		Definition	Unit	Min	Average	Median	Max	SD							Min	Average	Median	Max	SD	
E-8-94a	Order lead time	Time between a customer placing an order and receiving delivery	Working days																	
E-8-95a	Production lead time	Time in days from start of production (SOP) to release of finished products	Working days	n/a	n/a	n/a	n/a	n/a						n/a	n/a	n/a	n/a	n/a		
E-8-96a	— Internal Waiting time	Sum of waiting times, for example during set-up, or before and after QA/QC	Working days																	
E-8-97a	— Internal Production time	Value adding time of the production process not including set-up time or waiting time in between two separate steps	Working days																	
E-8-98a	— External QA/QC	If different release tests have to be performed it also includes waiting in	Working days																	
E-8-99a	Replenishment 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																	
Name <th>Definition</th> <th>Unit</th> <th>Min</th> <th>Average</th> <th>Median</th> <th>Max</th> <th>SD</th> <th colspan="6"></th> <th>Average</th> <th>Median</th> <th colspan="3"></th>		Definition	Unit	Min	Average	Median	Max	SD							Average	Median				
E-8-100a	Days on hand (DOH)	Average inventory less with stock > 30% divided by the Cost of Goods Sold (COGS)	Days																	
E-8-101a	Service level - delivery (OTF)	Perfect order fulfillment (percentage of orders shipped in time from your site (< 1 days of the agreed shipment day) and in the right quantity (i.e. 3% of the agreed quantity) and right quality) to your customer	%																	
E-8-102a	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 (i.e. 3% of the agreed quantity) and right quality) from your supplier	%																	
E-8-103a	Forecast accuracy	Actual orders received compared to the agreed order forecast	%																	
E-8-104a	Production schedule adherence	Number of released production orders as scheduled as a percentage of all production orders released within your heating period	%																	
E-8-105a	Priority orders	Number of priority orders as a percentage of all orders produced	%																	
E-8-106a	Production freeze period	Freezing period in which you do not allow any changes of your production schedule	Working days																	
E-8-107a	Number of stockouts	Number of out-of-stock events per month	Number per month																	
E-8-108a	Cycle time	Cycle time e.g. 30% of all products have a cycle time of 15-30 days, 10% of all products have a cycle time of more than 30 days	< 15 days 15-30 days > 30 days																	
E-8-109a	Raw material turns	Annual cost of raw materials purchased divided by the average raw material inventory	Number																	
E-8-110a	WIP turns	Annual cost of raw materials purchased plus annual cost of conversion divided by the average work in process inventory	Number																	
E-8-113a	Finished goods turns	Annual cost of goods sold divided by the average finished goods inventory	Number																	
Changeovers										Inventory management										
Name		Definition	Unit	Min	Average	Median	Max	SD							Min	Average	Median	Max	SD	
E-8-114a	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment	Minutes																	
E-8-115a	Country change	Country change	Minutes																	
E-8-116a	Format change	Format change	Minutes																	
E-8-117a	Product change	Product change	Minutes																	
E-8-118a	Number of Changeovers	Average number of changeovers performed per month including changing lots and changing formulae	Number																	
E-8-119a	Country change	Country change	Number																	
E-8-120a	Format change	Format change	Number																	
E-8-121a	Product change	Product change	Number																	

3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Commentary
E-8-122-L1	Line Number (auto-generated)	1					
E-8-123-L1	Line Description						
TPM performance							
OEE							
Definition see figure of this page (Tech-level performance segment)		Unit		Average			
E-8-124-L1	Loading = Scheduled Time / Calendar Time	%					
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours							
E-8-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time	%					
E-8-126-L1	<i>Downtime of which setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time	%					
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime							
E-8-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%					
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime							
E-8-128-L1	(OEE) Quality = (Input - Defects) / Input	%					
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)							
E-8-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a			
JIT Performance							
Changeovers		Unit	Min	Average	Median	Max	SD
-8-130a-e-L1	Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment.	Minutes				

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line

Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							Commentary		
E-8-140-L1	Line Number (auto-generated)					1			
E-8-141-L1	Line Description								
TPM performance									
OEE									
Definition see figure of this page (Tech-level performance segment)					Unit				
E-8-142-L1	Loading = Scheduled Time / Calendar Time				%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours									
E-8-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time				%				
E-8-144-L1	<u>Downtime</u> , of which, <u>changeovers</u> The time spent between different SKUs for setting up and cleaning the equipment as a percentage of the scheduled time				%				
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime									

Appendix

E-8-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time	%			
	<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime				
E-8-146-L1	(OEE) Quality = (Input - Defects) / Input	%			
	<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)				
E-8-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality	%		n/a	

JIT Performance							Commentary
Changeovers		Unit	Min	Average	Median	Max	
Changeover time	Time in minutes spent between different SKUs for setting up and cleaning the equipment	Minutes					
E-8-148a-e-L1	Country change	Minutes					
E-8-149a-e-L1	Format change	Minutes					
E-8-150a-e-L1	Product change	Minutes					

proceed

Technology: Drug Product - Inhalers

Please select the process steps and sub-steps/descriptors that you carry out at your site:

	Weighting / Mixing	Granulation	Sieving	Drying	Primary Packaging	Inspection	Inhaler assembly	Secondary Packaging
E-9-01a-h								
E-9-01b-1-2	☐ Wet	☐ Wet				☐ Auto	☐ 3rd party inhalers	
E-9-01c-1-2	☐ Dry	☐ Dry				☐ Manual	☐ Manufactured inhalers	
E-9-01f-1-2								
E-9-01g-1-2								

Note: Primary Packaging refers to packing into inhalers.
Note: Secondary Packaging refers to packing inhalers into boxes with leaflets

F Formulation
 PP Primary Packaging
 SP Secondary Packaging

Commentary

1: Cost and Structural KPIs

Production structure			Unit	Measure
Indicate the total volume of bulk goods that was produced at your site in the last year.				
E-9-02	Total		KG	
E-9-02-1	- thereof for aerosol-based inhaler production		%	
E-9-02-2	- thereof for powder-based inhaler production		%	
Indicate the total volume of bulk goods packed (Primary Packaging) at your site in the last year.				
E-9-03	Total		Millions Units	
Indicate the total volume of bulk goods packed (Secondary Packaging) at your site in the last year.				
E-9-12	Total		Million Packs	
Average packaging size				
E-9-13-1	Average KG per piece (Primary Packaging)		KG	
E-9-04	Average units per packed boxes (Secondary Packaging)		Units	

Commentary

Complexity Comments
Please highlight here the key drivers of complexity in your operation, in your opinion (comments will be reported without editing)

E-9-151

Batch & campaign structure in the last year			Formulation	PP	SP
E-9-17a-c	Number of batches / lots produced in the last year				
E-9-18	Number of campaigns in the last year				
E-9-152a-c	Number of machine hours operated in the last year				
		Min	Median	Max	
E-9-19a-c	Formulation batch size range (in KG)				
E-9-20a-c	Primary Packaging lot size range (in units)				
E-9-21a-c	Secondary Packaging lot size range (in				

Commentary

Age of production technology in the last year			Unit	Formulation	PP	SP
E-9-22a-c	Total number of machines		Number			
E-9-23a-c	Percentage of machines which are less than 3 years old		%			
E-9-24a-c	Percentage of machines that are between 3 and 5 years old		%			
E-9-25a-c	Percentage of machines that are between 6 and 10 years old		%			
E-9-26a-c	Percentage of machines that are between 11 and 15 years old		%			
E-9-27a-c	Percentage of machines that are older than 15 years		%			

Commentary

Level of automation in the last year			Unit	Formulation	PP	SP
E-9-28a-c	Percentage of machines that are manually operated		%			
E-9-29a-c	Percentage of machines that are operated with IT-support		%			
E-9-30a-c	Percentage of machines that are fully automated (without supervision/ from a control room)		%			

Commentary

Number of products in the last year			Unit	Formulation	PP	SP
E-9-31a-c	Number of different drug substances / bulks / blends produced at your plant		Number			
E-9-32a-c	Number of different SDUs produced at your plant		Number			
E-9-33a-c	Number of different SKUs produced at your plant		Number			

Commentary

Appendix

Cost structure in the last year						Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the General Information sheet.						
		Unit	Formulation	PP	SP	
E-9-34a-c	COGS (Cost of Goods Sold)	thousand	n/a	n/a	n/a	
E-9-35a-c	Conversion Costs	thousand	n/a	n/a	n/a	
E-9-36a-c	Material costs (inc. cost of API)	thousand				
E-9-37a-c	Direct material costs	thousand				
	Indirect material costs	thousand				
	Labor costs	thousand				
E-9-38a-c	Direct labor costs	thousand				
E-9-39a-c	thereof overtime costs	thousand				
E-9-153a-c	thereof contractor spend	thousand				
E-9-40a-c	Indirect labor costs	thousand				
E-9-41a-c	thereof overtime costs	thousand				
E-9-154a-c	thereof contractor spend	thousand				
	Plant, property and equipment costs	thousand				
E-9-43a-c	Costs for machines & tools	thousand				
E-9-44a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-9-45a-c	Costs for property and plant	thousand				
E-9-46a-c	thereof depreciation, amortisation (CAPEX)	thousand				
E-9-47a-c	Capex	thousand				
	Other costs	thousand				
E-9-48a-c	Corporate allocations	thousand				
E-9-49a-c	Other costs	thousand				
	Inventory write-off costs	thousand				
E-9-50a-c	Write-off costs due to shelf-life expiry	thousand				
E-9-51a-c	Write-off costs due to handling damages/losses	thousand				
E-9-52a-c	Write-off costs due to poor quality/out of spec	thousand				
E-9-53a-c	Write-off costs due to other reasons	thousand				

Specific Cost Items						Commentary
Figures should refer to the last financial year, and should be reported in local currency. Please see the local currency section on the Corporate Level sheet.						
		Unit	Formulation	PP	SP	
E-9-54a-c	Maintenance costs	thousand				
E-9-55a-c	Thereof preventive maintenance (Planned & condition-based activities)	thousand				
E-9-56a-c	QA and QC cost	thousand				
E-9-57a-c	Percentage of quality cost due to outsourced quality activities	%				
E-9-58a-c	Rework cost	thousand				
E-9-59a-c	Destruction cost (excl. write-offs)	thousand				

Headcount structure						Commentary
Please include all FTEs working at your plant on this technology independent from being on your payroll						
		Formulation	PP	SP	TOTAL	
E-9-60a-d	Direct labor	n/a	n/a	n/a	n/a	
E-9-61a-d	FTE in Production				n/a	
E-9-62a-d	FTE in Quality Control (e.g. QC lab testing, in-process testing)				n/a	
E-9-63a-d	Indirect labor	n/a	n/a	n/a	n/a	
E-9-64a-d	FTE in Quality Control (e.g. Incoming inspection, QC equipment maintenance)				n/a	
E-9-65a-d	FTE in Quality Assurance				n/a	
E-9-66a-d	FTE in Maintenance				n/a	
E-9-67a-d	FTE in Supply Chain				n/a	
E-9-68a-d	FTE in other functions				n/a	
E-9-69a-d	Overall number of FTEs working on this technology	n/a	n/a	n/a	n/a	

		Calendar time			
Unscheduled time			Scheduled time		
	Down time		Available time		
	Losses included Prevention Maintenance Losses due to material Labelings / Plant losses Energy efficiency Cleaning Repairs Working material / labor		Spared losses Losses included Effect losses Energy and production Repairing Reduced products		Start run time Amount produced / cycle time
			Quality losses Losses included Start-up losses Defective product Rejected products		Value added net operating time
Loading	QOE / Availability	QOE / Performance	QOE / Quality	QOE / Quality	

Appendix

TQM performance										Customer satisfaction										Complaints									
Metric										Metric										Metric									
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3A: Line Level Performance KPIs - Formulation

Add a Formulation Line

Remove a Formulation Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics									
E-9-122-L1	Line Number (auto-generated)		1						
E-9-123-L1	Line Description								
TPM performance									
OEE									
Definition see figure of this page (Tech-level performance segment)			Unit		Average				
E-9-124-L1	Loading = Scheduled Time / Calendar Time		%						
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Calendar Time</i> - usually 365 days, 8760 hours									
E-9-125-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%						
E-9-126-L1	<i>Downtime of which setup and cleaning</i> The time spent for setup and cleaning as a percentage of the scheduled time		%						
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <i>Downtime</i> - breakdowns (unplanned downtimes) + setup downtime									
E-9-127-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%						
<i>Amount Produced</i> - the number of units produced during the time period <i>Ideal Cycle Time</i> - the designed or optimum cycle time <i>Available Time</i> - the time the machine actually ran: scheduled time - downtime									
E-9-128-L1	(OEE) Quality = (Input - Defects) / Input		%						
<i>Input</i> - the number of units that were started through the process <i>Defects</i> - the number of defective units (even if they were subsequently salvaged)									
E-9-129-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a				
JIT Performance									
Changeovers			Unit	Min	Average	Median	Max	SD	Commentary
-9-130a-e-L1	Changeover time	Time in minutes spent between different time intervals	Minutes						

3B: Line Level Performance KPIs - Primary Packaging

Add a Primary Packaging Line

Remove a Primary Packaging Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics					
E-9-131-L1	Line Number (auto-generated)		1		
E-9-132-L1	Line Description				
TPM performance					
OEE					
Definition see figure of this page (Tech-level performance segment)			Unit		Average
E-9-133-L1	Loading = Scheduled Time / Calendar Time		%		
<i>Scheduled Time</i> - time during which the equipment was scheduled or expected to operate during the time period being analyzed					
<i>Calendar Time</i> - usually 365 days, 8760 hours					

					Commentary

E-9-134-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%			
E-9-135-L1	<u>Downtime of which setup, and cleaning</u>	The time spent for setup and cleaning as a percentage of the scheduled time	%			
	<u>Scheduled Time</u> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Downtime</u> - breakdowns (unplanned downtimes) + setup downtime					
E-9-136-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%			
	<u>Amount Produced</u> - the number of units produced during the time period <u>Ideal Cycle Time</u> - the designed or optimum cycle time <u>Available Time</u> - the time the machine actually ran: scheduled time - downtime					
E-9-137-L1	(OEE) Quality = (Input - Defects) / Input		%			
	<u>Input</u> - the number of units that were started through the process <u>Defects</u> - the number of defective units (even if they were subsequently salvaged)					
E-9-138-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a	

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-9-139a-e-L1	Changeover time	Time in <i>minutes</i> spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-9-158-a-e-L1		Country change	Minutes					
E-9-159-a-e-L1		Format change	Minutes					
E-9-160-a-e-L1		Product change	Minutes					

3C: Line Level Performance KPIs - Secondary Packaging

Add a Secondary Packaging Line

Remove Secondary Packaging a Line

NB: By 'Line' we mean a scheduling unit (e.g. granulator, encapsulator, packaging machine)
Please add a high-performing, low-performing and an average-performing line from your site.

