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Advances in Pharma Business Management and Research

Volume 1

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Lars Schweizer • Theodor Dingermann •
Otto Quintus Russe • Christian Jansen
Editors

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Preface

Since the autumn of 2016, Goethe University Frankfurt has been offering ambitious professionals from the pharmaceutical industry or related areas a unique opportunity to promote personal and professional advancement: the Master of Pharma Business Administration (Pharma MBA) program is the first and only part-time MBA program with a dedicated focus on the pharmaceutical industry.

Jointly developed by Goethe University Frankfurt, Goethe Business School, and the House of Pharma & Healthcare, the Pharma MBA offers an innovative combination of applied management fundamentals and pharma-specific business know-how along the pharmaceutical value chain. To ensure that the academic foundation and the practical relevance of the curriculum are perfectly matched, all modules draw on numerous practical examples and case studies or include impulse presentations of experienced practitioners of the pharma industry.

Pharma MBA graduates earn a Master of Business Administration (MBA) degree (90 ECTS CP) from both the AACSB-accredited Faculty of Economics and Business Administration and the Faculty of Biochemistry, Chemistry and Pharmacy at Goethe University Frankfurt.

A typical Pharma MBA cohort comprises a variety of international professionals from the pharmaceutical industry or related fields with several years of postgraduate work experience. Since 2016, participants from more than 30 national as well as international companies have commenced their studies on the university's modern and centrally located campus Westend of Goethe University Frankfurt. With already the fourth cohort starting in the autumn of 2019, the Pharma MBA program has established itself sustainably.

After completing the lecture phase in semesters 1–3, the 20 students of the inaugural Pharma MBA Class of 2018 finalized their studies at Goethe University Frankfurt with the completion of a master's thesis in the fourth semester. Abstracts of six selected master's theses are compiled and published in this first edition of the Pharma MBA's periodical. They are an outstanding testimony not only of the

diversity of the topics dealt with but also of the professional depth with which the topics were analyzed and perfectly illustrate the mission of the program to cover:

- Practically relevant basic knowledge on management in the pharmaceutical industry
- Detailed insights into innovative management concepts based on application examples and experience reports from pharmaceutical practice
- Current scientific findings and practical knowledge along the pharmaceutical value chain

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Frankfurt am Main, Hessen, Germany

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**Correction to: Introduction: Trends and Developments in the
Pharmaceutical and Life Sciences Industry C1**
Lars Schweizer and Theodor Dingermann

About the Editors

Lars Schweizer has been a Professor of Strategic Management at Goethe University Frankfurt since December 2007. Currently, he is the Academic Director of the Master of Pharma Business Administration as well as the Master of Digital Transformation at Goethe Business School. He holds a doctoral degree and postdoctoral degree (habilitation) from the University of Bamberg. He has published papers in journals such as the *Academy of Management Journal*, the *Strategic Management Journal*, the *Journal of Management, Industrial and Corporate Change*, the *Journal of General Management*, *Scandinavian Journal of Management*, the *Journal of Engineering and Technology Management*, the *International Journal of Biotechnology*, *Pharmaceutical Policy and Law*, and the *Journal of Business Research*. His main research focuses are mergers and acquisitions, strategic management, leadership, and organizational behavior as well as the pharmaceutical and biotechnology industries.

Theodor Dingermann (1948) studied pharmacy at the University of Erlangen-Nürnberg between 1973 and 1976. In 1980, he received his Ph.D. in biochemistry. From 1980 to 1982, he worked as a postdoctoral fellow at Yale University, New Haven, USA, with Prof. Dr. Dieter Söll. From 1990 to 2013, he was a Professor and Director of the Department of Pharmaceutical Biology at Goethe University Frankfurt/Main. Since 2013, he has been affiliated with the Goethe University as a Senior Professor. Prof. Dingermann received the Carl-Mannich-Medal Award from the German Pharmaceutical Society in 2010, and he was elected “Professor of the Year 2009” in Germany. He is editor-in-chief of the international scientific journal *DIE PHARMAZIE*, editor-in-chief of *Pharmakon*, the official journal of the German Pharmaceutical Society, and a member of the group of chief editors of the *Pharmazeutische Zeitung*.

Between 2005 and 2014, Prof. Dingermann was the Representative for Biotechnology for the State of Hessen. He is an elected member of the German Pharmaceutical Association’s Drug Commission (Arzneimittelkommission der Deutschen

Apothekerschaft) and since 1992 has been Chairman of the working group “recombinant DNA products” of the German Pharmacopoeia committee at the BfArM. From 1996 to 2000, he was Vice President and from 2000 to 2004 President of the German Pharmaceutical Society (DPhG). From 1998 to 2000, he served as Vice President of Goethe University Frankfurt/Main.

At GBS, Prof. Dr. Dingermann is the Academic Director of the [Master of Pharma Business Administration](#).

He is in great demand as a speaker at international events and author of numerous publications.

Otto Quintus Russe has been the Managing Director of the House of Pharma & Healthcare at Goethe University Frankfurt since 2014. He studied pharmacy at Goethe University Frankfurt from 2004 to 2008. After working in the pharmaceutical industry and public pharmacy, he completed his doctorate (2010–2014) on AMP-activated protein kinase as a target for the treatment of inflammatory nociception at the University Hospital Frankfurt.

Christian Jansen has been the Managing Director of Goethe Business School since 2013. Prior to joining GBS, Dr. Jansen worked as a consultant with McKinsey & Company for three years. He holds a diploma in Business Administration from Goethe University Frankfurt and a Master of Business Administration (MBA) degree from the University of Iowa, USA. In 2008, he completed his doctorate at the European Business School.

Introduction: Trends and Developments in the Pharmaceutical and Life Sciences Industry



Lars Schweizer and Theodor Dingermann

Abstract Currently, the pharmaceutical industry is facing rapid changes occurring e.g. as a result of biotechnology's development, the raising importance of IT/Big data as well as new tailor-made gene therapies or the CRISPR/CAS technology. This chapter is based on the observation that the management and science in the pharmaceutical industry is changing dramatically. The title of this book "Advances in Pharma Business Management and Research, Volume 1" reflects the diversity of the included studies and the goal to include and incorporate the different developments, trends, and challenges in the pharmaceutical industry. Thus, it comprises a number of interesting studies analyzing current challenges in the industry.

Currently, the pharmaceutical industry is facing rapid changes occurring e.g. as a result of biotechnology's development, the raising importance of IT/Big data as well as new tailor-made gene therapies or the CRISPR/CAS technology. One might ask why the pharmaceutical industry is so important and interesting. The simplest and most obvious answer lays in the most fundamental need of mankind: the will to survive. The discoveries in the pharmaceutical and biotechnology industries help to reduce mortality and to prolong life. This can surely be considered as one of the most important needs, if not *the* need and desire of all human beings.

Due to an oversight in editing, the second paragraph on page 3 was not removed, though it referred to an abstract which did not appear in this publication. We had asked the reader to ignore this section, and apologized for the error.

The original version of this chapter was revised. A correction to this chapter can be found at https://doi.org/10.1007/978-3-030-35918-8_8

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This book series is based on the observation that the management and science in the pharmaceutical industry is changing dramatically. Historically, competition in the pharmaceutical industry has been characterized by three factors. *First*, competitive advantage has been driven by blockbuster drugs, which were required to offset the cost of expensive hit-or-miss clinical trial programs. *Second*, almost all pharmaceutical companies have traditionally been vertically integrated from research and discovery through worldwide sales and marketing. *Third*, pharmaceutical companies have played a peripheral role as ‘suppliers’ in the health care system, provided marketing solutions to payers and providers. However, they had no intention in driving primary consumer demand or becoming involved in care, diagnosis, or decision-making.