Line characteristics							
E-9-140-L1	Line Number (auto-generated)	1					
E-9-141-L1	Line Description						
TPM performance							Commentary
OEE							
	Definition see figure of this page (Tech-level performance segment)		Unit		Average		
E-9-142-L1	Loading = Scheduled Time / Calendar Time		%				
	<u>Scheduled Time</u> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Calendar Time</u> - usually 365 days, 8760 hours						
E-9-143-L1	(OEE) Availability = (Scheduled Time - Downtime) / Scheduled Time		%				
E-9-144-L1	<u>Downtime of which changeovers</u>	The time spent between different SKUs for setting up and clearing the equipment as a percentage of the scheduled time	%				
	<u>Scheduled Time</u> - time during which the equipment was scheduled or expected to operate during the time period being analyzed <u>Downtime</u> - breakdowns (unplanned downtimes) + setup downtime						
E-9-145-L1	(OEE) Performance = (Amount Produced x Ideal Cycle Time) / Available time		%				
	<u>Amount Produced</u> - the number of units produced during the time period <u>Ideal Cycle Time</u> - the designed or optimum cycle time <u>Available Time</u> - the time the machine actually ran: scheduled time - downtime						
E-9-146-L1	(OEE) Quality = (Input - Defects) / Input		%				
	<u>Input</u> - the number of units that were started through the process <u>Defects</u> - the number of defective units (even if they were subsequently salvaged)						
E-9-147-L1	Overall Equipment Effectiveness = (OEE) Availability x (OEE) Performance x (OEE) Quality		%		n/a		

JIT Performance								Commentary
Changeovers		Unit	Min	Average	Median	Max	SD	
E-9-148a-e-L1	Changeover time	Time in <i>minutes</i> spent between different SKUs for setting up and cleaning the equipment.	Minutes					
E-9-149a-e-L1		Country change	Minutes					
E-9-150a-e-L1		Format change	Minutes					
		Product change	Minutes					

A.4 Questionnaire – QC Lab Benchmarking



Benchmarking in the Pharmaceutical Industry for Quality Control Labs

The Project

Since 2004, the Institute of Technology Management at the University of St. Gallen (ITEM-HSG), Switzerland is conducting an international benchmarking 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 2016 ITEM-HSG introduced a new benchmarking that aims for an analysis of Quality Control Labs in pharmaceutical companies in order to enable the participating companies to position their Quality Control Lab against a broad range of other pharmaceutical companies.

Your Commitment

Your participation is vital to the success of this unique study. Filling out the questionnaire takes about 30 minutes. The time to collect the data (e.g. performance indicators) differs from company to company.

Your Benefits

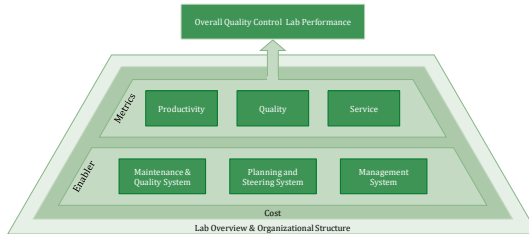
The questionnaire has been developed in cooperation with leading pharmaceutical companies under supervision of Prof. Dr. Thomas Friedli. This will help you to position your lab on the basis of our database.

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 utmost 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 the benchmarking framework that is the basis for the questionnaire structure



How to complete the form:

Please enter the figures for the respective metric.* All metrics should be average values for the year the data is collected for.

* If you are unable to provide a figure, please insert "n/a".

If you have any questions regarding the project please contact

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To the
questionnaire

General Information

Please provide some general information of your company below.

A01

Last Name

A02

First Name

A03

Position or Role

A04

Company Name

A05

Benchmarking Lab

A06

Country Lab is situated

A07

Telephone

A08

Email

A09

Address

Please fill in the year your data is collected for. This should always match a full calendar year (e.g. 2016).

A10

Year

Please chose which currency you use for filling in this questionnaire from the dropdown menu below.

A11

Currency

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CXXVIII

Lab Overview			
Lab Type / Technologies			
Please indicate for which technologies/products your QC Lab is performing tests for:			
Drug Substance			
B014	Chemicals (API)	☐ Yes ☐ No	
B016	Biologics	☐ Yes ☐ No	
Formulation, Filling and/or Packaging (Primary and Secondary)			
B010	Solids	☐ Yes ☐ No	
B013	Creams	☐ Yes ☐ No	
B014	Suppositories	☐ Yes ☐ No	
B011	Sterile liquids	☐ Yes ☐ No	
B019	Non-Sterile liquids	☐ Yes ☐ No	
B015	Patches	☐ Yes ☐ No	
B017	Inhalers	☐ Yes ☐ No	
Lab Focus			
Please indicate what kind of purpose your QC Lab has.			
B024	☐	Multi-purpose lab (If more than one DP or DS is tested, please consider yourself as a multi-purpose lab)	
B025	☐	Low volume lab	
B026	☐	High volume lab	
Lab Role			
Please indicate the degree of centralization of the QC Lab.			
B034	☐	Our lab is only responsible to conduct testing for the site where the lab is located.	
	☐	Our lab is responsible to conduct testing for multiple sites.	
If the lab is responsible to conduct testing for multiple sites, please indicate to what degree this lab does testing for other sites.			
B036	Proportion of tests for other sites to overall number of tests within QC Lab.	Unit	Figure
		%	
Mutual Recognition Agreement (MRA)			
Please indicate if you do re-testing for batches produced in another country with no MRA in place and thus batches from these countries must undergo batch re-testing.			
B044	☐	Yes, batch re-testing is done at our QC Lab for our own production in a third-country.	
	☐	No, batch re-testing is done by another company (CMO re-testing) or another location of our company.	
If yes, please indicate to what degree in-country batch re-testing is conducted.			
B046	Proportion of batch re-testing to overall amount of testing within QC Lab.	Unit	Figure
		%	
Regulatory Approval			
Please indicate if your lab has regulatory approval. Regulatory approval means any approvals by health authorities in a country or organization (e.g. FDA).			
B054	☐	Food & Drug Administration (FDA)	
B055	☐	European Medicines Agency (EMA)	
B056	☐	Pharmaceuticals and Medical Devices Agency in Japan (PMDA)	
B057	☐	China Food and Drug Administration (CFDA)	
B058	☐	World Health Organization (WHO)	
B059	☐	Other approval, please specify below	
Age of Testing Methods			
Please indicate if new testing methods (not an update of an existing methods) have been introduced to the lab. All categories below should sum up to 100%.			
B064	Testing methods which were introduced less than 3 years ago	Unit	Figure
		%	
B065	Testing methods which were introduced between 3 and 5 years ago	Unit	Figure
		%	
B066	Testing methods which were introduced between 6 and 10 years ago	Unit	Figure
		%	
B067	Testing methods which were introduced more than 10 years ago	Unit	Figure
		%	
Active vs. Inactive Testing Methods			

Appendix

Please indicate the proportion of active methods that are regularly used in your lab. Inactive methods are those methods that are still in the system but are not used anymore (e.g. due to expiration, termination of products tested with this method).			
		Unit	Figure
B07	Proportion of active methods that are regularly used within QC Lab	%	
Age of Equipment			
Please indicate the age of your lab equipment. All categories below should sum up to 100%.			
B08a	Lab instruments which are less than 3 years old	%	
B08b	Lab instruments which are between 3 and 5 years old	%	
B08c	Lab instruments which are between 5 and 10 years old	%	
B08d	Lab instruments which are more than 10 years old	%	
Level of Automation			
Please indicate the level of automation in your lab. Please include instruments in sample preparation as well as testing. All categories below should sum up to 100%.			
B09a	Percentage of instruments that are manually operated (supervision at any time is needed)	%	
B09b	Percentage of instruments that are operated with IT-support (temporary supervision is sufficient)	%	
B09c	Percentage of instruments that are fully automated (without supervision)	%	
No. of Products tested & Countries filed			
Please indicate the total number of products tested and the number of countries that your lab runs tests for (e.g. one product tested with two different methods and/or specifications for country specific regulatory = 2).			
B10a	Total number of products tested	No.	
B10b	Total number of countries filed	No.	
FTE Structure			
Please include all FTEs working on your site, in your Quality Control Lab and your Quality Assurance department (on-site & network) independent from being on your payroll. If you are unable to provide a figure please insert "n/a".			
	Name	Definition	Unit
			Figure
Total Site FTEs			
B11a	Site Permanent FTEs	Number of permanent site FTEs.	No.
B11b	Site Temporary FTEs	Number of temporary site FTEs.	No.
B11c		Total	n/a
Quality Control (QC) FTEs			
B12a	QC Permanent FTEs	Number of permanent Quality Control FTEs.	No.
B12b	QC Temporary FTEs	Number of temporary Quality Control FTEs.	No.
B12c		Total	n/a
Quality Assurance (QA) FTEs			
Site Level			
Site Level includes all QA FTE that are <u>on-site</u> , supporting <u>on-site</u> QA activities.			
B13a	QA Permanent FTEs	Number of permanent Quality Assurance FTEs.	No.
B13b	QA Temporary FTEs	Number of temporary Quality Assurance FTEs.	No.
B13c		Total	n/a
Network Level On-Site			
Network Level On-Site includes all QA FTE that are <u>on-site</u> , supporting <u>off-site</u> QA activities.			
B14a	QA Permanent FTEs	Number of permanent Quality Assurance FTEs.	No.
B14b	QA Temporary FTEs	Number of temporary Quality Assurance FTEs.	No.
B14c		Total	n/a
Network Level Off-Site			
Network Level Off-Site includes all QA FTE that are <u>off-site</u> , supporting <u>on-site</u> QA activities.			
B15a	QA Permanent FTEs	Number of permanent Quality Assurance FTEs.	No.
B15b	QA Temporary FTEs	Number of temporary Quality Assurance FTEs.	No.
B15c		Total	n/a

Lab Volumes			
Please include all processed batches independent from where these batches were produced and if batches were actually tested (e.g. number of batches from other sites that are processed at your lab should be included)			
316	Drug Substance Batches	Total number of drug substance batches processed in the last year.	No.
317	Intermediate Batches	Total number of intermediate batches processed in the last year.	No.
318	Raw Material Batches	Total number of raw material batches processed in the last year.	No.
319	Stability Batches	Total number of stability batches processed in the last year.	No.
320	Drug Product Batches	Total number of drug product batches (completed all processing stages up to, but not incl. final packaging) processed in the last year.	No.
321	Packaged Product Batches	Total number of packaged product batches processed in the last year.	No.
322	Component & Packaging Material Batches Receipts	Total number of component & packaging material batches receipts in the last year.	No.
323	Total		n/a

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Appendix

Organizational Structure				
Please fill in the respective figures below. If you are unable to provide a figure please insert "n/a".				
Name		Definition	Unit	Figure
General metrics				
C01	Span of Control	Number of employees to supervisors (employees directly reporting to this supervisor).	No.	
C02	Reporting Layers	Number of management levels from analyst to the highest ranking quality manager at the site (e.g. Worker - Supervisor - Manager of the department - Quality Head = 4 Levels)	No.	
C03	Qualified Technicians	Employees with prior work related qualification in your lab as a percentage of all lab employees (e.g. trained/certified employees at previous company who do not require re-training in your organization). If your organization does re-train certified employees = 0 %)	%	
C04	Employees Fluctuation	Employees leaving your lab due to personal reasons, terminations, expired work contracts, retirements etc. as a percentage of all lab employees.	%	
C05	Cross-trained Analysts	Proportion of employees to total lab employees that are cross-trained in order to conduct various type of tests and tasks within the lab.	%	
C06	Group Work	Percentage of lab employees that are organized in teams in order to facilitate day-to-day work more efficient.	%	
C07	Training	Number of training days per lab employee (all kinds of training off- and on the job) in the last year.	Days	
C08	Sick Leave	Total time of employees absent (e.g. sick leave, maternity leave) as a percentage of the total working time.	%	
C09	Number of Suppliers for Consumables	Number of suppliers for consumables.	No.	
QC Direct FTE Structure				
Direct employees are all those employee that are doing directly batch-related work (e.g. testing analysis). Full-time equivalent (FTE) allows part-time workers' working hours to be standardized against those working full-time. The standardized figure is 1.0, which refers to a full-time worker. 0.5 refers to an employee that works half full-time hours.				
C10a	Drug Substance Testing FTE	Number of direct drug substance testing FTEs.	No.	
C10b	Intermediate Testing FTE	Number of direct intermediate testing FTEs.	No.	
C10c	In Process Control Testing FTE	Number of direct IPC testing FTEs.	No.	
C10d	Raw Material Testing FTE	Number of direct raw material testing FTEs.	No.	
C10e	Stability Testing FTE	Number of direct stability testing FTEs.	No.	
C10f	Drug Product Testing FTE	Number of direct drug product testing FTEs.	No.	
C10g	Packaged Product Testing FTE	Number of direct packaged product testing FTEs.	No.	
C10h	Microbial Environmental Testing FTE	Number of direct environmental testing FTEs.	No.	
C10i	Microbial Product Testing FTE	Number of direct microbial product testing FTEs.	No.	
C10j	Component & Packaging Testing FTE	Number of direct component & packaging testing FTEs.	No.	
C10k		Total	n/a	
QC Indirect FTE Structure				
Indirect employees are all those employee that are doing indirectly batch-related work (e.g. documentation). Full-time equivalent (FTE) allows part-time workers' working hours to be standardized against those working full-time. The standardized figure is 1.0, which refers to a full-time worker. 0.5 refers to an employee that works half full-time hours.				
C11a	Drug Substance Testing FTE	Number of indirect drug substance testing FTEs.	No.	
C11b	Intermediate Testing FTE	Number of indirect intermediate testing FTEs.	No.	
C11c	In Process Control Testing FTE	Number of indirect IPC testing FTEs.	No.	
C11d	Raw Material Testing FTE	Number of indirect raw material testing FTEs.	No.	
C11e	Stability Testing FTE	Number of indirect stability testing FTEs.	No.	
C11f	Drug Product Testing FTE	Number of indirect drug product testing FTEs.	No.	
C11g	Packaged Product Testing FTE	Number of indirect packaged product testing FTEs.	No.	
C11h	Microbial Environmental Testing FTE	Number of indirect environmental testing FTEs.	No.	
C11i	Microbial Product Testing FTE	Number of indirect microbial product testing FTEs.	No.	
C11j	Component & Packaging Material Testing FTE	Number of indirect component material testing FTEs.	No.	
C11k	Management & Administration FTE	Number of QC management & administration FTEs.	No.	
C11l	Analytical Development FTE	Number of analytical development FTEs.	No.	
C11m	Other QC FTE	Number of other QC FTEs.	No.	
C11n		Total	n/a	

QA FTE Structure			
Site Level			
<i>Site Level includes all QA FTE that are <u>on-site</u>, supporting <u>on-site</u> QA activities.</i>			
212a	Validation FTE	Number of validation FTEs (e.g. method validation, equipment validation, process validation).	No.
212b	Batch Disposition FTE	Number of batch disposition FTEs (incl. batch record review).	No.
212c	Quality Compliance and Auditing FTE	Number of quality compliance and auditing FTEs.	No.
212d	Quality Systems FTE	Number of quality systems FTEs (e.g. responsible for Annual Product Quality Reviews, Stability Reports, Change Controls.)	No.
212e	Management & Administration FTE	Number of QA management & administration FTEs.	No.
212f	Other QA FTE	Number of other QA FTEs.	No.
212g	Total		n/a
Network Level On-Site			
<i>Network Level On-Site includes all QA FTE that are <u>on-site</u>, supporting <u>off-site</u> QA activities.</i>			
213a	Quality Compliance and Auditing FTE	Number of quality compliance and auditing FTEs.	No.
213b	Quality Systems FTE	Number of quality systems FTEs.	No.
213c	Management & Administration FTE	Number of QA management & administration FTEs.	No.
213d	Total		n/a
Network Level Off-Site			
<i>Network Level Off-Site includes all QA FTE that are <u>off-site</u>, supporting <u>on-site</u> QA activities.</i>			
214a	Quality Compliance and Auditing FTE	Number of quality compliance and auditing FTEs.	No.
214b	Quality Systems FTE	Number of quality systems FTEs.	No.
214c	Management & Administration FTE	Number of QA management & administration FTEs.	No.
214d	Total		n/a
Overtime			
215a	QC	Proportion of spent overtime hours to total hours in QC.	%
215b	QA	Proportion of spent overtime hours to total hours in QA.	%
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Comment			

Enabler						
Please rate to what degree your lab fulfills the enablers below.						
Question	1	2	3	4	5	Don't know
Maintenance & Quality System						
Preventive Maintenance						
D1	To what degree is there a formal program for maintaining your lab equipment?	There is no formal maintenance program	Formal program exists but is not widely visible	Formal program exists and is visible but is adhered to unevenly	Formal program is regularly adhered to but not regularly updated	Formal program strictly adhered to and updated regularly
		☐	☐	☐	☐	☐
D2	To what degree are maintenance jobs (e.g. calibration programs) documented, and maintenance plans and checklists posted close to instruments?	Jobs, plans, and checklists are not documented & posted	Jobs, plans, and checklists are rarely documented & posted	Jobs, plans, and checklists are sometimes documented & posted	Jobs, plans, and checklists are regularly documented & posted	Jobs, plans, and checklists are always documented & posted
		☐	☐	☐	☐	☐
D3	To what degree is potential bottleneck lab equipment identified and supplied with additional spare parts?	Bottleneck equipment is not identified	Bottleneck equipment is identified but not supplied with spare parts	Bottleneck equipment is supplied with spares, but unevenly across the lab	Bottleneck equipment is supplied with spare parts across the lab	Bottleneck analysis is regularly refreshed, and equipment supplied with spares
		☐	☐	☐	☐	☐
D4	To what degree is the maintenance program continuously optimized based on a dedicated failure analysis?	Dedicated failure analysis is not carried out	Dedicated failure analysis is carried out but not used to optimize maintenance	Failure analysis is used to optimize maintenance, but unevenly across the lab	Failure analysis is used to optimize the maintenance program across the lab	Regularly-refined failure analysis is used to optimize maintenance
		☐	☐	☐	☐	☐
D5	To what degree does the maintenance department focus on assisting analysts perform their own preventive maintenance?	Analysts receive no assistance relating to preventive maintenance	Analysts receive little assistance relating to preventive maintenance	Analysts receive some assistance relating to preventive maintenance	Analysts receive significant assistance relating to preventive maintenance	Analysts receive extensive assistance relating to preventive maintenance
		☐	☐	☐	☐	☐
D6	To what degree are analysts actively involved in the decision making process when buying new equipment?	Analysts are not involved in buying new equipment	Analysts are rarely consulted when buying new equipment	Analysts are sometimes consulted when buying new equipment	Analysts are regularly consulted when buying new equipment	Analysts are extensively involved in buying new equipment
		☐	☐	☐	☐	☐
D7	To what degree is your equipment maintained internally vs. externally?	<20% of maintenance is conducted internally	20% - 40% of maintenance is conducted internally	40% - 60% of maintenance is conducted internally	60% - 80% of maintenance is conducted internally	>80% of maintenance is conducted internally
		☐	☐	☐	☐	☐
D8	To what degree is your preventive maintenance effort focused on proactive activities rather than reactive activities?	<20% of activities are focused on proactive maintenance	20% - 40% of activities are focused on proactive maintenance	40% - 60% of activities are focused on proactive maintenance	60% - 80% of activities are focused on proactive maintenance	>80% of activities are focused on proactive maintenance
		☐	☐	☐	☐	☐
Technology Assessment & Usage						
D9	To what degree is the lab situated at the leading edge of new technology?	We do not seek to use leading edge technology	We rarely incorporate leading edge technology	We sometimes incorporate leading edge technology	We regularly incorporate leading edge technology	We seek to stay at the frontier of leading edge technology
		☐	☐	☐	☐	☐
D10	To what degree do you screen the market for new production technology and assess new technology concerning its technical and financial benefit?	We do not screen for and assess new technology	We rarely screen for and assess new technology	We sometimes screen for and assess new technology	We regularly screen for and assess new technology	We are always screening for and assessing new technology
		☐	☐	☐	☐	☐
D11	To what degree is the lab effectively using new technology?	We have not introduced new technology in the last 5 years	We are interested in improving technology but do not devote much capex to this	We seek to introduce new technology, and devote some capex to this	We seek to introduce new technology, and devote a significant portion of capex	Our lab is used to pilot new technology within our network
		☐	☐	☐	☐	☐
D12	To what degree does the lab rely on vendors for its equipment?	<20% of equipment from vendors	20% - 40% of equipment from vendors	40% - 60% of equipment from vendors	60% - 80% of equipment from vendors	>80% of equipment from vendors
		☐	☐	☐	☐	☐
D13	To what degree is proprietary process technology and equipment used to gain a competitive advantage?	We use off-the-shelf process technology and equipment	We buy equipment on the market and use it with minimal modification	We buy equipment on the market, and carry out some modification as needed	We buy equipment on the market, and continuously modify to suit our needs	We build equipment to fit our needs - if it doesn't exist on the market we build it
		☐	☐	☐	☐	☐
D14	To what degree do you put an emphasis on smart lab system implementation?	We do not put an emphasis on smart lab system implementation	We put little emphasis on smart lab system implementation	We put some emphasis on smart lab system implementation	We put emphasis on smart lab system implementation but rarely review new smart solutions	We put remarkable emphasis on smart lab system implementation and regularly review new smart solutions
		☐	☐	☐	☐	☐
Housekeeping						

D15	To what degree do employees strive to keep the lab neat and clean?	Housekeeping is not a core part of our improvement initiatives	Housekeeping is a small part of our improvement initiatives	Housekeeping is a reasonable part of our improvement initiatives, and a part of our training program	Housekeeping is a significant part of our improvement initiatives and training program	Housekeeping is a core part of our improvement initiatives, and we perform regular audits	
		☐	☐	☐	☐	☒	
D16	To what degree are tools and consumables put in their place (e.g. usage of a shadow board)?	We do not have formal housekeeping procedures	Formal housekeeping procedures exist but are not widely visible	Formal housekeeping procedures exist and are visible, but are adhered to unevenly	Formal housekeeping procedures are adhered to across the lab	Regularly-updated formal housekeeping procedures are adhered to across the lab	
		☐	☐	☐	☐	☒	
D17	To what degree are housekeeping checklists used to continuously monitor the condition and cleanliness of our equipment?	We do not have housekeeping checklists	Housekeeping checklists exist but are not widely visible	Housekeeping checklists exist and are visible, but are adhered to unevenly	Housekeeping checklists are adhered to across the lab	Regularly-updated housekeeping checklists are adhered to across the lab	
		☐	☐	☐	☐	☒	
D18	To what degree do you do a regular review of the "As-is" situation (e.g. by doing a walkthrough) in your lab in order to identify potential improvement areas (e.g. by doing a gap analysis)?	We do not do a regular review of the "As-is" situation	We rarely do a review of the "As-is" situation	We sometimes do a review of the "As-is" situation	We regularly do a review of the "As-is" situation but do not always use tools to identify improvement areas	We regularly do a review of the "As-is" situation and use tools to identify improvement areas	
		☐	☐	☐	☐	☒	
Process Management							
D19	To what degree are direct and indirect processes documented?	Documentation does not exist	Documentation exists but is not widely visible	Documentation exists and is visible but is enforced unevenly	Documentation is regularly enforced but not regularly updated	Documentation strictly enforced and updated regularly	
		☐	☐	☐	☐	☒	
D20	To what degree is process quality continually measured using process metrics?	No clear definition of metrics	Few clearly defined metrics, but no regular usage	Some standardized metrics and occasional usage	Comprehensive set of standardized metrics and continuous usage	Comprehensive set of standardized metrics with leading and lagging indicators and continuous usage	
		☐	☐	☐	☐	☒	
D21	To what degree are dedicated process owners defined and responsible for planning, managing, and improving their processes?	No dedicated process owners	Some ownership of processes	Dedicated process owners, but little responsibility attached	Dedicated process owners responsible for planning & management	Dedicated process owners responsible for planning, management and improvement	
		☐	☐	☐	☐	☒	
D22	What proportion of the equipment in the lab is currently under statistical process control (SPC)?	<20% of equipment	20% - 40% of equipment	40% - 60% of equipment	60% - 80% of equipment	>80% of equipment	
		☐	☐	☐	☐	☒	
D23	To what degree are standardized tools in place for root cause analysis, to get a deeper understanding of the influencing factors (e.g. DMAIC)?	No tools in place	Some tools in place but not standardized	Standardized tools in place, but used unevenly	Standardized tools used regularly	Standardized tools used regularly and a core part of training	
		☐	☐	☐	☐	☒	
Standardization and simplification							
D24	To what degree is standardization emphasized as a strategy for continuous improvement of lab processes and equipment?	We do not communicate standardization as part of our improvement program for the lab	Standardization is communicated but not emphasized in the lab	Standardization is emphasized, but unevenly across the processes and equipment	Standardization is emphasized across both processes and equipment, but not core to our improvement program	Standardization is core to our improvement program for both processes and equipment	
		☐	☐	☐	☐	☒	
D25	To what degree are documented operating procedures used to standardize processes (e.g. set-ups)?	Documentation does not exist	Documentation exists but is not used to drive adherence	Documentation exists and is visible but is adhered to unevenly	Documentation is regularly adhered to but not regularly updated	Documentation strictly adhered to and updated regularly	
		☐	☐	☐	☐	☒	
D26	To what degree are optimized lab operating procedures (e.g. shortened set-ups) documented as best-practice processes and rolled-out throughout the whole quality organization?	Best practice is not documented	Best practice is documented but not rolled-out	Best practice is documented and rolled-out unevenly across the quality organization	Best practice is shared across the quality organization, but not regularly	Best practice is shared across the quality organization regularly	
		☐	☐	☐	☐	☒	
D27	To what degree are standardized functional descriptions used to reduce the period of vocational training for new employees?	Standardized functional descriptions do not exist	Standardized functional descriptions exist but are not used in training	Standard functional descriptions inform training but do not reduce the period	Standard functional descriptions inform training and reduce the period a little	Standard functional descriptions inform training and reduce the period significantly	
		☐	☐	☐	☐	☒	
D28	To what degree are standardized lab equipment (e.g. standardized design, standardized spare parts) used to achieve a high up time of the equipment?	Equipment is not standardized	A minor part of the equipment is standardized	Some equipment is standardized	Most of the equipment is standardized	Equipment is standardized throughout the lab	
		☐	☐	☐	☐	☒	
D29	To what degree do you pursue lowering material costs with the help of standardized equipment (e.g. for spare parts) and standardized consumables?	Equipment and consumables are not standardized	Little standardization of equipment and consumables exists, but reduction of material costs is not measured	Some standardization of equipment and consumables exists, but does not reduce material costs	Use of standardized equipment and consumables reduces costs a little	Use of standardized equipment and consumables reduces costs significantly	
		☐	☐	☐	☐	☒	
Planning & Steering System							
Set-up reduction							
D30	To what degree do you continuously work to lower set-up and cleaning times in your lab?	We do not seek to continuously improve set-up and cleaning times	Continuously improving times is a small part of our improvement initiatives	Continuously improving times is a reasonable part of improvement initiatives	Continuously improving times is a significant part of our improvement initiatives	Continuously improving times is a core part of our improvement initiatives	
		☐	☐	☐	☐	☒	