Nowadays, pharmaceutical companies face daunting stock market expectations, short-term operating pressures on earnings, and increased regulatory requirements. As a result, pharmaceutical firms need to adjust their strategy in various ways. E.g., (1) they turn to mergers and acquisitions in order to plug strategic holes and accelerate operational improvements, (2) they enter into strategic alliances, and (3) they focus their activities on specific core areas. Hence, the future success will require pharmaceutical firms to develop new capabilities on many fronts. *First*, they have to dedicate resources in order to stay informed of technology developments and integrate the most promising technologies and (gene) therapies in-house. *Second*, the efficient storage and effective retrieval of the vast quantities of data provided by the new technologies have to be assured. *Third*, pharma companies will have to hire the right talent for each specific task and pay attention that they effectively work together. *Fourth*, development and marketing must continuously be informed over the advances in research and discovery, because they have to create targeted products for smaller subpopulations of diseases. *Fifth*, pharmaceutical companies will have to create more effective tools for portfolio selection and management.

Looking at the firm level, one needs to consider some additional trends and developments. (1) From a competitive perspective, biotechnology challenges the historical bases of competition (blockbuster drugs, vertical integration, role as supplier) in the pharmaceutical industry. (2) Knowledge and technology are not only transforming drug discovery, they are also redefining the business structure of the pharmaceutical industry. Many new players focus on narrow elements of the pharmaceutical business, from clinical trials to specialty manufacturing to genomic databases and screening capability. This trend is called deconstruction of the value chain leading to increased outsourcing activities. (3) Consumers are gaining more and more access to information and establishing greater control over decisions about their care. Accelerating progress in genetic understanding creates the possibility for pharmaceutical firms to segment patients on the basis of genomic descriptors and tailor therapy according to their specific needs. As a result pharmaceutical firms need to become more consumer-centric.

The title of this book “*Advances in Pharma Business Management and Research, Volume 1*” reflects the diversity of the included studies and the goal to include and incorporate the different developments, trends, and challenges in the pharmaceutical industry. Thus, this book comprises a number of interesting studies analyzing current challenges in the industry.

To start with, **Nadine Schneider** is putting her focus on the regulatory environment. Her study is entitled “*Relevance of instruments for measurements of Quality of Life in the AMNOG context*”, where she analyzed the endpoint “Health-related Quality of Life (HrQoL)” from different perspectives. Among the four outcomes “morbidity”, “mortality”, “adverse effects” and “HrQoL” the latter is the most subjective and also a relatively new outcome. This study covers in addition to standard analytical tools also interviews to investigate different perspectives regarding the relevance of this endpoint in comparison to the others. At the end it comes down to the question: “Is the endpoint HrQoL a fully equivalent outcome category within the assessment process in the AMNOG context?” This study was supervised by Dr. Matthias Pfannkuche.

The focus of **Daria Mikhailova** study is put on the firm-level. She analyzed “*The quality management system for R&D project and portfolio management in a pharmaceutical company*”. She especially evaluated critically the relationships between elements of project quality and other project performance dimensions. She approached this question by adopting a systems perspective to quality and answering the question on how elements of a project management quality system are interrelated to achieve project excellence in a generic pharmaceutical research and development setting. Among other results Daria concluded that higher quality levels of project management processes help to eliminate trade-offs between project performance dimensions and decrease total cost of ownership of the developed products. This study was supervised by Dr. Hans Martin Schwarm.

The study of **Johannes Heusler** is entitled “*Brexit and Its Impact on Pharmaceutical Law - Implications for global pharma companies*”. By that, he combines a macro- and a micro-level perspective analyzing the impact of the UK leaving the European Union on pharmaceutical firms with a special focus on the regulatory environment. The future development as well as the post-Brexit relationship between the UK and the EU are hard to predict. The study at hand provides a comprehensive evaluation of potential changes to the regulatory framework and their consequences, focusing on the following key areas: (1) Marketing authorizations and drug approval procedures, (2) Drug manufacturing: rules on Good Manufacturing Practice (GMP) and quality of pharmaceutical products, (3) Pharmacovigilance, as well as (4) Clinical trials. Based on his analysis, Johannes derives recommended actions like the installation of a Brexit Working Group within pharmaceutical firms in order to deal with the resulting challenges. This study was supervised by Dr. Ursula Schickel.

Gaining and retaining valuable human resources is a key and constant challenge for pharma firms. The study of **Silke Baasner** is entitled “*Implementation of*

Measurable and Sustainable Actions to Improve Employee's Engagement and Business Performance - Global Medical Clinical & Regulatory Affairs (GMCRA) – A Role Model at Fresenius Kabi” and deals with this challenge. In order to bring a high performance culture to life and to add value to the company the management of GMCRA at Fresenius Kabi has started the initiative *Excellence@GMCRA*. To evaluate the status regarding employee engagement a computer assisted web questionnaire on feedback culture at GMCRA, focusing on leadership behavior and staff development, was performed. The study at hand describes the results as well as the actions implemented by the management like (1) onboarding program for new employees with a buddy concept, (2) regular 1:1 meetings with superiors and employee, and (3) individual personal development plan (PDP) for each employee. As a result of these measures the bond of employees to the company was increased, the engagement of employees was fostered, and the performance of the employees were improved. This study was supervised by Dr. Fabian Urban.

The empirical study of **Martin Lange** and **Alina Hernandez-Bark** deals also with the increasing importance of human resources and organizational effectivity and efficiency as a key success factor for pharmaceutical firms. It is entitled “*Leadership Models and Work Behavior: An Empirical Analysis of Consequences of Authentic and Transformational Leadership*”. Throughout the course of the 20th century, a multitude of empirical studies show primarily positive relationships between different constructs of leadership models and desirable variables of organizational behavior. However, the selection of analyzed leadership models and their consequences is very heterogeneous. The study at hand has the objective to contribute to Leadership Research by applying a comparative empirical study in the – until today—often neglected study population of in-house and sales personnel within the pharmaceutical industry. For this purpose, an online employee survey with N=137 participants from a leading pharmaceutical company in Germany was conducted. Based on contemporary leadership theory, a range of Hypotheses regarding consequences of modern leadership models is empirically tested. The results of the study reconfirm Identification with Manager, Trust and Loyalty as well as Employee Satisfaction as consequences of Authentic and Transformational leadership. Work context as in-house vs. sales setting shows moderating effects on some of the leadership-consequences relationships.

The study of **Elmar Hörner** analyzes the management of intrafirm relationships in the form of strategic alliances—a collaboration form that has been increasing continuously and significantly since the beginning of the 1990 in the pharmaceutical industry. It is entitled “*Alliance Management at Merck - Establishing an operational 100-day plan for alliance launches and management*” and takes a firm-level perspective. This research is motivated by the observation that the pharmaceutical industry has been facing many challenges in the past 20 years leading to a change and adaptation in business models. One of the adaptations is the increasing importance and raising number of strategic alliances. The study at hand analyzes the launch phase of an alliance and proposes an operational 100-day plan for the use during

different sub-phases in the context of the German pharmaceutical firm Merck KGaA based in Darmstadt. The focus is put on the role and skills of Alliance Management during the lifecycle of the partnership. This plan is validated by a survey with alliance managers at Merck KGaA and includes the following phases: (1) Preparation of Alliance Launch, (2) Alliance Launch/Develop Alliance Strategy, (3) Execute Alliance, (4) Evaluate Alliance Strategy, and (5) Managing the Alliance. This study was supervised by Dr. Eva Koscher.