Appendix

D31	To what degree do analysts practice set-ups to reduce the time required?	Analysts do not practice set-ups	Analysts rarely practice set-ups	Analysts sometimes practice set-ups	Analysts regularly practice set-ups	Analysts practice set-ups extensively	
		☐	☐	☐	☐	☐	
D32	What proportion of equipment set-ups are scheduled so that the testing process is not affected (e.g. to shorten lead time)?	<20% of set-ups	20% - 40% of set-ups	40% - 60% of set-ups	60% - 80% of set-ups	>80% of set-ups	
		☐	☐	☐	☐	☐	
D33	To what degree are optimized set-up and cleaning procedures documented as best-practices and rolled-out throughout the whole lab?	Best practices are not documented	Best practices are documented but not rolled-out	Best practices are documented and rolled-out unevenly across the lab	Best practices are shared across the whole lab, but not regularly	Best practices are shared across the whole lab regularly	
		☐	☐	☐	☐	☐	
Pull approach							
D34	Do you use a pull system (Kanban squares, containers or signals) for your consumables?	We do not use a pull system for our consumables and it is not planned to introduce it	We do not use a pull system for our consumables but we want to introduce it	We are currently introducing a pull system for all our consumables	We have a pull system in place for all our consumables	We have a pull system in place for all our consumables and continuously improving it	
		☐	☐	☐	☐	☐	
D35	To what degree do you test according to forecast?	We do not test according to forecast	We do little testing according to forecast	We do some of our test according to forecast	We do most of our test according to forecast to get maximum capacity utilization	We do most of our test according to forecast but still can react flexible to short-term changes	
		☐	☐	☐	☐	☐	
D36	To what degree do you have tools installed for a regular demand and FTE capacity analysis?	We have no instruments installed to analyze demand and FTE capacity and no intend to do it in the future	We do not have any instruments installed to analyze demand and FTE capacity but intend to do it soon	We are currently rolling-out instruments to analyze demand and FTE capacity	We have one instrument installed for demand analysis or FTE capacity analysis	We have instruments installed for both, demand analysis and FTE capacity analysis	
		☐	☐	☐	☐	☐	
Layout optimization							
D37	To what degree are your processes located close together so that material handling and consumable storage are minimized?	Related processes are not located close together	A minor part of related processes is located close together	Some related processes are located close together	Most related processes are located close together	Related processes are located close together across the whole lab	
		☐	☐	☐	☐	☐	
D38	What proportion of testing substances/products are classified into groups with similar processing requirements to reduce set-up times?	<20% of substances/products	20% - 40% of substances/products	40% - 60% of substances/products	60% - 80% of substances/products	>80% of substances/products	
		☐	☐	☐	☐	☐	
D39	To what degree does the layout of the lab facilitate low inventories and fast throughput?	Lab layout is not optimized for inventories and throughput	Layout is optimized in one or two parts of the lab	Layout is optimized in some parts of the lab	Layout is optimized in most parts of the lab	Layout is optimized across the lab	
		☐	☐	☐	☐	☐	
D40	To what degree can your lab layout be characterized as separated into "mini-labs", i.e. testing substances/products have been classified based on their specific requirements?	Layout does not resemble "mini-labs"	Layout resembles "mini-labs" in one or two parts of the lab	Layout resembles "mini-labs" in some parts of the lab	Layout resembles "mini-labs" in most parts of the lab	Layout resembles "mini-labs" across the lab	
		☐	☐	☐	☐	☐	
D41	To what degree does your testing processes from incoming testing material to release involve almost no interruptions and can be described as a full continuous flow?	Continuous flow is not a core part of our lab objective	Continuous flow is a small part of our lab objective	Continuous flow is a reasonable part of our lab objective	Continuous flow is a significant part of our lab objective	Continuous flow is a core part of our lab objective	
		☐	☐	☐	☐	☐	
D42	To what degree do you use "Value Stream Mapping" as a methodology to visualize and optimize processes?	VSM is not used	VSM is rarely used	VSM is sometimes used	VSM is regularly used	VSM is extensively used	
		☐	☐	☐	☐	☐	
Planning adherence							
D43	To what degree do you meet your daily lab testing plans?	<20% of days	20% - 40% of days	40% - 60% of days	60% - 80% of days	>80% of days	
		☐	☐	☐	☐	☐	
D44	To what degree do you know the root causes of variance in your lab working schedule and continuously try to eliminate them?	We do not have a clear view of root causes of variation	We have some view of the root causes, but do not work on eliminating them	We have a good view of the root causes, but unevenly work on eliminating them	We have a good view of the root causes and regularly work on eliminating them	We have a clear view of the root causes and continuously work on eliminating them	
		☐	☐	☐	☐	☐	
D45	To what degree does your lab have flexible working shift models in order to easily adjust labor capacity according to current demand changes?	We do not have flexible shift models	We have flexible shift models for a minor part of the employees in the lab	We have flexible shift models for some employees in the lab	We have flexible shift models for most employees in the lab	We have flexible shift models for all employees throughout the whole lab	
		☐	☐	☐	☐	☐	
D46	Beyond flexible working shifts, do you assign extra resources within the lab for testing during peak loads or do you outsource activities?	We don't have a clear strategy how to handle peak loads	We rarely follow one of the two objectives during peak loads	We do sometimes assign extra resources or outsource activities during peak loads	We regularly assign extra resources or outsource activities during peak loads	We are always assigning extra resources or outsource activities during peak loads	
		☐	☐	☐	☐	☐	
D47	To what degree do you prefer to increase productivity over short lead time or vice versa?	We don't have a clear strategy but are not the trade-off	We only follow one of the two objectives	We try to follow both objectives but are not very successful	We aim to find the optimal balance between increasing productivity and short lead time	We found the optimal balance between increasing productivity and short lead time	
		☐	☐	☐	☐	☐	
Visual management							

D48	To what degree do you utilize performance charts to show weekly/monthly/annual performance objective?	We do not utilize performance charts in the lab	Performance charts are used for a few processes only	Performance charts across most processes show objectives	Performance charts across all key processes show objectives	Regularly-updated charts across all key processes show objectives	
		☐	☐	☐	☐	☐	☒
D49	To what degree do you utilize charts showing the current performance status (e.g. current RFT rate) in your lab?	We do not utilize current performance charts in the lab	Performance charts are used for a few processes to show current KPIs	Performance charts across most processes show current KPIs	Performance charts across all key processes show current KPIs	Regularly-updated charts across all key processes show current KPIs	
		☐	☐	☐	☐	☐	☒
Management System							
Management commitment and company culture							
D50	To what degree does the head of quality and management empower employees to continuously improve processes and reduce failure?	Head of quality and management do not seek to empower lab employees	Head of quality and management promotes continuous improvement activity through other means	Head of quality and management seek to empower lab employees, but unevenly	Head of quality and management regularly seek to empower employees	Head of quality and management actively seek to empower all lab employees on a continuous basis	
		☐	☐	☐	☐	☐	☒
D51	To what degree are the head of quality and management personally involved in improvement projects?	Head of quality and management are not involved in improvement projects	Head of quality and management are involved in setting objectives for improvement, but no further	Head of quality and management are sometimes personally involved in improvement projects	Head of quality and management are regularly personally involved in improvement projects	Head of quality and management are personally involved in virtually all improvement projects	
		☐	☐	☐	☐	☐	☒
D52	To what degree does your site have an open communication culture, encourage the flow of information between the production and lab?	We always have trouble with communication between the production and lab	We often have trouble with communication between the production and lab	We sometimes have trouble with communication between the production and lab	We have an open communication culture enabling flow of info between the production and lab	We have an open communication culture, with a very good flow of info between the production and lab	
		☐	☐	☐	☐	☐	☒
D53	To what degree are problems (e.g. complaints) traced back to their origin to identify root causes?	We do not trace problems of this type to their origin	We rarely trace problems to their origin	We trace problems to their root cause if they repeat	We trace most problems to their root cause	We rigorously examine all problems, and identify root causes	
		☐	☐	☐	☐	☐	☒
D54	To what degree do you align the achievement of quality standards between production and QC/QA (e.g. shared responsibility or primarily the task of QA/QC)?	We do not seek to align the approach to achieve quality standards between production and QC/QA	We rarely align the approach to achieve quality standards between production and QC/QA	We sometimes seek to align the approach to achieve quality standards between production and QC/QA	We regularly align the approach to achieve quality standards between production and QC/QA	We always align the approach to achieve quality standards between production and QC/QA	
		☐	☐	☐	☐	☐	☒
D55	To what degree do your employees continuously strive to reduce waste in processes (e.g. waste of time, consumables)?	Waste reduction is not a core activity	Waste reduction is a focus for specialized employees only	Employees strive to reduce process waste in some processes	Employees strive to reduce process waste in most processes	Employees strive to reduce all kinds of waste in every process	
		☐	☐	☐	☐	☐	☒
D56	To what degree do you prefer improvement programs initiated and promoted by the site lab and not the global organization and vice versa?	We don't have a clear strategy how to handle this trade-off	We try to have both but initiatives are not aligned and not very successful	We aim to find a balance between corporate improvement programs and site improvement initiatives	We have a balance between corporate improvement programs and site improvement initiatives	We found the optimal balance between corporate improvement programs and site improvement initiatives	
		☐	☐	☐	☐	☐	☒
Employee involvement and continuous improvement							
D57	To what degree have you implemented tools and methods to deploy a continuous improvement process in your lab?	We do not have a continuous improvement program	Continuous improvement processes are not supported by tools	We have some tools and methods to support continuous improvement	We have multiple tools and methods to support continuous improvement	Comprehensive tools and training in place to support continuous improvement	
		☐	☐	☐	☐	☐	☒
D58	To what degree are your analysts involved in writing standard operating procedures (SOPs)?	Analysts are not involved in developing SOPs	Analysts are rarely consulted when developing SOPs	Analysts are sometimes consulted when developing SOPs	Analysts are regularly consulted when developing SOPs	Analysts are extensively involved in developing SOPs	
		☐	☐	☐	☐	☐	☒
D59	To what degree do lab employee actively drive suggestion programs (not excl. linked to a suggestion system in place)?	Employees do not actively drive suggestion programs	Employee engagement with suggestion programs is very limited	Employees are sometimes engaged in suggestion programs	Employees are actively engaged in suggestion programs	Employees are extensively involved in driving suggestion programs	
		☐	☐	☐	☐	☐	☒
D60	To what degree do your analysts have the authority to correct problems (e.g. with equipment, testing methods) when they occur without consulting a supervisor?	Problem solving is not carried out by analysts	Very few analysts have the authority to correct problems	Some analysts have the authority to correct problems	Most analysts have the authority to correct problems	Analysts have the authority to actively correct problems	
		☐	☐	☐	☐	☐	☒
D61	To what degree do supervisors focus on assisting analysts to perform their own problem solving?	Analysts receive no assistance relating to problem solving	Analysts receive little assistance relating to problem solving	Analysts receive some assistance relating to problem solving	Analysts receive significant assistance relating to problem solving	Analysts receive extensive assistance relating to problem solving	
		☐	☐	☐	☐	☐	☒
D62	To what degree does your site form cross-functional project teams to solve problems in your lab?	Our site does not utilize cross functional teams	Our site rarely utilizes cross functional teams	Our site sometimes utilizes cross functional teams	Our site regularly utilizes cross functional teams	Our site makes extensive use of cross functional teams	
		☐	☐	☐	☐	☐	☒
D63	To what degree does your lab follow a vision based approach to continuous improvement integrating constraints into the vision rather than an incremental approach?	We solely rely on incremental steps to continuous improvement	We mostly rely on incremental steps to continuous improvement	We follow a vision based approach with solely qualitative objectives	We follow a vision based approach with qualitative objectives integrating constraints into the vision	We follow a vision based approach with quantitative/measurable objectives integrating constraints into the vision	
		☐	☐	☐	☐	☐	☒

Appendix

D64	Does global quality organization have a lab certification program for best performing labs?	We don't have and are currently not planning to have a lab certification program ☐	We do not have a lab certification program but will launch it soon ☐	We are currently launching a lab certification program ☐	We have a lab certification program but once a lab is certified there is no review in place ☐	We have a lab certification program and continuously review the lab certificates ☐	☒
Functional integration and qualification							
D65	To what degree do you put emphasize on analysts cross-training to the required level so that they can fill-in for others when necessary?	We do not have cross-trained lab analysts ☐	We have too few cross-trained lab analysts ☐	We have some cross-trained lab analysts but less than the required level ☐	We have a high number of cross-trained lab analysts but less than the required level ☐	We have the optimal balance between cross-trained analysts and the required level ☐	☒
D66	To what degree is information and skill-evaluation from official feedback meetings used in further training?	The information is not used ☐	The information is used, but not in any broad program. Employees do <u>standard trainings</u> ☐	Some of the information is used in further trainings ☐	Most of the information is used in further trainings ☐	The information is used systematically in further training ☐	☒
D67	To what degree does your site invest in the training and qualification of your lab employees?	We do not invest in the training and qualification of our lab employees ☐	We invest a little in training, but do not offer qualifications for lab employees ☐	We have some trainings and offer one or two qualifications for lab employees ☐	We have a dedicated development and qualification program for lab employees ☐	We continuously seek to improve our dedicated training and qualification program for lab employees ☐	☒
D68	To what degree do your cross-trained analysts rotate on the job performing different tasks?	Our cross-trained analysts do not rotate ☐	Our cross-trained analysts rarely rotate ☐	Our cross-trained analysts sometimes rotate ☐	Our cross-trained analysts regularly rotate ☐	Our cross-trained analysts extensively rotate ☐	☒

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Comment

Productivity



Please fill in the respective figures below. If you are unable to provide a figure please insert 'n/a'.

Name	Definition	Unit	Figure

General metrics

101	Handled Samples	Total number of samples managed by lab (not necessarily tested but incl. e.g. sample splitting for shipment) in the reporting period.	No.	
102	Dedicated Equipment	Percentage of equipment that is dedicated to a specific product (e.g. drug product solids) that is tested.	%	
103	Equipment Utilization Rate	Ratio between output that is actually achieved with the installed equipment, and the potential output which could be achieved with it, if capacity was fully used.	%	
104	Number of samples per run	Number of different samples that can be tested together in one run due to same testing method (pooling).	No.	
105	Stock-time for Consumables	Number of days consumables are on stock before usage for testing (e.g. solvents, reagents, gloves, filters, etc.).	days	
106	SOPs	Number of Standard Operating Procedures (SOPs) or other formal written instructions (excluding the testing methods themselves) in the lab.	No.	

Tests

Number of individual sample items (test items) analyzed is equal to number of tests. Testing multiple sample items (test items) at the same time is counted as multiple tests. If you do a purity test that leads into 10 different results for impurity this is still only counted as one test.

107a	Drug Substance Tests	Number of drug substance tests in the reporting period.	No.	
107b	Intermediate Tests	Number of intermediate tests in the reporting period.	No.	
107c	In Process Control Tests	Number of in process control tests in the reporting period.	No.	
107d	Raw Material Tests	Number of raw material tests in the reporting period.	No.	
107e	Stability Tests	Number of stability tests in the reporting period.	No.	
107f	Drug Product Tests	Number of drug product tests in the reporting period.	No.	
107g	Packaged Product Tests	Number of packaged product tests in the reporting period.	No.	
107h	Microbial Environmental Tests	Number of microbial environmental tests (i.e. absence from microbes in clean rooms (e.g. on surface and personnel gear)) in the reporting period.	No.	
107i	Microbial Product Tests	Number of microbial product tests (i.e. absence from microbes (e.g. bacteria and viruses) in products) in the reporting period.	No.	
107j	Component & Packaging Material Tests	Number of component and packaging material tests (incl. primary and printed packaging material) in the reporting period.	No.	
107k		Total	n/a	

Throughput rate

108a	Drug Substance Throughput rate	Number of drug substance testing samples analyzed per week in the reporting period.	No./wk.	
108b	Intermediate Throughput rate	Number of intermediate testing samples analyzed per week in the reporting period.	No./wk.	
108c	In Process Control Throughput rate	Number of IPC testing samples analyzed per week in the reporting period.	No./wk.	
108d	Raw Material Throughput rate	Number of raw material testing samples analyzed per week in the reporting period.	No./wk.	
108e	Stability Throughput rate	Number of stability testing samples analyzed per week in the reporting period.	No./wk.	
108f	Drug Product Throughput rate	Number of drug product testing samples analyzed per week in the reporting period.	No./wk.	
108g	Packaged Product Throughput rate	Number of packaged product samples analyzed per week in the reporting period.	No./wk.	
108h	Microbial Environmental Throughput rate	Number of microbial environmental testing samples analyzed per week in the reporting period.	No./wk.	
108i	Microbial Product Throughput rate	Number of microbial product testing samples analyzed per week in the reporting period.	No./wk.	
108j	Component & Packaging Material Throughput rate	Number of component & packaging material testing samples analyzed per week in the reporting period.	No./wk.	
108k		Total	n/a	

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Comment

Quality				
Overall Quality Control Lab Performance Methods Productivity Quality Efforts Equipment Maintenance & QCW System Training and Testing System Management System Staff Lab Overview & Organizational Structure				
Please fill in the respective figures below. If you are unable to provide a figure please insert "n/a":				
Name		Definition	Unit	Figure
General metrics				
P01	Lab Deviation Events	Number of events where an unexplained discrepancy from the routine processes occurs in the reporting period. Lab deviations comprise all events where an error occurs due to technical, human factors or environmental factors that cause differences from the routine processes.	No.	
P02	Recurring Deviations	Percentage of lab deviations that have already occurred in the reporting period. A deviation is recurring when a second deviation with the same root cause occurs within a one-year rolling period in the same process/system.	%	
P03	CAPAs Overdue	Proportion of CAPAs on lab deviations that went overdue in the reporting period to total number of CAPAs.	%	
P04	Customer Complaints Requiring Investigations	Total number of customer complaints requiring investigations in the reporting period.	No.	
P05	Product Re-Tests due to Complaints	Percentage of product re-tests (due to complaints by the customer) from overall number of tests in the reporting period.	%	
P06	Routine Product Re-tests	Number of routine product retests in the reporting period. Product retesting occurs when a material has reached the end of its initial shelf life and requires re-testing (re-analysis) to assess conformity to the registered specification(s). The test material was not progressed to formulation / further processing due to lack of demand. The intention of retesting is to prevent waste.	No.	
P07	Annual Product Quality Reviews (APQR)	Number of conducted verifications (reviews) that confirm the acceptability of the manufacturing and packaging processes in the reporting period.	No.	
P08	APQR On-Time Rate	Percentage of conducted verifications (reviews) that were on-time in the reporting period.	%	
P09	Stability Reports	Number of stability reports confirming stability at the time of testing and at different times during storage.	No.	
P10	Change Controls opened	Number of changes to product, process, equipment, testing methods and other changes which are tracked in a formal system.	No.	
P11	Audits	Number of audits by external parties (e.g. regulatory agencies, other companies) in the reporting period.	No.	
P12	Method Transfers	Number of Method Transfers in the reporting period. A method transfer is the formal process of transferring the analytical know-how from the sending unit to the receiving unit which must demonstrate the ability to do the analytical procedure(s) reliably and accurately.	No.	
P13	Test Method Validations	Number of test method validations performed in the reporting period.	No.	
Analytical Right First Time				
P14a	Drug Substance Testing RFT	Percentage of "total number of test without any deviation" out of "total number of tests" in the reporting period. Deviation= Each test repeated not due to confirmed OOS/OOT/OOE result regardless to the reason (human error, equipment error, low method performance, etc.). Data which is not part of a formal Deviation Management system (e.g. Trackwise) has to be collected manually on a continuous basis.	%	
P14b	Intermediate Testing RFT		%	
P14c	In Process Control Testing RFT		%	
P14d	Raw Material Testing RFT		%	
P14e	Stability Testing RFT		%	
P14f	Drug Product Testing RFT		%	
P14g	Packaged Product Testing RFT		%	
P14h	Microbial Environmental Testing RFT		%	
P14i	Microbial Product Testing RFT		%	
P14j	Component & Packaging Material Testing RFT		%	
P14k	Total Avg.		n/a	
Lab Investigation				
P15a	Drug Substance Lab Investigation	Number of lab investigations in the reporting period. A lab investigation is undertaken for deviation events to understand the root cause of the error when a test result is out of specification (OOS).	No.	
P15b	Intermediate Lab Investigation		No.	
P15c	In Process Control Lab Investigation		No.	
P15d	Raw Material Lab Investigation		No.	
P15e	Stability Lab Investigation		No.	
P15f	Drug Product Lab Investigation		No.	
P15g	Packaged Product Lab Investigation		No.	
P15h	Microbial Environmental Lab Investigation		No.	
P15i	Microbial Product Lab Investigation		No.	
P15j	Component & Packaging Material Lab Investigation		No.	
P15k	Total		n/a	
Invalidated OOS				

168a	Drug Substance Invalidated OOS	Number of occurrence when the assessment of a testing OOS result does not confirm the previous OOS result but testing results appear to be accurate.	No.	
168b	Intermediate Invalidated OOS		No.	
168c	In Process Control Invalidated OOS		No.	
168d	Raw Material Invalidated OOS		No.	
168e	Stability Invalidated OOS		No.	
168f	Drug Product Invalidated OOS		No.	
168g	Packaged Product Invalidated OOS		No.	
168h	Microbial Environmental Invalidated OOS		No.	
168i	Microbial Product Invalidated OOS		No.	
168j	Component & Packaging Material Invalidated OOS		No.	
168k			Total	n/a
Total OOS				
173a	Drug Substance OOS	Number of confirmed OOS in the reporting period.	No.	
173b	Intermediate OOS		No.	
173c	In Process Control OOS		No.	
173d	Raw Material OOS		No.	
173e	Stability OOS		No.	
173f	Drug Product OOS		No.	
173g	Packaged Product OOS		No.	
173h	Microbial Environmental OOS		No.	
173i	Microbial Product OOS		No.	
173j	Component & Packaging Material OOS		No.	
			Total	n/a

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Comment

Service

Overall Quality Control Lab Performance

Productivity

Quality

Costs

Material

Equipment

Manufacture & Quality Control

Processing and Release Control

Management Systems

Goal

Lab Overview & Organizational Structure

Please fill in the respective figures below. If you are unable to provide a figure please insert "n/a".

Name	Definition	Unit	Figure

Process Times

Which of the following figures are you able to provide?

Waiting & Prep.

Testing

Release

Substance/Material entering QC

Completion of QC and QA

Cycle Time

Lead Time

Release Time

☐

Lead Time

☐

Cycle Time

☐

Release Time

Lead Time

DS Testing Lead Time

Intermediate Testing Lead Time

IPC Testing Lead Time

Raw Material Testing Lead Time

Stability Testing Lead Time

Drug Product Testing Lead Time

Packaged Product Testing Lead Time

Microbial Environmental Testing Lead Time

Microbial Product Testing Lead Time

Component & Packaging Material Testing Lead Time

Time from substance/material entering QC until completion of QC and QA work, including all waiting time, storage time and order processing time.

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

Total Avg.

n/a

Cycle Time

DS Testing Cycle Time

Intermediate Testing Cycle Time

IPC Testing Cycle Time

Raw Material Testing Cycle Time

Stability Testing Cycle Time

Drug Product Testing Cycle Time

Packaged Product Testing Cycle Time

Microbial Environmental Testing Cycle Time

Microbial Product Test Cycle Time

Component & Packaging Material Testing Cycle Time

Value adding time in QC to complete the analytical tests from start to finish (incl. secondary review). Not including waiting time, storage time and order processing time.

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

No. of days

Total Avg.

n/a

CXLII

Release Time				
3084	DS Release Time	Time after finishing testing (incl. secondary review) to release of the products including all waiting times. Secondary review should be only included in cycle time.	No. of days	
3085	Intermediate Release Time		No. of days	
3086	IPC Release Time		No. of days	
3087	Raw Material Release Time		No. of days	
3088	Stability Release Time		No. of days	
3089	Drug Product Release Time		No. of days	
3090	Packaged Product Release Time		No. of days	
3091	Microbial Environmental Release Time		No. of days	
3092	Microbial Product Test Release Time		No. of days	
3093	Component & Packaging Material Release Time		No. of days	
			Total Avg.	n/a
Adherence to Schedule (ATS)				
3074	Drug Substance Testing Adherence	Percentage of drug substance testing batches that were tested as scheduled in the reporting period.	%	
3075	Intermediate Testing Adherence	Percentage of intermediate testing batches that were tested as scheduled in the reporting period.	%	
3076	In Process Control Testing Adherence	Percentage of in process control testing batches tests that were tested as scheduled in the reporting period.	%	
3077	Raw Material Testing Adherence	Percentage of raw material testing batches that were tested as scheduled in the reporting period.	%	
3078	Stability Testing Adherence	Percentage of stability testing batches that were tested as scheduled in the reporting period.	%	
3079	Drug Product Testing Adherence	Percentage of drug product testing batches that were tested as scheduled in the reporting period.	%	
3080	Packaged Product Testing Adherence	Percentage of packaged product testing batches that were tested as scheduled in the reporting period.	%	
3081	Microbial Environmental Testing Adherence	Percentage of microbial environmental testing batches (i.e. absence from microbes in clean rooms (e.g. on surface and personnel gear)) that were tested as scheduled in the reporting period.	%	
3082	Microbial Product Testing Adherence	Percentage of microbial product testing batches (i.e. absence from microbes (e.g. bacteria and viruses) in products) that were tested as scheduled in the reporting period.	%	
3083	Component & Packaging Material Testing Adherence	Percentage of packaging material testing batches (incl. primary and printed packaging material) that were tested as scheduled in the reporting period.	%	
			Total Avg.	n/a
Adherence to Lead Time (ATL)				
3084	Drug Substance Testing ATL	Percentage of drug substance testing batches that were on time in the reporting period.	%	
3085	Intermediate Testing ATL	Percentage of intermediate testing batches that were on time in the reporting period.	%	
3086	In Process Control Testing ATL	Percentage of in process control testing batches tests that were on time in the reporting period.	%	
3087	Raw Material Testing ATL	Percentage of raw material testing batches that were on time in the reporting period.	%	
3088	Stability Testing ATL	Percentage of stability testing batches that were on time in the reporting period.	%	
3089	Drug Product Testing ATL	Percentage of drug product testing batches that were on time in the reporting period.	%	
3090	Packaged Product Testing ATL	Percentage of packaged product testing batches that were on time in the reporting period.	%	
3091	Microbial Environmental Testing ATL	Percentage of microbial environmental testing batches (i.e. absence from microbes in clean rooms (e.g. on surface and personnel gear)) that were on time in the reporting period.	%	
3092	Microbial Product Testing ATL	Percentage of microbial product testing batches (i.e. absence from microbes (e.g. bacteria and viruses) in products) that were on time in the reporting period.	%	
3093	Component & Packaging Material Testing ATL	Percentage of packaging material testing batches (incl. primary and printed packaging material) that were on time in the reporting period.	%	
			Total Avg.	n/a

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Cost				
Please fill in the respective figures below. If you are unable to provide a figure please insert "n/a". Please use your local currency that you indicated on the "General Information" sheet. Please insert figure in thousand (e.g. 100'000 -> 100).				
Name	Definition	Unit	Figure	
H01	Total QO Costs	All costs of the quality organization in the reporting period.	Thousand	n/a
H02	Total QC Costs	All costs of the Quality Control Lab in the reporting period.	Thousand	n/a
H02a	Labor	All labor costs.	Thousand	
H02b	Materials (e.g. consumables)	All materials (e.g. consumables) costs.	Thousand	
H02c	Equipment	Costs for instruments, tools and spare parts (incl. electricity).	Thousand	
H02d	Maintenance	All maintenance costs including routine and no- routine maintenance.	Thousand	n/a
H02d1	Internal Maintenance	Internal cost of maintenance of lab equipment and facilities.	Thousand	
H02d2	External Maintenance	Cost for maintenance of lab equipment and facilities that are maintained by a third-party.	Thousand	
H02e	Depreciation	All depreciation costs.	Thousand	
H02f	Services	All service costs (incl. costs for employment of external parties to provide services) that are included in QC lab expenses.	Thousand	n/a
H02f1	Contract Lab	Cost of testing carried out by a third-party lab.	Thousand	
H02f2	Sample Packaging	Cost of sample management activities (transport, weighing, packaging, labelling etc.) carried out by a third-party.	Thousand	
H02f3	Lab Glassware	Cost for collecting, washing and returning glassware to the lab.	Thousand	
H02f4	Waste Disposal	Cost of waste management activities carried out by a third-party including waste collection, packaging and disposal.	Thousand	
H02f5	Archiving	Cost of document transport and storage, carried out by a third-party.	Thousand	
H02f6	Administration	Cost of administration activities carried out by a third-party, which may include document authoring or formatting, data management and secretarial duties.	Thousand	
H02f7	Information Technology	Cost of IT services provided by a third-party.	Thousand	
H02f8	Other QC Service Costs	All other QC service costs not included in any category above.	Thousand	
H02g	Other QC Costs	All other QC costs not included in any category above.	Thousand	
H03	Total QA Costs	All costs of the Quality Assurance in the reporting period.	Thousand	
H04	Other QO Costs	All other costs of the quality organization in the reporting period.	Thousand	
H05	Site Absorption	Site absorption costs are all manufacturing costs of finished products (incl. materials, labor and manufacturing overhead) in the reporting period.	Thousand	

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Comment

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

marten.ritz@unisg.ch

A.5 Questionnaire – Global Quality Benchmarking Study

2020 Quality Benchmarking Study

Introduction

2020 Quality Benchmarking Study

A Global Initiative to Baseline Pharmaceutical Quality Management

Welcome to the 2020 Quality Benchmarking Study (QBS)! Dun & Bradstreet and the University of St.Gallen are partnering to conduct this study, which is funded by the U.S. Food and Drug Administration (FDA). The study will benchmark manufacturing performance and quality management practices in comparison to global baselines and reported activities of peer establishments in the pharmaceutical industry.