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Relevance of Instruments for Measurements of Quality of Life in the AMNOG Context: An Analysis of the Endpoint Health-Related Quality of Life from Different Perspectives



Nadine Schneider

Abstract In the assessment of the additional therapeutic benefit of newly approved drugs, different patient-relevant outcomes are used, such as Health-related Quality of Life (HrQoL). Among the four outcomes (morbidity, mortality, adverse effects), HrQoL is the most subjective and also a relatively new outcome. This thesis focuses on the relevance of HrQoL data within the AMNOG process, including available instruments for the measurement of HrQoL. Moreover, interviews were conducted to investigate different perspectives regarding the relevance of this endpoint in comparison to the others. Until now, HrQoL is perceived more as a supportive tool rather than an equivalent criterion. Possible reasons for that are technical limitations (response rate, validated questionnaires) as well as differences with regard to the profile of requirements for the pharmaceutical company concerning the market authorization (study design).

1 Relevance of Instruments for Measurements of Quality of Life in the AMNOG Context

1.1 *An Analysis of the Endpoint Health-Related Quality of Life from Different Perspectives*

Since the Act on the Reform of the Market for Medicinal Products (AMNOG) came into effect, the pharmaceutical companies have been facing an additional burden with regard to the reimbursement negotiations with the statutory health insurances.

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Manufacturers are free to set their price for a newly approved drug in the first year after market access. Since 2011, they need to prove the additional therapeutic benefit of the new drug in order to negotiate the reimbursement price according to the therapeutic value (Wenzl and Paris 2018). The political goal was saving the sick funds 2.2 billion € per year by stemming the rapidly increasing pharmaceutical expenditures (Leverkus and Chuang-Stein 2016). Moreover, it was introduced to create a fair competition and to focus more on the patients' well-being.

The assessment of an additional therapeutic benefit is based on patient-relevant outcomes, such as mortality, morbidity and Health-related Quality of Life (HrQoL) in comparison to the standard of care. The level of additional benefit in comparison to an appropriate comparative therapy is categorized as: major, significant, marginal, not quantifiable, none or less (Leverkus and Chuang-Stein 2016). The choice of comparator is very crucial for the pharmaceutical company and it is determined by the G-BA (Federal Joint Committee), which is the highest decision making body. The decision is based on label and medical guidelines, the criteria for determining the appropriate comparator is written in G-BA's rules of procedure (G-BA 2018).

The added benefit, determined by the G-BA, is highly beneficial for the pharmaceutical company with regard to the reimbursement negotiations with the SHI. If the G-BA finds that the drug does not have any additional benefit, the SHI will pay no more than what the equivalent products (often generic drugs) already cost. Thus, the company's goal is to show an added benefit and a higher value of their newly launched drug compared to the appropriate comparative therapy to achieve a sustainable reimbursement price. In general, this requires a strategic rethinking from the pharmaceutical companies with regard to their market access strategy. They will have to learn to live with an unpredictable market access process (Sieler et al. 2015).

Among the four outcomes, HrQoL is the most subjective and also a relatively new outcome (Blome et al. 2017). The use of patient reported outcomes (such as HrQoL) in comparative effectiveness research can be challenging, for instance when it comes to the selection of appropriate instruments or interpretation of results. HrQoL data are difficult to obtain, complex and subjective. Furthermore, there are technical limitations with regard to the different questionnaires available. The G-BA only accepts certain validated questionnaires for the assessment of an additional benefit.

This master thesis focuses on the analysis of the outcome category Health related Quality of Life (HrQoL) by evaluating the different perspectives of the involved parties. The goal is to analyze the importance of HrQoL data and their significance for patient-relevance within the AMNOG process. What does an improvement of HrQoL mean for a patient in a certain indication? Moreover, how do IQWiG and G-BA evaluate HrQoL? Is this endpoint a fully equivalent outcome category within the assessment process?

2 Methods

To analyze the relevance of HrQoL data in the assessment of an additional benefit, two major strategies were pursued:

1. The primary focus of this master thesis lays on the assessment of drugs in rheumatic indications. Therefore, five newly (2015 until 2017) approved drugs in the indication areas psoriasis, psoriatic arthritis and rheumatoid arthritis were chosen and analyzed to find out whether HrQoL data were included in the dossier or not. Moreover, it was documented if G-BA and IQWiG accepted the data and if these data were crucial for the granting of an additional benefit.
2. To investigate potential differences regarding the relevance of HrQoL data within the AMNOG process, interviews with different parties were conducted: With a representative from a pharmaceutical company, vfa (Verband Forschender Arzneimittelhersteller, Association of Research-Based Pharmaceutical Companies) and with a rheumatologist/clinician. Furthermore, definitions and statements published by G-BA and IQWiG will be provided to represent the view of the regulatory authorities. This master thesis is a qualitative approach rather than a quantitative one. The goal was to get a comprehensive picture about the relevance of HrQoL data and the used instruments with their strengths and weaknesses within the AMNOG process.

3 Results and Conclusions

It seems that the endpoint HrQoL is still the most difficult endpoint to have in the benefit assessment. This is because of several reasons: Firstly, HrQoL data are based on a subjective assessment. Secondly, especially validated instruments used for the measurement are limited. Thirdly, it seems that HrQoL data are experienced rather as a supportive tool than as an equivalent criterion.

For the assessment of HrQoL patients are asked to fill in different questionnaires about their well-being or pains. Each person experiences pain in a different kind of way and in a different intensity. Moreover, the experience of pain can be influenced by different factors e.g. mental state or the personal attention of the doctor. Thus, it is very difficult to get an objective assessment about the change of HrQoL caused by a certain medication. How well represented is the change of HrQoL through this kind of questionnaires? The answer to this question is of course dependent on the indication and also on the available disease-specific questionnaires. Nevertheless, the goal of validated questionnaires is to transform a subjective opinion into an objective evaluation that quantifies the patient perception. The three main properties for the determination of outcome questionnaires are objectivity, reliability (reproducibility) and validity (content, construct, criterion) (Hamilton et al. 2017).

Difficulties also exist with regard to technical and/or organizational limitations such as low response rate or the lack of validated and suitable questionnaires. G-BA and IQWiG do not accept HrQoL data with a response rate lower than 80%. This can be challenging to achieve, depending on the indication. In rheumatic diseases, patients may not be able to fill in the form properly because their hand and finger joints hurt. Generally speaking, pain is often the reason why patients are not able to fill in the questionnaire, this being also true for other indications such as cancer. Another reason can be that the patients suffer from depression and thus are not willing to fill in the form. Sometimes the self-assessment is impaired by the disease, e.g. in case of schizophrenia and Alzheimer's disease. Furthermore, elderly people often have difficulties with that task. Some also report that some of the questionnaires are too long or that they need to fill in several ones. There are many reasons for a low response rate which are challenging to overcome. With respect to G-BA and IQWiG a low response rate leads to invalid data and a possible imbalance between the study arms, thus the data will be excluded from the assessment.

Apart from the response rate, another problem is the lack of validated and suitable questionnaires. IQWiG requests a generic and a disease-specific questionnaire for the assessment of HrQoL. However, depending on the indication, there is often no validated disease-specific questionnaire so far. In the dossiers submitted for RA drugs, the pharmaceutical company only uses the SF-36, which is a generic tool. It seems that this questionnaire works quite well for the assessment of the general health status, but there is no single question included about disease-specific problems. Patients with RA often suffer from pain in the joints. Since mostly the fingers are impaired, they are not able to get dressed or cook. For instance, they need a special solution to open a bottle of water, which often means that they need help in their daily routine. This is different for PsO and PsA, since in these two indications the pharmaceutical company mostly uses the DLQI (Dermatology Life Quality Index) questionnaire. This is a disease-specific form that addresses 10 questions with regard to skin specific problems e.g. "...how much has your skin affected any social or leisure activities?" An assessment of an improvement of HrQoL works quite well for these two indications. The introduction of new disease-specific instruments means a big effort and is not that easy to implement. A new questionnaire needs to be validated with regard to reliability, internal consistency, unidimensionality and responsiveness. Moreover, the language availability needs to be considered. Most clinical studies are international and thus the questionnaire needs to be available in a large number of languages, which means a big effort in terms of time and money (Doward et al. 2004).