Help grow the economy and improve public health by sharing information about your establishment's quality management practices. Participate and learn how your establishment compares to its peers through a free, customized quality metrics industry comparison report prepared for you by Dun & Bradstreet and the University of St.Gallen.

You will need to consult with colleagues and your internal records in order to complete some of the questions. We ask that you fill out the questionnaire as completely as possible.

Throughout the questionnaire, you will encounter terms that are underlined like this. To see a definition of these terms, please refer to the glossary associated with this document.

Survey Respondent Contact Information

Your Contact Information

Please tell us how we can reach you for any follow-up questions about your responses, and to deliver your benchmarking report. All fields are required.

First Name:	
Last Name:	
Job Title:	
Country Calling Code:	
Telephone Number (including area code):	
E-mail Address:	

D-U-N-S® Number:	
Establishment Name:	
Doing Business As name (if any):	
Street Address:	
City:	
State/Province:	
Postal Code:	
Country:	
Country Calling Code:	
Telephone Number (with Area Code):	
Fax Number (with Area Code):	
Website Address:	

Manufacturing Activities

Manufacturing Activities

The questions on this page will ask about manufacturing activities performed at your establishment. Please consider processing, testing, packaging, storing, and other activities when selecting your responses.

What type(s) of manufacturing does your establishment perform? Please select all that apply.

- ☐ Label/Relabel
- ☐ Manufacture Active Pharmaceutical Ingredient (API)
- ☐ Manufacture Finished Dosage Form (FDF)
- ☐ Manufacture Pharmaceutical Intermediates
- ☐ Pack/Repack
- ☐ Particle Size Reduction
- ☐ Testing Laboratory
- ☐ Other:

Do you currently market products in the United States?

- ☐ Yes
- ☐ No, but we have an application pending
- ☐ No, and we don't have any applications pending

In which of the following categories do you market products in the United States, or have an application pending? Please select all that apply.

- ☐ Abbreviated New Drug Application (ANDA)
- ☐ Active Pharmaceutical Ingredient (API) or Bulk Ingredient |
- ☐ Biologics License Applications (BLA)
- ☐ Combination Products (Device/Drug or Device/Biologic)
- ☐ Cosmetic
- ☐ New Drug Application (NDA)
- ☐ OTC Monograph
- ☐ Unapproved Drug
- ☐ Other:

Please indicate the dosage form(s) for products that you either market in the United States, or have a pending application to do so. Please select all that apply.

- ☐ Aerosol
- ☐ Gas
- ☐ Capsule
- ☐ Liquid
- ☐ Ointment/Suppositories
- ☐ Positron Emission Tomography (PET)
- ☐ Parenteral Drug
- ☐ Powder
- ☐ Tablet
- ☐ Transdermal or Topical Delivery System
- ☐ Other:

What type(s) of manufacturing does your establishment perform? Please select all that apply.

- ☐ Contract Manufacturing Organization (CMO)
- ☐ Generics producer (own brand)
- ☐ Patented drugs producer (own brand)

Since you identified your establishment as a CMO, please indicate the percentage of contract manufacturing activities, including testing, your business performs.

- ☐ 1%–20%
- ☐ 21%–40%
- ☐ 41%–60%
- ☐ 61%–80%
- ☐ 81%–99%
- ☐ 100%

OPEX KPIs

Which of the following products does your site produce? Please select all that apply.

- ☐ Chemical/Small Molecules Drug Substances/API
- ☐ Biologic/Large Molecule Drug Substances
- ☐ Sterile Drug Products
- ☐ Non-sterile Drug Products

OPEX Performance

Operational Excellence (OPEX) Performance and Key Performance Indicators (KPIs) in areas such as maintenance, quality, delivery and people.

The next set of questions will ask you to provide key performance indicators (KPIs) for a 12-month period. You may choose the 12-month period that is most appropriate and convenient for your internal systems (e.g. a calendar year, fiscal year, or 12-month rolling period).

Please indicate the starting month of the 12-month period you have chosen.

Year:

Context Factors

The metrics in this section are not key performance indicators themselves, but will provide context for the KPIs related to maintenance, quality, delivery, and people below.

Total number of FTEs:

Please include all full-time equivalents working at your establishment, including contractors and temporary employees. To enter decimal numbers, use a period (.) as a decimal point. For example, if your establishment has ten and a half full-time equivalents, enter "10.5" into the box.

	Chemical/Small Molecules Drug Substances/API	Biologic/Large Molecule Drug Substances	Sterile Drug Products	Non-sterile Drug Products
Number of FTEs by Technology:				
Total FTEs assigned to the technology, including contractors and temporary employees				
Days on hand (DOH):				
Average Inventory value less write downs x 365 divided by the Cost of Goods Sold (COGS)				
Test Volume:				
Number of release and long-term stability tests conducted per year (number of tests equals number of individual sample items analyzed)				
Batches Produced:				
Number of all batches produced (production started in the reporting period)				

Maintenance KPIs

Please provide the average of KPIs for the 12-month period starting with the month you indicated above. You do not need to type the percent symbol (%) in the box itself. For example, if a proportion is 999 out of a thousand, enter "99.9" in the box.

	Chemical/Small Molecules Drug Substances/API	Biologic/Large Molecule Drug Substances	Sterile Drug Products	Non-sterile Drug Products
Maintenance FTEs / Total FTEs:				
Proportion of Maintenance FTEs as a percentage of Total FTEs assigned to the technology				
Unplanned maintenance:				
Proportion of time spent on maintenance that was unplanned as a percentage of the overall time spent on maintenance				

Quality KPIs

Please provide the average of KPIs for the 12-month period starting with the month you indicated above. For decimal numbers, please use a period as the decimal point. For percentages, you do not need to type the percent symbol (%) in the box itself. For example, if a proportion is 11 out of a thousand, enter "1.1" in the box.

	Chemical/Small Molecules Drug Substances/API	Biologic/Large Molecule Drug Substances	Sterile Drug Products	Non-sterile Drug Products
Quality FTEs / Total FTEs: Proportion of Quality FTEs as a percentage of Total FTEs assigned to the technology				
Rejected Batches: Number of rejected batches (not meeting established requirements and therefore quarantined for scrap, rework or reprocessing) in the reporting period				
Deviations: Number of all deviations that have occurred in the 12 months reporting period				
Recurring Deviations: Number of recurring deviations in the reporting period. A deviation is recurring when a closed CAPA has previously addressed the same root cause in the same process/equipment.				
Deviation Closure Time: Average deviation closure time in days				
Confirmed Out-of- Specification (OOS) Results: Number of release and long-term stability test results that fall outside the				

specifications or acceptance criteria, where the OOS result is confirmed

Invalidated OOS results:

Number of release and long-term stability test results that fall outside the specifications of acceptance criteria, where OOS result was identified as an aberration of the measurement process

Delivery KPIs

Please provide the average of KPIs for the 12-month period starting with the month you indicated above. For decimal numbers, please use a period as the decimal point. For percentages, you do not need to type the percent symbol (%) in the box itself. For example, if a proportion is 11 out of a thousand, enter "1.1" in the box.

Chemical/Small
Molecules Drug
Substances/API

Biologic/Large
Molecule Drug
Substances

Sterile Drug
Products

Non-sterile
Drug Products

Dosage Units:

Total number of dosage units distributed in the reporting [period](#)

Customer

Complaints:

Number of **product quality** complaints received for the products in the reporting period

**Service Level –
Delivery (OTIF):**

Perfect order
fulfillment
(percentage of orders
shipped in time from
your establishment
(+/- 1 days of the
agreed shipment
day) and in the right
quantity (+/- 3% of
the agreed quantity)
and accurate quality)
to your customers

**Service Level –
Supplier (OTIF):**

Perfect order
fulfillment
(percentage of orders
shipped in time to
your establishment
(+/- 1 days of the
agreed shipment
day) and in the right
quantity (+/- 3% of
the agreed quantity)
and accurate quality)
**from your
suppliers**

**Adherence to
standard lead time
(Lab):**

Proportion of batches
that have been tested
& released within the
defined standard lead
time as a percentage
of all batches tested
and released

People KPIs

Please provide the average of KPIs for the 12-month period starting with the month you indicated above. For decimal numbers, please use a period as the decimal point. For percentages, you do not need to type the percent symbol (%) in the box itself. For example, if a proportion is 11 out of a thousand, enter "1.1" in the box.

	Chemical/Small Molecules Drug Substances/API	Biologic/Large Molecule Drug Substances	Sterile Drug Products	Non-sterile Drug Products
Safety level: Reported incidents due to accidents that required medical consultation per <u>year</u>				
Sick leave: Proportion of time absent due to sick leave as a percentage of the total working time per employee. Do not include parental or family leave.				

Organization Enablers

Organization Enablers

Enablers serve as an Operational Excellence (OPEX) Performance maturity assessment and will help to understand performance gaps. These are often associated with high operational performance. The enablers explored in this section focus on organizational practices.

To what degree are product and process development linked to ensure close collaboration?

- ☐ Product development and process development teams do not work together.
- ☐ Product development and process development do reach out to work together when either side has an urgent need (e.g. for trouble-shooting).
- ☐ Product development and process development have established channels to work together when either side feels it is beneficial.
- ☐ Product development and process development teams follow a defined procedure to ensure regular exchange.
- ☐ Product development and process development teams work extensively together to ensure full alignment at all times.
- ☐ Not applicable/Don't know

If you have any further comments about the collaboration between product and process development, you may enter them here.

What is the primary focus of your process performance and product quality monitoring system?

- ☐ Metrics are primarily based on operational performance and not actively collected for process improvement.
- ☐ Metrics focusing on quality are used to improve compliance, but are only reviewed within the quality unit.
- ☐ Metrics are visually displayed and routinely reviewed by employees to inspire continuous improvement.
- ☐ Metrics are visually displayed and routinely reviewed by employees. Leading indicators have been identified, they are used to improve quality.
- ☐ Metrics are visually displayed and routinely reviewed by employees. Leading indicators have been identified, are utilized in predictive analyses, and they are used to improve quality.
- ☐ Not applicable/Don't know

If you have any further comments about your process performance and product quality monitoring system, you may enter them here.

To what extent does your quality system facilitate continual improvement?

- ☐ We have a quality system that is not used for continuous improvement.
- ☐ We have a quality system that is only used for continuous improvement if there is a specific request.
- ☐ We have a quality system that is routinely used for continuous improvement.
- ☐ We have a quality system that is routinely used for continuous improvement and we incorporate external feedback (e.g. customer feedback, external audits).
- ☐ We can demonstrate PQS (Pharmaceutical Quality System) effectiveness and drive all types of post-approval changes to facilitate continuous improvement.
- ☐ Not applicable/Don't know

If you have any further comments about your quality system's facilitation of continual improvement, you may enter them here.

Do you establish formal knowledge management program with your suppliers (e.g. direct product components, substances) and contract manufacturers ensuring you are immediately informed about all important changes?

- ☐ There is no formal knowledge management program with suppliers and contract manufacturers.
- ☐ There is a knowledge management program with suppliers and contract manufacturers, but it is not applied in practice.
- ☐ There is a formal knowledge management program with suppliers and contract manufacturers. It is part of the structured supplier onboarding, but not followed up after that.
- ☐ There is a formal knowledge management program with suppliers and contract manufacturers. It is part of the structured supplier onboarding and applied in our routine collaboration.
- ☐ There is a formal knowledge management program with suppliers and contract manufacturers. It is part of the structured onboarding, routinely applied and our partners are audited to adhere to the process.
- ☐ Not applicable/Don't know

If you have any further comments about knowledge management with your suppliers, you may enter them here.

To what degree do you receive feedback from your internal and external customers on quality delivery performance (e.g. on time in full rate)?

- ☐ We do not receive feedback from our customers.
- ☐ We only receive feedback from our customers when there are complaints.
- ☐ We gather feedback from our customers in an annual customer satisfaction survey.
We have a process to routinely gather feedback from our customers.
- ☐ We have an established feedback process with our customers that gives them opportunity to provide timely information on every order.
- ☐ Not applicable

If you have any further comments about your customer feedback system, you may enter them here.

Social & Employee Enablers

Social and Employee Enablers

Enablers serve as an Operational Excellence (OPEX) Performance maturity assessment and will help to understand performance gaps. These are often associated with high operational performance. The enablers explored in this section focus on organizational practices as it relates to employees and social behaviors.

To what degree do shop floor employees know how products impact patients?

- ☐ Employees cannot explain, and senior management doesn't communicate, how the product impacts patients.
- ☐ Employees can explain how patients use the products but not the impact of quality. Senior management only communicates about the effect of quality and supply when it is the dedicated purpose (e.g. part of townhall's agenda once per year).
- ☐ Employees can explain how patients use the products and the impact of quality. Senior management highlights the effect of quality and supply even if it is not the dedicated purpose of the communication (e.g. during gemba walks).
- ☐ Employees can explain how patients use the products and the impact of Critical Quality Attributes. Employees can hear directly from patients.
- ☐ Employees can explain patient expectations, how the products are used, and the impact of Critical Quality Attributes. Employees have external opportunities to connect with patient support efforts.
- ☐ Not applicable/Don't know

If you have any further comments about your shop floor employees' awareness of products' impact on patients, you may enter them here.

To what degree is your senior management involved in evaluating the outcome of process performance and product quality review?

- ☐ Senior management is not involved in evaluating the outcome of process performance and product quality review.
- ☐ Senior management only approves or confirms that process performance and product quality review was conducted.
- ☐ Senior management is briefed about critical outcomes of process performance and product quality reviews by middle management.
- ☐ Senior management discusses the outcome of process performance and product quality review in detail with the colleagues who conducted the review.
- ☐ Senior management does not only discuss the outcome of process performance and product quality review but also drives deriving improvement actions.
- ☐ Not applicable/Don't know

If you have any further comments about senior management's involvement, you may enter them here.

To what degree do you engage your shop floor employees to identify improvement ideas and to act on these?

- ☐ We do not engage shop floor employees to identify improvement ideas.
- ☐ We engage shop floor employees to identify improvement ideas by providing a suggestion system.
- ☐ We engage shop floor employees to identify improvement ideas by providing a suggestion system and dedicated training how to identify improvement ideas.
- ☐ We engage shop floor employees to identify improvement ideas by providing a suggestion system and dedicated training how to identify improvement ideas. There is a transparent evaluation process and employees always receive feedback.
- ☐ We engage shop floor employees to identify improvement ideas by providing a suggestion system and dedicated training how to identify improvement ideas. There is a transparent evaluation process, employees always receive feedback and selected shop floor employees are involved in executing resulting improvement projects.
- ☐ Not applicable/Don't know

If you have any further comments about shop floor employees' role in identifying ideas for improvement, you may enter them here.

What proportion of your shop floor employees are cross-trained, so they can fulfill a broad range of tasks (e.g. perform several jobs on the same line or across several lines) and substitute for colleagues if necessary?

- ☐ 1%–20% of shop floor employees
- ☐ 20%–40% of shop floor employees
- ☐ 40%–60% of shop floor employees
- ☐ 60%–80% of shop floor employees
- ☐ >80% of shop floor employees
- ☐ Not applicable/Don't know

If you have any further comments about cross-training, you may enter them here.

To what degree are Quality Excellence and Continuous Improvement trainings rolled out to train employees in tools (e.g. Lean/Six Sigma)?

- ☐ We do not run Quality Excellence and Continuous Improvement trainings.
- ☐ Some Quality Excellence and Continuous Improvement trainings are provided from time to time. However, there is no structured concept in place.
- ☐ We run a structured generic Quality Excellence and Continuous Improvement training program. However, it relies on off-the-shelf approaches provided by external trainers and certification organizations.
- ☐ We run a structured program of Quality Excellence and Continuous Improvement trainings tied to our individual needs. The structured training program is developed, tied/customized to our organization's needs and deployed by our internal specialists (train the trainer approach).
- ☐ We run a structured program of Quality Excellence and Continuous Improvement trainings tied to our individual needs. The structured training program is developed, tied/customized to our organization's needs and deployed by our internal specialists (train the trainer approach). There is a defined process to evaluate the effectiveness of the training program.
- ☐ Not applicable/Don't know

If you have any further comments about your training program, you may enter them here.

Technical & Tool Enablers

Technical and Tool Enablers

Enablers serve as an Operational Excellence (OPEX) performance maturity assessment and will help to understand performance gaps. These are often associated with high operational performance. The enablers explored in this section focus on organizational practices as it relates to technology and other tools used in your processes.

To what degree are potential bottleneck machines identified and proactively supplied with additional spare parts?

- ☐ Bottleneck machines are not identified.
- ☐ Bottleneck machines are identified, but not in a dedicated process and not supplied with additional spare parts proactively.
- ☐ Bottleneck machines are identified in a dedicated process, but not supplied with additional spare parts proactively.
- ☐ Bottleneck machines are identified in a dedicated process, but only some are supplied with additional spare parts proactively.
- ☐ Bottleneck machines are identified in a dedicated process, which is updated regularly, and fully followed up by supplying additional spare parts proactively.
- ☐ Not applicable/Don't know

If you have any further comments about your treatment of bottleneck machines, you may enter them here.

What is your use of statistical tools to measure, track, and implement continuous improvement? For example, this could be a knowledge base of the relevant multifactorial relationships (e.g., between formulation, process, and quality attributes).

- ☐ Identify and collect data that measures manufacturing performance
- ☐ Identify, collect, and analyze manufacturing performance data
- ☐ Link performance data to business objectives and communicate performance to the organization
- ☐ Use statistical techniques to quantify process performance, and establish baselines for key attributes
- ☐ Use statistical techniques to drive performance improvement and establish culture of continuous improvement including management reviews
- ☐ Not applicable/Don't know

If you have any further comments about your use of statistical tools, you may enter them here.

To what degree do you use statistical process control (SPC) in your processes?

- ☐ SPC not or rarely utilized, no equipment with real-time monitoring
- ☐ SPC partly (>30%) utilized, no equipment with real-time monitoring
- ☐ SPC often utilized (>60%), little (<30%) equipment with real-time monitoring
- ☐ SPC always utilized, some (>30%) equipment with real-time monitoring
- ☐ SPC always utilized, >80% of equipment under real-time monitoring
- ☐ Not applicable/Don't know

If you have any further comments about your use of statistical process control, you may enter them here.

Do you apply a formal quality risk management (QRM) process for all products and are your employees trained accordingly?

- ☐ We do not have a formal quality risk management process.
- ☐ We have a formal quality risk management process. However, it is not always applied and employees are not trained on the procedures.
- ☐ We have a formal quality risk management process. It is always applied for all new products/processes and SMEs (Subject matter experts) are trained according to it.
- ☐ We have a formal quality risk management process. It is always applied for all new products/processes and all relevant employees are trained accordingly.
- ☐ We routinely review our existing quality risk management documentations (e.g. review initial assessments and mitigations based on production experience after a certain time). Procedures are clearly defined and employees are trained accordingly.
- ☐ Not applicable/Don't know

If you have any further comments about your quality risk management process, you may enter them here.

To what degree do you make use of standardized tools and procedures (e.g. FMEAs, 5 Whys, Ishikawa) for root cause analysis (RCA) to get a deeper understanding of the influencing factors?

- ☐ Standardized tools/procedures for RCA are not in place
- ☐ Standardized tools/procedures for RCA are in place, but rarely used (<50% of investigations) without systematically rolled-out trainings
- ☐ Standardized tools/procedures for RCA are in place and widely used (>50% of investigations), and trainings are rolled out systematically
- ☐ Standardized tools/procedures for RCA are in place and widely used (>50% of investigations), and trainings are rolled out systematically; RCA effectiveness is assessed
- ☐ Standardized tools/procedures for RCA are in place and widely used (>50% of investigations), and trainings are rolled out systematically; RCA effectiveness is assessed and trainings are adapted accordingly
- ☐ Not applicable/Don't know

If you have any further comments about your tools and procedures for root cause analysis, you may enter them here.

Do you measure corrective and preventive action (CAPA) effectiveness and identify CAPAs that are not effective?

- ☐ We only use our CAPA system for documentation, i.e. we do not review the overall list of CAPAs, proportions of overdue CAPAs, or trends.
- ☐ We use our CAPA system for documentation and review, e.g. the overall list of CAPAs, proportions of overdue CAPAs, or trends.
- ☐ We have defined measures in place and are able to assess the overall effectiveness of the CAPA system. Furthermore, distinct ineffective CAPAs can be identified.
- ☐ We have defined measures in place assessing the overall effectiveness of the CAPA system and identifying distinct ineffective CAPAs. Additional actions for all ineffective CAPAs are derived.
- ☐ We have defined measures in place assessing the overall effectiveness of the CAPA system, identifying distinct ineffective CAPAs and deriving additional actions. The measures are reviewed and updated regularly.
- ☐ Not applicable/Don't know

If you have any further comments about your CAPA system, you may enter them here.

To what degree have you implemented 5S (Sort, Set in Order, Shine, Standardize, Sustain) and continuously improve it?

- ☐ We do not have formal procedures in place to implement 5S.
- ☐ Formal procedures for putting all tools and fixtures in their place exist, but are only partly (<50% of areas) adhered to.
- ☐ Formal procedures for putting all tools and fixtures in their place exist that are fully adhered to, but are static not optimized.
- ☐ Formal procedures for putting all tools and fixtures in their place exist that are fully adhered to, they are adapted/optimized unregularly, e.g. when requested by management.
- ☐ Formal procedures for putting all tools and fixtures in their place exist that are fully adhered to; optimization constantly is our priority.
- ☐ Not applicable/Don't know

If you have any further comments about your 5S program, you may enter them here.

To what degree do you utilize charts/boards showing the current performance status (KPIs) in your manufacturing areas and QC labs?

- ☐ We do not utilize performance charts.
- ☐ Performance charts are used in some areas (<50%) to show KPIs, but not systematically used and updated.
- ☐ Performance charts across some areas (<50%) show KPIs and are systematically used and updated.
- ☐ Performance charts across most areas (>50%) in manufacturing and QC show KPIs and are systematically used and updated.
- ☐ Performance charts across all areas in manufacturing and QC show KPIs. The set-up and structured usage of performance boards is continuously reviewed and improved.
- ☐ Not applicable/Don't know

If you have any further comments about your use of performance charts, you may enter them here.

Management Comments

Establishment Management Comments

How well does the marketplace reward your company's investment for this specific manufacturing site in continuous improvement and mature quality systems?	1 - Not At All	2 - Poorly	3 - Neither Low or High	4 - Positive	5 - High	6 - Unsure
	☐	☐	☐	☐	☐	☐

Because you selected "Positive" or "High" to Question 1.a., please select as many items from the list below that represent marketplace acknowledgement of value.

	Yes	No	Unsure
Increased Sales	☐	☐	☐
Increased Market Share	☐	☐	☐
Increased Stock Value	☐	☐	☐
Increased Brand Recognition	☐	☐	☐

Please use the space below to provide additional input related to this topic.

In your role as a leader, what management practices and operational processes help you to balance the pressure for continuous improvement with shareholder expectations?

Summation

Thank you for completing the Quality Benchmarking Study! You have reached the end of the questionnaire.

Completing a survey online will produce a page which displays a record of your responses.

2020 Quality Benchmarking Study

GLOSSARY OF TERMS

5S:	5S is used to eliminate waste in the workplace and to uncover dysfunctional ways of work. The five S's comprise sort, set in order, shine, standardize, and sustain.
5 Whys:	A guided team exercise for identifying the root cause of a problem. Five Whys is used in the “analyze” phase of the Six Sigma (define, measure, analyze, improve, control) methodology.
Batch:	A specific quantity of a drug or other material that is intended to have uniform character and is produced according to a single manufacturing order during the same cycle of manufacture.
API:	Active Pharmaceutical Ingredient
Bottleneck Machine:	A bottleneck machine is one machine in a chain of processes/machines, such that its capacity limits the capacity of the whole chain.
CAPA:	Corrective And Preventive Action
CMO:	Contract Manufacturing Organization
Context Factors:	Background information on the site, such as size and FTEs, technology, and product program. They allow to build meaningful peer groups for comparisons (“compare apples with apples”).
Continual Improvement:	Recurring activity to increase the ability to fulfil requirements. (ISO 9000:2005).
Critical Quality Attributes (CQA):	A CQA is a physical, chemical, biological, or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality.
DUNS Number:	The Data Universal Numbering System is a proprietary system developed and managed by Dun & Bradstreet that assigns a nine-digit unique numerical identifier to a single business entity.

Effectiveness:	Effectiveness describes the “degree to which something is successful in producing a desired result; success.”
Enabler:	Enablers represent capabilities of an organization that are associated with reaching a high operational performance.
Establishment:	A place of business under one management, at one general physical location.
FTE:	Full-Time Equivalent
Failure Mode and Effects Analysis (FMEA):	The process of reviewing as many components, assemblies, and subsystems as possible to identify potential failure modes in a system and their causes and effects.
Invalidated OOS:	Number of release and long-term stability test results that fall outside the specifications or acceptance criteria where the source of the OOS result is identified as an aberration of the measurement process.
Ishikawa:	An Ishikawa diagram is a diagram that shows the causes of an event and is often used in manufacturing and product development to outline the different steps in a process, demonstrate where quality control issues might arise and determine which resources are required at specific times. It is also referred to as a fishbone diagram.
ITEM-HSG:	Institute of Technology Management at the University of St.Gallen
KPI:	Key Performance Indicator
Manufacture Finished Dosage Form (FDF):	A dosage form is the physical form in which a drug is produced and dispensed, such as a tablet, a capsule, or an injectable.
OpEx:	Operational Excellence
OOS:	Out of Specification - Number of release and long-term stability test results that fall outside the specifications or acceptance criteria.
OTC Monograph:	The safety, effectiveness, and labelling of OTC active ingredients.



OTIF:	On Time and In Full
Positron Emission Tomography (PET):	Imaging technique that uses radioactive substances to visualize and measure metabolic processes in the body.
QC:	Quality Control
RCA:	Root Cause Analysis
Six Sigma:	A data-driven method for improving, optimizing and stabilizing business and manufacturing processes.
SPC:	Statistical Process Control. For example, batch records could include a series of charts depicting acceptance ranges, confidence intervals, and distribution plots (inter- and intra-batch) showing measurement results. (See also FDA Guidance for Industry PAT [...], 2004).

A.6 Survey – OPEX across Manufacturing and Quality Control

1 Instructions

Operational excellence across manufacturing and quality control

Survey based study

The study

Since years the University of St.Gallen is offering Operational Excellence (OPEX) benchmarking programs in the areas of pharmaceutical manufacturing and quality control labs. Based on the benchmarking data there seems to be only limited correlation between effectiveness of manufacturing operations and quality control. Diverse performance patterns between manufacturing and quality control in the same production sites can be observed.