It seems that HrQoL data are still perceived rather as a supportive tool than as an equivalent outcome. Especially in rheumatic indications, other outcomes have much more relevance than HrQoL within the assessment process. That can also be due to the difficulties to evaluate the clinical relevance of potential differences. What is meaningful for the patient? The minimal clinically important difference (MCID) is defined as the minimal differences in scores of an outcome measure that is perceived by patients as beneficial or harmful (Keurentjes et al. 2012).

Apparently the relevance of HrQoL data is higher in oncological disease where the disease caused a significant reduction of lifetime. In these kind of indications a substantial improvement of HrQoL, whereas morbidity and mortality are the same as with the appropriate comparative therapy, will be enough for a major added benefit (Hecken 2016).

One of the major problems is the different profile of requirements for the pharmaceutical company. For the market authorization, the focus lies on a reasonable benefit/risk ratio, which means that while designing the clinical trials the outcomes mortality, morbidity and adverse effects are much more important. HrQoL is so far no criterion within the market authorization process. Very often the trials are big international studies, which means a big effort recruiting the patients. Primarily the pharmaceutical company's goal is to obtain market authorization in the preferred countries, which also means dealing with different authorities at the same time. The pharmaceutical company is focused on fulfilling the requirements of EMA and/or FDA and that means a lot of strategic planning before running the clinical trial. The second priority is the benefit assessment in Germany where the focus is more on a patient-relevant added benefit including the aspect HrQoL data. This situation forces the pharmaceutical company to plan the clinical trials in accordance with EMA/FDA for the market authorization, but at the same time the pharmaceutical company also needs to plan the clinical trials for G-BA/IQWiG and a lot of other HTA bodies in Europe and outside from Europe to obtain a beneficial assessment for the reimbursement negotiations with the health insurances. Since the requirements differ in certain aspects, this is a really challenging and costly situation. That could prospectively force the pharmaceutical companies to rethink their market access strategy. It will get more unattractive aiming for a market authorization in Germany, if the AMNOG process is not going to improve. However, since Germany is one of the biggest markets (fourth largest worldwide) (Bütow 2017) in the pharmaceutical sector, this will not happen that fast.

Moreover, the AMNOG process could also, to a certain extent, influence the decision about which indication area it is worth to invest in concerning research activity. In some cases even really innovative new treatment options do not obtain the appropriate added benefit, which would enable the company to amortize their investment/expenses. It is not worthwhile for a company to invest in a drug which will be compared to a generic standard of care.

4 Outlook

Today HrQoL is not an equivalent criterion in the assessment of an added benefit of new drugs. However, the importance and the relevance to include such data have been increasing over time. The authorities have already started to sanction the lack of HrQoL data, at least for certain indications (Hecken 2016). The relevance to include sufficient HrQoL data is getting more important for the pharmaceutical company as well. To overcome the limitations the pharmaceutical company is facing, especially

with regard to different requirements each authority demands, the set of rules needs to be adapted.

IQWiG and G-BA should be more flexible and willing to adapt to individual solutions. An example: On the one hand, the ministry of health wants to support research in the field of new antibiotics. But on the other hand, this research is not worth financially for the pharmaceutical companies since the added benefit will most probably be compared to a generic product. The pharmaceutical companies have no chance to amortize their expenses. To solve this problem, an individual solution needs to be implemented like in the case of orphan drugs.

It would be desirable that the whole AMNOG process gets more pragmatic with regard to the medical daily practice. Partly the required high numbers of patients, which should be included in the clinical trials, are not realistic and are difficult to fulfill. Furthermore, the requested duration of the clinical trials sometimes makes no sense with regard to the mode of action of the new drug. An artificial prolongation of the study duration only to fulfill the requirements is not only very costly for the pharmaceutical company but also doubtful in terms of ethics, especially for the patients in the placebo arm. Individual and disease-specific solutions are needed here.

Speaking about HrQoL data, the question is which time frame is the optimal one for the assessment of an increase of HrQoL? In indications where depression or other perceptual disorders are increased, this could also influence the self-assessment and the assessment of their well-being. This would then lead to a non representative picture of the HrQoL status. It should be possible to adapt the design of the clinical trial in accordance with the specific requirements for the assessment of HrQoL data.

An individual adaptation of the study design only makes sense if validated and well-designed disease-specific questionnaires exist. And this for every indication. Moreover, it would be advantageous if questionnaires, which are accepted for EMA and FDA, are also accepted by IQWiG and G-BA, such as the EQ-5D form. Generally speaking, more flexibility concerning the choice of questionnaires and a greater alignment to the requirements needing to be fulfilled to obtain market authorization would be preferable.

Taken all these considerations together, the AMNOG process needs to be further developed, both for the assessment of HrQoL data and with regard to the general very technical-driven requirements. It is indeed important to regulate the price system in the pharmaceutical market, but with a certain dose of common sense and an understanding of what is important for the patients and for the well-being of the whole population. The pharmaceutical market still has a big medical need of new innovative and “cost-intelligent” drugs. The AMNOG process should not interfere with the devolvement of innovation in Germany.

There are also further developments with regard to the market access sector, which will influence the conduction of clinical trials. There will be a new Clinical Trial Regulation in 2019, which means a major change concerning the conduction of clinical trials. The new Regulation (Clinical Trial Regulation EU No. 536/2014) has the goal to harmonize the assessment and supervision process for clinical trials throughout the EU (European Medicine Agency 2014). This Regulation will repeal

the existing EU Clinical Trial Directive (EC) No. 2001/20/EC. The key benefits of the regulation are harmonized electronic submission and assessment process for clinical trials conducted in multiple member states, improved collaboration with regard to information-sharing and decision-making. Furthermore, an increased transparency of information on clinical trials and the highest standard of safety for all participants are also of importance (European Medicine Agency 2018). Similar efforts to improve the conduction of clinical trials are seen by the FDA (Food and Drug Administration US 2018). Changes regarding the planning and conduction of clinical trials will automatically influence future Health Technology Assessments. The impact of these changes on the outcome category HrQoL and its consequent implementation in the trial design will be seen and further analyzed in the future.

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Quality Management System for R&D Project and Portfolio Management in Pharmaceutical Company



Daria Mikhailova

Abstract Project management is an established multi-disciplinary knowledge area with widely accepted methodologies and ample body of research, which, however, has two major points of debate: explanations of project performance and theoretical foundation. Though general and quality-based project excellence assessment models exist, only a few studies have quantitatively demonstrated relationships between elements of project quality and other project performance dimensions. To fill this research gap, current study adopts a systems perspective to quality and answers the question on how elements of a project management quality system are interrelated to achieve project excellence in generic pharmaceutical research and development setting. Results of the study support performance frontiers theory by indicating that higher quality levels of project management processes help to eliminate trade-offs between project performance dimensions and decrease total cost of ownership of developed products. In addition, project management quality serves as the foundation for sustainable effectiveness of project management, also under conditions of external suppliers' failure. Utilized systems approach revealed not only linear relations (e.g. surrogates of system performance), but also more complex non-linear modifying, feedback loop (system learning) relations, and system evolution.

1 Introduction

Project management (PM) is an established multi-disciplinary knowledge area with widely accepted methodologies and ample body of research, which, however, has two major points of debate: explanations of project performance and theoretical foundation (Padalkar and Gopinath 2016). Discussions on project performance start from project success and failure criteria (Atkinson 1999), and proliferate in the dimension of critical success factors (Cooke-Davies 2002; Müller and Jugdev

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2012). In order to conceptualize empirical research findings and link notions of success criteria and success factors, general business excellence model was adapted to project management context (Westerveld 2003) and later augmented with organizational aspect of project quality to form a quality-based project excellence assessment model (Basu 2014). However, only a few studies have quantitatively demonstrated relationships between elements of project quality and other project performance dimensions (Harter et al. 2000). Therefore, there is a research gap between the conceptual holistic understanding of project excellence and empirical evidence to support it. In order to fill this research gap, current study adopts a systems perspective to quality (Kuhn 1974).

The research question is formulated as follows: how elements of a project management quality system are interrelated to achieve project excellence? To answer this question, a descriptive model of a project management quality system is created for the generic pharmaceutical research and development (R&D) setting, and the interconnections between its elements are studied in the light of capabilities relationships theories.

2 Theoretical Background

2.1 Theories

In the quality management literature, quality is mostly seen as a dimension of competitive advantage (Flynn et al. 1994). Trade-off theory (Skinner 1969) stipulates that competitive capabilities are contesting in nature and improvement in one dimension would imply a trade-off in another. This theory was partially supported by empirical evidence; however, accumulating counter-examples have led to the emergence of another research stream in capabilities relationship field—cumulative capabilities theory (De Meyer et al. 1989). This theory emphasizes a particular order in the development of competitive capabilities that is important to achieve sustainable improvements. It uses quality as the foundation for further capabilities acquisition, followed by dependability, speed and cost efficiency.

In the context of New Product Development (NPD) project management research, and supported by classical project management theory (Graves 1989), the existence of trade-offs between dimensions of NPD performance is largely assumed (Smith and Reinertsen 1997). However, empirical evidence regarding these trade-offs is mixed (Swink et al. 2006). It has been proposed that specific techniques can simultaneously improve NPD cost, time and quality by reducing waste in NPD project management activities via a higher level of processes maturity (Harter et al. 2000). This view is congruent with cumulative capabilities theory so that quality of project management processes form the foundation of achieving next levels of performance frontier. At the same time, due to diminishing returns from quality investments after a certain quality level is reached, there is global performance frontier that is established by state-of-the-art NPD project management (Swink et al. 2006).

Another similar approach is seen in excellence models (EFQM 2013; Westerveld 2003) that consist of Enablers (processes, behaviors, products and services, strategy, resources, and partnerships) and Results (for business, customers, people, and society). A causal relationship is assumed between Enablers and Results, and a positive feedback loop from Results to Enablers is achieved by learning, creativity, and innovation.

Mentioned theories provide a structure for studying the impact of project management processes quality on other project excellence dimensions. More specifically, they allow to conceptually describe functional-level quality management system in NPD project management in general and pharmaceutical R&D project and portfolio management in particular that can be used for systematic assessment of relationships between system components.

2.2 Pharmaceutical Project Management Quality System Model

In order to study the structure of the quality system, a Pharmaceutical Project Management Quality System (PPMQS) Model was created (Fig. 1).

This model is primarily based on the Pharmaceutical Production System Model (Friedli et al. 2017) and consists of Enabling (processes and behavior) and Result (outcomes and their metrics) systems.

Enabling system (Fig. 1, categories A, B, and C) was changed to suit project management context. It is based on IMSI Project Management Assessment Model (Holmes and Walsh 2005) and international standards for quality management in projects (ISO 2017) and portfolio management (ISO 2015). Individual enablers in category A (Fig. 1) represent project management knowledge areas. The system of category A enablers defines Project Management Quality Maturity (category B). Project governance (category C) represents portfolio management processes (ISO 2015) as viewed from a project management perspective.

Result system (Fig. 1, categories D, E, and F) was developed by analogy to Pharmaceutical Production System Model and consists of several aggregation levels of quality metrics that define Pharmaceutical Project Management Quality System (PPMQS) Excellence. At the lowest level of aggregation, individual quality metrics form compound scores of internal Operational Stability and external Supplier Reliability (categories D). Current study adopts product life-cycle approach for Effectiveness measurement of new product development (Suomala 2015). Therefore, Operational Stability incorporates post product launch metric of product quality, and Supplier Reliability category is derived from commercial supplier performance metrics. PPMQS Effectiveness (category E) is a compound score of Operational Stability and Supplier Reliability (categories D). PPMQS cost Efficiency metric (category E) is defined as a proportion of project management costs in overall

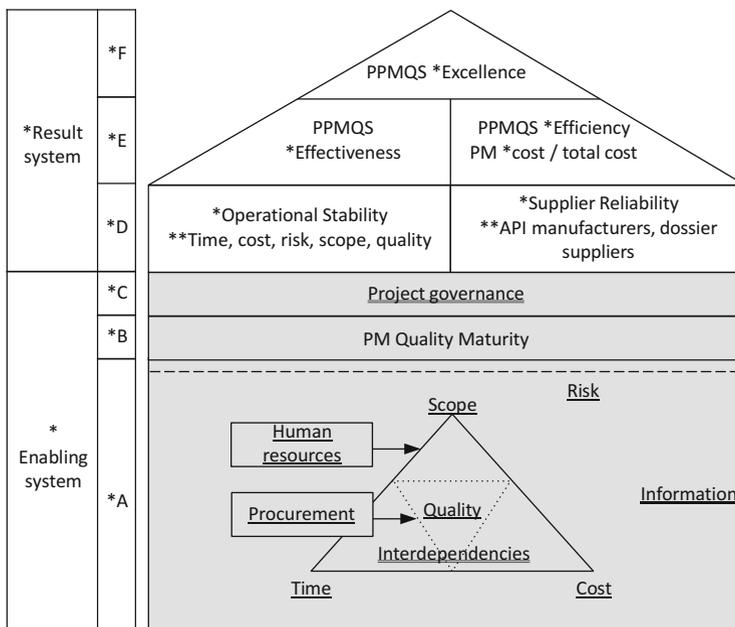


Fig. 1 Pharmaceutical project management quality system model. Coding: simple text—own definition by analogy; text with single asterisk (*)—adaptation from (Friedli et al. 2017); text with double asterisk (**)—own sub-categories and suppliers choice; underlined text—categories based on (Holmes and Walsh 2005); double underlined text—categories based on (ISO 2015, 2017) (“Information” is a compound category from several sources); grey background—own compilation of Enabling system

product development costs. PPMQS Excellence (category F) comprises both PPMQS Effectiveness and Efficiency (categories E).

2.3 Hypotheses

Based on the quality systems theories, the following hypotheses were formulated for testing in the pharmaceutical generic R&D project management context:

H1 *There is a positive link between PPMQS Effectiveness and Efficiency.*

As shown in (Friedli et al. 2017), pharmaceutical manufacturing data has proven cumulative development of effectiveness and efficiency capabilities, however, for NPD only Efficiency (but not Effectiveness) metrics were demonstrated to be positively influenced by interdependencies capabilities (Brettel et al. 2011). In a more narrow sense, project management Effectiveness and Efficiency in the new product development process are expected to be positively related, at least at higher degrees of project management maturity.

H2 *There are individual KPIs on the Operational Stability and Supplier Reliability level that can serve as surrogates for PPMQS Effectiveness.*

The goal of identification of surrogate metrics that can reliably represent whole Pharmaceutical Project Management Quality System Effectiveness was substantiated by two considerations: facilitation of analyses with compound Effectiveness score sub-components and individual KPIs, and practical interest for system monitoring and system interventions.