This survey takes on the phenomena described above and asks for industry's perception if there are differences in operational performance, level of maturity and status of compliance between manufacturing and quality control at their production sites. In addition, the specific organization of and strategy to Operational Excellence will be part of the analyses. Furthermore, we are looking for your approaches to deal with interdepartmental barriers and levers for alignment.

Scope & Commitment

The questionnaire is seeking responses from pharmaceutical production sites. Site leaders, local heads of production/quality or site OPEX specialists are perfectly qualified and kindly asked to fill the questionnaire. Responses from above-site functions on behalf of one site (or multiple sites) are also very welcome. Kindly note that the scope of the questionnaire is always a particular production site and not the entire company (answers are expected to differ between different sites of the company network). In case you want to provide insights for more/multiple sites, please fill one questionnaire for each site.

Filling the questionnaire will take less than 20 minutes. There is no data gathering needed as this study is focusing on qualitative insights rather than benchmarking numbers.

Benefits

We will provide a result summary of the research outcomes to all participating sites after completing the study and analyses. Therefore, please make sure to name a point of contact. As a matter of course there are no costs associated with taking the survey and receiving the result summary.

Furthermore, we are open and happy to discuss the topic of OPEX across manufacturing and quality control with all interested parties and share our experience. Please approach the research team.

Confidentiality of responses

Your answers stay fully confidential with the research teams. We will not disclose the names of participating sites nor any specific answers. Only anonymized results will be communicated to public.

Thank you very much for your participation

Structural Context & Infrastructure				
Manufacturing vs. Quality Control Labs	OPEX Organization	Corporate Structure	Responsibilities	Support functions
	OPEX Strategy	Prioritization	Execution	Background / History
	Level of Excellence			
	Differences in Performance	Cost	Quality	Delivery
	Differences in Maturity	Visual Management	Process Management	Standardization
	Differences in Compliance	Observations audits	Citations inspections	Customer Complaints
	Barriers and Levers			
	Knowledge transfer	Resource Allocation	Complexity in activities	CI culture

If you have any additional questions concerning the project please contact:

Institute of Technology Management, University of St.Gallen (ITEM-HSG)
Transfer Center for Technology Management, University of St.Gallen (TECTEM)
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2 General Information

General Information

Contact Information

Last Name

First Name (s)

Position or role

Company Name

Production Site / Location

Telephone

Fax

E-mail

Adress

Please select your site location

If your country is not listed, please specify below

☐ Switzerland

☐ USA

☐ etc.

3 Structural Context & Infrastructure

Structural Context & Infrastructure

OPEX Organization

Corporate Structure

Does your company have a corporate / above-site OPEX organization?

- ☐ Yes
- ☐ No

Besides the general OPEX organization: Does your company run a corporate / above site organization **dedicated to OPEX per department manufacturing or quality control?**

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

Support functions

Does your company provide corporate / above-site support (e.g. training, tools) to drive forward OPEX in manufacturing and quality control at your site?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

Responsibilities on site

Who is responsible for fostering, prioritizing and driving-forward Operational Excellence **in manufacturing** at your site ?

	Corporate level	Site OPEX	Dedicated	Production staff
Manufacturing	☐ OPEX organization	☐ organization	☐ production OPEX organization	☐ not dedicated to OPEX

Who is responsible for fostering, prioritizing and driving-forward Operational Excellence in **quality control** at your site ?

	Corporate level	Site OPEX	Dedicated lab	Lab staff not
QC Lab	☐ OPEX organization	☐ organization	☐ OPEX organization	☐ dedicated to OPEX

OPEX Strategy

Execution

Who executes OPEX and improvement projects in **manufacturing** at your production site ?

	Corporate level	Site OPEX	Dedicated	Production staff
Manufacturing	☐ OPEX organization	☐ organization	☐ production OPEX organization	☐ not dedicated to OPEX

Lab staff not
dedicated to
OPEX

No

Who executes OPEX and improvement projects in **quality control** at your production site ?

QC Lab	☐ Corporate level OPEX organization	☐ Site OPEX organization	☐ Dedicated lab OPEX organization	☐ Lab staff not dedicated to OPEX

Prioritization

Do you follow a formalized OPEX or lean roadmap at your production site?

☐ Yes

☐ No

Does the roadmap include department specific targets and actions?

☐ Yes, for both (Manufacturing and QC Lab)

☐ Yes, only manufacturing

☐ Yes, only QC Labs

☐ No department specific targets

Background / History

When did you start dedicated OPEX initiatives in manufacturing and quality control, e.g. rolling out a structured program at your site?

Manufacturing QC Labs

4 Level of Excellence

Levels of Excellence

Differences in Performance

Cost

Where is the higher attention for increasing efficiency or decreasing costs?

☐ Manufacturing

☐ QC Labs

☐ Equal

Do you currently follow active, specific targets for increasing efficiency or decreasing costs in manufacturing and quality control?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

Quality

Do you see either manufacturing or lab deviations as bigger issue and field for future improvement in your production site?

☐ Manufacturing

☐ Labs

☐ Equal

Delivery

What part of the site internal value chain (and respective department) do you consider especially as bottleneck for on-time release and delivery?

- ☐ Manufacturing
- ☐ Labs
- ☐ Equal

In case there are defined lead times for production and testing processes: Do you see a better average adherence to defined standard lead times (ATL) in manufacturing or quality control?

- ☐ Manufacturing
- ☐ Labs
- ☐ Equal

Differences in Maturity**Visual Management**

Where do you see the higher maturity in applying Visual Management tools (e.g. performance boards at the floor or in the lab) and structurally using these to steer the daily business (e.g. huddle meetings)?

- ☐ Manufacturing
- ☐ Labs
- ☐ Equal

Do you use boards (or digital screens) to visually display current performance (KPIs) and targets in the departments?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

If you use boards (or digital screens) to visually display current performance (KPIs) and targets in the departments when did you start using them?

Manufacturing QC Lab

Do you follow a corporate or site-level standard to design and use visual boards / screens? Or do approaches across departments differ?

- ☐ Corporate Standard
- ☐ Site Standard
- ☐ Different across departments

Cross-Training

Where do you currently see a higher proportion of cross-trained employees (shop floor Employees or analysts can fulfill multiple roles in their department) at your site?

- ☐ Manufacturing
- ☐ QC Labs
- ☐ Equal

Do or did you actively foster cross-training ?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

If you did or do actively foster cross-training, when did you start fostering a higher level of cross-training ?

Manufacturing QC Lab

Do you follow corporate or site-level targets for the proportions of cross-trained employees? Or do departments set own targets at your site?

- ☐ Corporate Standard
- ☐ Site Standard
- ☐ Different across departments

5S

Where do you see the higher maturity in applying 5S principles (e.g. shadow boards) at your site?

- ☐ Manufacturing
- ☐ QC Labs
- ☐ Equal

Did or do you actively apply 5S principles in manufacturing and quality control at your site?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

If you actively apply 5 S principles in manufacturing and quality control at your site, when did you start introducing 5S?

Manufacturing QC Lab

Do you follow a corporate or site-level standards to implement and sustain 5S? Or do approaches across departments differ?

- ☐ Corporate Standard
- ☐ Site Standard
- ☐ Different across departments

Differences in Compliance

Audits

What department performs better / receives fewer observations (on average) in internal and external audits ?

- ☐ Manufacturing
- ☐ QC Labs
- ☐ Equal

Does your company run an internal corporate audit program for manufacturing areas and quality control labs?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

Inspections

Does the majority of citations received / actions indicated in inspections concern either the areas of manufacturing or quality control?

- ☐ Manufacturing
- ☐ QC Labs
- ☐ Equal

Customer Complaints

Does the majority of customer complaints cause follow-up activities (investigating potential issues) in either manufacturing or quality control?

- ☐ Manufacturing
- ☐ QC Labs
- ☐ Equal

5 Barriers and Levers**Barriers and Levers****Information & Knowledge transfer**

Do you see information & knowledge transfer across manufacturing and quality control as a barrier to align OPEX at your site?

- ☐ Yes ☐ No

Do you actively foster information & knowledge transfer across manufacturing and quality to share successful OPEX practices at your site?

- ☐ Yes ☐ No

Please briefly describe your approach for information & knowledge transfer across manufacturing and quality to share successful OPEX practices at your site:

Resource Allocation

Do your manufacturing and quality control departments struggle with driving OPEX due to lack of dedicated resources?

Manufacturing ☐ Yes ☐ No

QC Lab ☐ Yes ☐ No

Do you follow an integrated site-level strategy to allocate and distribute resources (e.g. lean experts) to departments according to the actual need?

- ☐ Yes ☐ No

Please briefly describe your site's approach for allocating OPEX and CI resources to manufacturing and quality control labs:

Complexity in activities

Which of the following products does your site produce? Please select all that apply.

- ☐ Small Molecules DS / API ☐ Large Molecules / Bio DS ☐ Non-sterile Drug Products ☐ Sterile Drug Products

Is your QC only responsible to conduct testing related to the production at the same site or do you test for multiple sites? If your site tests centralized, what proportion of your overall tests is for other locations?

- ☐ Own Site
☐ Multiple sites / Centralized testing

%

Please briefly describe the level of complexity at your production site compared to other sites of your company network. Do you see complexity of activities in particular as a challenge in manufacturing or quality control?

CI Culture

Do you see a comparably higher maturity / cultural readiness and focused mindset for continuous improvement in your manufacturing areas or qc labs?

- ☐ Manufacturing
☐ Labs
☐ Both

Is embedding a continuous improvement culture a current priority in either your manufacturing areas or qc labs (running structured initiatives to proactively engage operators and analysts)?

- ☐ Manufacturing
☐ Labs
☐ Both

Please briefly describe your site's approach for embedding a continuous improvement culture in your manufacturing areas and quality control labs. Do you follow a cross-functional approach at the site or is it driven departmental?

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University of St.Gallen

6 Endseite

Thank you very much for your participation!

A.7 Interview Guideline – Deep Dive Successful Practices

A) *Part 1 - Welcome & Introduction:*

- a. Personal introduction of attendees
- b. Consent & confirmation to record the interview and use findings in an anonymized manner in the thesis
- c. Explanation of interview scope and mode of operations
- d. Introduction of thesis topic and high-level overview of findings from re-search phases 1 & 2

B) *Part 2 - Supplementary Details Survey Responses:*

- a. Please briefly outline the approach to OPEX at your production site in your own words and give a short overview on the organizational set-up and strategy.
- b. Does your site's approach to OPEX comprise both departments manufacturing and quality control in an integrated manner?
- c. Please give a brief overview of the OPEX history in manufacturing and quality control. Have OPEX initiatives been initially started in parallel across both departments or in a sequential order?
- d. How do responsibilities for definition, prioritization, and execution of OPEX projects differ between manufacturing and quality control at your production site?
- e. How many resources / FTEs are dedicated to OPEX in manufacturing and quality control? Are cross-departmental OPEX resources (OPEX site organization) available and capable to agilely support manufacturing or quality control according to the current needs and priorities?

C) *Part 3 - Detailed Discussion Case Focus Topic:*

Based on your survey responses, following successful practices in the field of OPEX across manufacturing and QC have been identified at your production site. Please provide us with additional explanation on:

Case A

- a. Standardized cross-departmental best practice exchange
- b. Structured interdepartmental Gemba Walks

- c. Aligned roadmap comprising both manufacturing and QC, embedded in site strategy
- d. One integrated cross-departmental idea management system

Case B

- e. Common, cross-functional framework for OPEX implementation: Defined by corporate, driven by the site, implemented by the department
- f. Cross-departmental best practice sharing during Gemba walks
- g. Formalized process for regular feedback between OPEX functions in manufacturing and quality control

Case C

- h. Setting-up PLTs (Project/Product Leadership Teams) for each product or project. Holding periodic cross-functional meetings within PLTs including QC, QA, Production, Supply Chain, Project Management, Business Development
- i. Defining and executing OPEX projects as employee development opportunities (e.g. 6 Sigma belt certification)

D) Part 4 - Conclusion & Outlook:

- a. Double-check for additional/final comments on the topic
- b. Summary of interview take-aways
- c. Next steps of study & thesis completion
- d. Offer to share final results and further exchange on the topic

A.8 Curriculum Vitae

Name	Marten Ritz
Date of birth	January 18, 1993 in Goslar, Germany
Nationality	German

Experience

Since 06/2021	Institute of Technology Management , St.Gallen (CH): <i>Postdoctoral Project Leader – Production Management</i>
10/2019 – 05/2021	Institute of Technology Management , St.Gallen (CH): <i>Head of Competence Center – Operational Excellence</i>
05/2018 – 05/2021	Institute of Technology Management , St.Gallen (CH): <i>Research Associate – Operational Excellence</i>
08/2017 – 03/2018	Laboratory for Machine Tools (WZL) , Aachen (D): <i>Master's Candidate & Research Assistant – Technology Planning</i>
04/2017 – 07/2017	Institute of Technology Management , St.Gallen (CH): <i>Research Intern – Operational Excellence</i>
05/2016 – 03/2017	Laboratory for Machine Tools (WZL) , Aachen (D): <i>Research Assistant – Technology Planning</i>
10/2015 – 02/2016	Mubea Fahrwerksfedern GmbH , Attendorn & Weissensee (D): <i>Bachelor's Candidate – Manufacturing Technologies & Investments</i>
04/2015 – 06/2015	Mubea Fahrwerksfedern GmbH , Attendorn (D): <i>Intern – Manufacturing Technologies & Investments</i>
09/2013 – 10/2013	Mann + Hummel GmbH , Bad Harzburg (D): <i>Intern – Technical Service</i>
07/2011 – 09/2011	H.C. Starck GmbH , Goslar (D): <i>Production Support – Special Metal & Ceramic Powders</i>

Education

08/2018 – 07/2021	University of St.Gallen , St.Gallen (CH): Management, especially Business Innovation <i>Degree: Doctor of Philosophy</i>
04/2016 – 03/2018	RWTH Aachen University , Aachen (D): Production Engineering, especially Corporate Optimization <i>Degree: Master of Science</i>
10/2011 – 03/2016	RWTH Aachen University , Aachen (D): Mechanical Engineering, especially Production Engineering <i>Degree: Bachelor of Science</i>
08/2004 – 06/2011	Christian-von-Dohm Gymnasium , Goslar (D): <i>Degree: Abitur</i>