H3 *There is a positive link between Enabling and Result systems of PPMQS.*

Positive feedback loop from “Results” to “Enablers” in excellence models (EFQM 2013) is expected to be translated into a gradual increase in project management maturity and project governance levels that are supposed to drive PPMQS Effectiveness and Efficiency.

3 Empirical Analysis

3.1 Methodology

Current work utilizes case study approach to test stated hypotheses on a sample of 30 R&D projects within a multinational generic pharmaceutical company (STADA) completed in 2 year period between 07/2015 and 07/2017.

3.1.1 Characterization of PPMQS Enabling and Result Systems

For the Enabling system, typical maturity model was developed as a five-step progression from an awareness of project management methodology needs (level 1) to best-in-class optimized process with the focus on continuous improvement (level 5) based on IMSI Project Management Assessment Model (Holmes and Walsh 2005) and industry standards (ISO 2015, 2017), which were adapted to generic pharmaceutical industry (Babler 2010; Bode-Greuel and Nickisch 2008). Data was collected via project-level questionnaires filled by responsible project managers. The questionnaire’s face validity was established by three independent experts. Subsequently, the questionnaire was pre-tested on one of the participants (five projects).

After data acquisition from the overall sample, the validity of the questionnaire was re-assessed based on the following parameters (statistical approach from (Abramowitz and Weinberg 2016)):

- Reliability analysis per category: Cronbach’s Alpha (CA) > 0.6.
- Confirmatory factor analysis (CFA) per category as per criteria specified in Table 1. Heywood cases were excluded from corresponding categories.

For categories that passed validation, factor scores (method—regression) were recorded, and exploratory factor analysis (EFA) was used to identify common

Table 1 Parameters and acceptance criteria of confirmatory factor analysis

Parameters	Acceptance criteria
Extraction method principal axis factoring (PAF)	Percent of variance explained—minimum 50%
Analysis of correlation matrix	Convergence of replication within stated number of iterations
Fixed number of factors = 1	Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) ≥ 0.5
100 maximum iterations for convergence	Bartlett's test of sphericity with significance < 0.05
No rotation	

factors underlying the complete survey as per parameters specified in Table 1, except the following: number of factors for extraction—based on Eigenvalues > 1 ; Varimax rotation if > 1 factor extracted; factor loadings for principal factor > 0.7 . Factor scores for major factor were used as PM Quality Maturity score (Fig. 1, category B). The questionnaire was considered to be validated if most of the categories passed CA and CFA requirements, and if EFA for the whole questionnaire resulted in at least one valid factor.

Key performance indicators (KPIs) were chosen for assessment of the Result system of PPMQS, and an additional statistical analysis was performed to select KPIs with suitable reliability within the sample:

- Reliability analysis per category: CA > 0.6 .
- CFA per category as per criteria specified in Table 1. Heywood cases were excluded from corresponding categories.
- For categories that passed validation, factor scores (method—regression) were recorded for subsequent analysis (sub-categories within Operational Stability and category Supplier Reliability).
- Individual KPIs that passed validation within categories were used for data aggregation (Operational Stability and PPMQS Effectiveness scores).

Validated quality metrics from both Enabling and Result systems were used in the final statistical analysis to explore interrelationships between PPMQS components in order to test the proposed hypotheses.

3.2 Testing of Hypotheses

Hypothesis 1: correlation between PPMQS Effectiveness and Efficiency. Bivariate Pearson's Correlation on the overall sample and sub-sample of high performers (top 25%) for PM Quality Maturity score was calculated for PPMQS Effectiveness score and PPMQS Efficiency variable. Value, sign, and significance of correlation were used for interpretation of the existence of a positive link between these two parameters.

Hypothesis 2: identification of KPIs that can be used as surrogates for PPMQS Effectiveness. Bivariate correlation matrix of KPIs with PPMQS Effectiveness score was created to identify possible candidates to investigate similarity of distribution (KPIs with correlation significant at 0.05 level 2-tailed). Subsequently, linear relationship between PPMQS Effectiveness and candidate surrogates was checked via scatter plots and SPSS Test for linearity within means comparison analysis. Distribution assessment was done by splitting overall projects sample into categories of high-performers (top 25% of projects) and low performers (bottom 25% of projects) for the respective KPI. Afterwards, an independent samples t-test for equality of means was conducted for PPMQS Effectiveness score variable between these two groups with 95% confidence interval. KPIs that showed a mean difference significant at 0.05 level 2-tailed were considered to be good surrogates for PPMQS Effectiveness.

Hypothesis 3: identification of connections between Enabling and Result systems of PPMQS Model. Overall projects sample was split into high (top 50%) and low (bottom 50%) PM Quality Maturity projects and further subdivided into quadrants according to respective KPI performance (high—top 50% and low—bottom 50% of projects). An independent samples t-test for equality of means with 95% confidence interval was conducted for PPMQS Effectiveness surrogate variables between two groups of high and low KPI performers for low and high PM Quality Maturity groups. Afterwards, the effect of PM Quality Maturity on the mean difference and the significance level of the t-test was evaluated. Groups that showed a mean difference significant at 0.05 level 2-tailed were used to study mean differences on individual Enabler level with the same method.

4 Empirical Findings

4.1 Characterization of Enabling and Result Systems

Questionnaire validation resulted in 7 (out of initial 10) confirmed categories for the enablers of Scope, Time, Cost, Quality, Information, Procurement, and Interdependencies. Exploratory factor analysis based on confirmed enablers' factor scores resulted in 1 common factor explaining 66.5% of the variance for the whole system. This result corresponds to the initial goal of measuring overall project management maturity. Project governance did not form 1 reliable category, and corresponding individual questions were subsequently analyzed separately.

KPIs validation resulted in 3 (out of 4) confirmed compound categories: Cost, Quality, and Supplier Reliability. Category Scope did not pass validation as an entity, and corresponding KPIs (regulatory and market scope parameters) were analyzed separately. Bivariate correlations between Result system KPIs were investigated for linearity, and the following KPIs were found to have a linear relationship:

- Service rating and Risk increase—positive relationship;
- Supplier overall rating and Significant deviations—negative relationship.

4.2 Testing of Hypotheses

No correlation was found between PPMQS Effectiveness and Efficiency. This result holds for the overall sample and high performers for PM Quality Maturity subgroup.

Based on bivariate correlation matrix between PPMQS Effectiveness and individual KPIs, the following KPIs were selected for linear relationship check: Risk increase, Cost vs. baseline, Cost vs. plan, Supplier overall rating, Supply rating, Service rating. All KPIs except “Service rating” showed required degree of linearity. Comparison of mean values for PPMQS Effectiveness between project groups which showed high or low performance for candidate surrogate KPIs via independent samples t-test showed mean difference significant at 0.05 level for Risk increase, Cost vs. baseline, Supplier overall rating and Supply rating. All these KPIs were considered to be good surrogates for PPMQS Effectiveness from a statistical viewpoint.

Out of all studied individual KPIs of the Result system, the following two KPIs have a different effect depending on the level of PM Quality Maturity:

- Supplier overall performance. For low maturity projects, mean difference in the surrogate for PPMQS Effectiveness “Cost vs. baseline” is significant at 0.01 level. For surrogate “Risk increase” it is marginally not significant ($p = 0.059$). No such relation can be demonstrated for high maturity projects.
- Significant deviations. For low maturity projects, there is a negative difference in the surrogate for PPMQS Effectiveness “Supplier overall performance”, which is significant at 0.01 level. For other surrogates, negative difference holds and is marginally not significant for “Cost vs. baseline” ($p = 0.057$) and not significant for “Risk increase”. No such relation can be demonstrated for high maturity projects. This result is in line with negative bivariate correlation between Supplier overall rating and Significant deviations.

These results demonstrate that there is a connection between Enabling and Result systems of PPMQS. In particular, low PM Quality Maturity level reveals a strong dependence of overall PPMQS Effectiveness on external suppliers. This effect is compensated by higher PM Quality Maturity levels. The second result shows that with less rigorous supplier selection process (at lower levels of PM maturity) higher project effectiveness is realized via quality drawbacks (lower post-launch production quality).

5 Discussion

Positive validation of both Enabling and Result systems components within studied sample demonstrates the suitability of applied PPMQS model to the pharmaceutical R&D project and portfolio management context. At the same time, despite evidence from pharmaceutical production regarding the positive correlation between quality

system Effectiveness and Efficiency (Friedli et al. 2017), no such correlation could be found for the project management quality system. It should be noted that mean PM Quality Maturity level across all knowledge areas for high performers group (top 25% of the projects) was 2.32 (compared to 1.60 for low performers, on the scale from 1.0 to 5.0), therefore it could not be excluded that presence of correlation between PPMQS Effectiveness and Efficiency might be demonstrated for higher PM maturity levels.

In accordance with Excellence models (EFQM 2013), a connection was found between Enabling and Result systems of PPMQS. PM Maturity level does not have a direct influence on project Effectiveness; however, it acts as a modifier on the dependence of Effectiveness on external suppliers. This relationship partially proves Excellence models assumptions on the feedback loop from project Results to project Enablers as seen on the functional, but not individual project level. Therefore, Excellence model learning mechanism occurs across projects. In addition, study demonstrates that investments in project management processes are justified in settings of high supplier dependence (e.g., for pipelines with a substantial proportion of in-licensed projects).

Several KPIs were found to be representative of overall system: risk increase is a characteristic of high levels of uncertainty of pharmaceutical new product development; actual cost in comparison to baseline (decision point) is a measure of governance decision quality; supplier ratings emphasize the importance of partnerships quality and learning in accordance with the Excellence model (EFQM 2013).

An interesting result regarding the negative relationship between supplier rating and post-launch production quality was investigated further and demonstrated the existence of trade-offs assumed by classical project management theory (Graves 1989) between project performance dimensions during the development process and after product launch. In combination with the absence of correlation between Effectiveness and Efficiency, this result at first glance supports trade-off theory as opposed to cumulative capabilities theory. However, this conclusion holds only in conjunction with low PM quality maturity. Therefore, higher quality levels of project management processes help to eliminate trade-offs between project performance dimensions in accordance with performance frontiers theory (Swink et al. 2006) and decrease total cost of ownership of developed products.

Present study made two main contributions to the research domain. First, it supported quality-based understanding of project excellence by demonstrating that project management quality serves as the foundation for sustainable effectiveness of project management, also under conditions of external suppliers' failure. Second, utilized systems approach to project quality allowed comprehensive analysis of interconnections between system components, which helped to reveal not only linear relations (as for identified surrogates of system performance), but also more complex non-linear modifying, feedback loop (system learning) relations, and system evolution (changing the level of performance frontier).

Identified patterns of the pharmaceutical project management quality system require further research. Notably, the generalizability of the findings should be investigated, e.g. via a multiple case study approach. Cross-sectional studies of

generic pharmaceutical companies with significantly different levels of project management quality maturity would allow to increase sample size and examine causal relationships between quality system components.

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Brexit and Its Impact on Pharmaceutical Law: Implications for Global Pharma Companies



Johannes Heusler

Abstract With the United Kingdom's (UK) referendum on the 23rd of June 2016 the majority of the British electorate voted for a withdrawal of the UK from the European Union. The term Brexit was already established some time before, but now it became reality. Based on the outcome of the referendum, on 29th of March 2017 Prime Minister Theresa May officially handed in the application for the exit according to Article 50 of the Treaty on the European Union. As a consequence, the UK will have to leave the European Union until the 29th of March 2019.

After the momentous referendum vote and connected withdrawal decision, a lot of discussion about the economic, legal and social outcomes of the first in history withdrawal of an EU member state arose. There are still many uncertainties on how the exit will look like and what the consequences are. Brexit and also its potential implications for the regulatory environment within the health care system quickly became one of the hot topics within the pharmaceutical industry. Due to the highly regulated environment surrounding medicinal products throughout their life cycle, the favours of the Union have become more vital than in any other sector of industry.

The derogation coming along with the UK's withdrawal are therefore expected by many to hit pharma exceedingly hard. Especially multinational pharmaceutical companies operating in the UK might be affected in various ways and areas and therefore need to prepare for changes by identifying key business issues, mitigating risks and creating plans for multiple scenarios.

The future development as well as the post-Brexit relationship between the UK and the EU are hard to predict. As negotiations are ongoing some tendencies on how the future relationship could look like became apparent. However, there are still many open questions for the industry as well as for the regulators. This might lead to serious risks but maybe also opportunities connected with the different Brexit scenarios and their impact on pharmaceutical law.

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This master thesis provides a comprehensive evaluation of potential changes to the regulatory framework and their consequences, while focusing on the following key areas:

- Marketing authorisations and drug approval procedures
- Drug manufacturing: rules on Good Manufacturing Practice (GMP) and quality of pharmaceutical products
- Pharmacovigilance
- Clinical trials

The evaluation finally aims for providing guidance for global pharma companies, which are facing challenges in that specific area. What are the potential impacts and risks that are connected with different Brexit scenarios and the related changes to the regulatory environment for pharmaceuticals? Which aspects do impacted companies need to consider in order to prepare for different Brexit scenarios?

To answer those questions, the master thesis is focusing on review and discussion of currently available publications and literature in this field and evaluate different options and scenarios. The scenarios are assessed regarding their impact on the pharmaceutical industry, while summarizing potential risks and possible mitigation actions. The review also takes into consideration expert opinions from regulators and industry associations. The master thesis is supposed to scrutinize the currently available information and summarize the potential impact on the regulatory environment. This is the basis to derive guidance for companies to prepare for the different scenarios, taking into account their respective probability of occurrence. Impact on health authorities, e.g. the European Medicines Agency (EMA), and consequences for health care systems related to the discussed aspects are also taken into consideration. Own ideas for problem solutions are introduced as applicable.

The master thesis is reflecting the state of affairs as of the 7th of August 2018.

Due to procedural reasons any publication or event after this date is not considered anymore. The following chapters represent a compendious aggregation of the master thesis content but not the full text of the original master thesis.

1 Brexit Scenarios

The UK's withdrawal from the European Union is supposed to be set in stone since Prime Minister Theresa May officially handed in the respective invocation according to Article 50 of the Treaty on European Union on 29th of March 2017. According to the given procedure for leaving the EU the period for related negotiations is limited to two years. Unless there will be an agreed extension, the EU treaties will cease to apply on 29th of March 2019 at midnight. The statutory negotiations technically started when the UK submitted the notification letter. This chapter provides an overview on the guidelines for the Brexit negotiations as agreed by the group representing the remaining EU27 member states in the EU Council late April 2017. Furthermore, the possibility of a transitional period as well as four basic exit scenarios resulting in different types of post-Brexit relationship between the EU and

the UK are assessed: The EEA scenario, the EFTA scenario, the FTA scenario and the WTO scenario.

The WTO no-deal scenario is expected to have the maximum impact on the pharma industry with total separation of the UK systems for pharmaceutical regulation from the EU. According to the overall assessment, a hard Brexit seems to be the most likely scenario considering the current state of affairs, but there is still hope that at least some kind of free trade and mutual recognition agreement will be negotiated. Considering the limited time until the withdrawal becomes effective, the political disagreement that is still predominant in the UK as well as the sagging negotiations between both parties, the risk that the UK will leave the EU without a deal must not be underestimated.

2 Impact on the Drug Regulatory Framework

This chapter addresses the potential impact of the UK's withdrawal from the European Union on the European drug regulatory framework. Still, there are many uncertainties connected with the UK's withdrawal from the European Union and the resulting non-applicability of European pharmaceutical legislation. Following the progress of ongoing discussions and negotiations it seems to be rather unlikely that the EU will seek any EEA or EFTA membership. Instead the future relationship seems to be strongly dependent on how successful the negotiators will be in swiftly reaching a consensus on a bilateral contractual framework outlining the terms and conditions of the future relationship, including agreements on free movement of medicines and mutual recognition of related regulation and procedures. At this stage the impact on pharmaceutical law is accordingly undetermined and may vary significantly depending on the possible mutual recognition of drug regulatory key issues.

After considering the general drug regulatory environment selected the following key aspects are discussed in the respective sub-chapters: Relocation of the EMA, Marketing authorisations, drug manufacturing, pharmacovigilance and clinical trials.

3 Recommended Actions for Companies

Unfortunately, the most probable post-Brexit scenario seems to be that the UK will become a third country after leaving the EU, entailing significant changes of the drug regulatory environment. Even if there is hope that agreements of mutual recognition will be put in place subsequently, the industry needs to prepare for the regulatory consequences related to the 'no deal third country situation', which is about to become reality end of March 2019. Relying on the transitional period or betimes available arrangements is considered highly risky.

In a summary report that was published by the European Commission in March 2018 following a technical seminar addressing questions related to pharmaceuticals, the authority clearly expressed concerns regarding the level of preparedness of the industry (Boehm 2018). In the meantime, the situation may have changed as most likely more and more companies have become aware of the seriousness of the situation. However, it is assumed that there is still need for action in the industry, justifying the elaboration of recommendations for companies as outlined below.

Pharmaceutical companies play a critical role in ensuring continued supply of medicines after Brexit and in minimizing expected disruptions and impact on public health in the UK and the EU.

The first step to prepare for Brexit is to identify and analyse the company specific key business issues and areas requiring adaptations. This is prerequisite for creating mitigation strategies and concrete action plans. The consequences can be quite serious. In the worst case the companies might even be forced to revoke products from the market. The sooner the companies start acting the lower is the risk of running into Brexit-related regulatory non-compliances or supply issues.

The list of questions that should be carefully assessed by the companies is quite long, including the following examples: Which organizational changes are necessary? Which processes need to be adapted? Which products and supply chains are affected? Which transfers of pharmacovigilance, manufacturing, testing or release activities are needed and what are the different options?

Pharmaceutical companies that seek market access of their products in the UK and in the EU member states in the future must have at least a legal entity in both territories representing the marketing authorisation holder for each product. This is primarily impacting companies that used to have their centralised marketing authorisations based in the UK. Without transferring the marketing authorization holder to one of the remaining EU/EEA member states, such products may not anymore be released to the EU/EEA market after exit day. Of course such changes usually are associated with additional financial and human resources. Detailed planning of such transfers and related timelines in alignment with other ongoing regulatory activities related to the concerned products is indispensable, especially if there are numerous licences concerned. Companies should act as soon as possible in order to make sure the required resources are available in due time, supporting a smooth transition and transfer of activities.

Related artworks changes, usually affecting folding boxes and patient information leaflets, should be initiated in due time to ensure undisrupted supply of regulatory compliant medicinal products after the MHA transfer.

Pending requests for transfers of RMS responsibility to an EU/EEA member state should be initiated immediately. It is essential to assess the suitability of the new RMS country. For example, all available formulations and strengths of the products must be registered in the proposed EU/EEA member state. The transfer of RMS responsibility must be agreed by both MHRA and the competent authority of the to-be RMS.

Companies that used to have legal representatives for clinical trials in the UK need to assess the need for transfers of this role to an EU/EEA member state.

Depending on the number of trials requiring such changes the transfer of the legal entity could trigger a substantial amendment for all multinational or global clinical trials with any EU/EEA country participating in countries where a grouped amendment for all studies will not be possible. Similar to the transfer of licenses, a detailed plan and timetable would be necessary to integrate the change into other substantial amendments or initial clinical trials to reduce the resource burden.

Acquisition of key personnel such as the QP or the QPPV might also represent a challenge for companies that need to transfer those roles and related activities from the UK to a site in the EU/EEA. Therefore, companies should not wait too long to start recruiting or staff relocation activities. In addition, there might also be opportunities for internal talent management and selective personnel development in order to fill such positions.

Transfers of regulatory relevant activities, such as importation, QP certification, release testing or storage of reference samples is usually connected with high efforts and costs regarding sourcing and qualification. In the best case the company has already labs or release/importation organisations in place in the EU/EEA that can act as acceptor site for such activities. Especially if a new location needs to be established, the investment and expenditure of time usually is incomparably higher. Outsourcing of selected activities to contractors could be an option.

Due to expected bottlenecks regarding the processing of regulatory relevant changes by the authorities, respective preparation and submission of marketing authorization holder transfers and variations should be made sufficiently early. Any last-minute action should be avoided.

It is strongly advised to proactively get in touch with relevant authorities, e.g. EMA and seek support and advice, especially in case of open questions regarding the changing regulatory environment.

Building up safety stocks of material that was already released to saleable stock could help to bypass a certain period of pending approvals and safeguard companies against running into supply issues. Some of the major pharmaceutical companies such as Novartis and AstraZeneca already informed the public about plans to increase their stockpiles for that reason (Mancini 2018) and (Sabbagh 2018). Indeed, this seems to be a good backup, at least for companies that are not sure if they will manage to have all necessary transfers and approvals in place allowing for regular and compliant release of their products post-Brexit.

Companies operating in the EU and the UK are usually impacted in several ways and the challenges they are facing mostly prove to be rather complex. It is therefore recommended to establish a cross-functional Brexit Working Group within the company including drug regulatory subject matter experts as well as representatives from the impacted sites and departments such as manufacturing, quality, artwork management, drug safety, clinical development and legal. Supportive functions like informatics or human resources (e.g. when it comes to recruiting of relevant key personnel) might be involved as needed. Depending on the identified key issues, management should clearly define the respective roles and responsibilities of this taskforce. In addition, it is essential to establish reporting structures, escalation pathways and business processes facilitating a functioning co-operation of executing

departments regarding the timely implementation of agreed actions. Close collaboration between all involved sites and functions is indispensable. For example, the Brexit Working Group could perform the following tasks:

- Initiate and track necessary actions according to a detailed action plan that is based on the ongoing impact assessment. Regular reviews and reassessments are obligatory due to the many uncertainties regarding the political development and potentially changing regulatory implications as Brexit negotiations are running. At this point a lot of information is still pending.
- Provide support for the transfers and redistribution of activities and staff relocation as applicable.
- Coordinate marketing authorisation transfers, orphan drug designation transfers and variations regarding manufacturing, import testing as well as release activities and drive respective dossier preparation.
- Ensure close collaboration with relevant health authorities, e.g. EMA and MHRA, meaning that the Brexit Working Group is accountable for the overall plans and at the same time remains in close exchange with the appropriate contact persons at the authorities. If possible, the working group should be the single point of contact for any Brexit-related communication with authorities. At a minimum any such health authority communication should be aligned with the working group as a coordinating function.
- Keep stakeholders informed and escalate issues to upper management as needed.
- Increase internal awareness about the expected changes of the pharma regulatory framework and the resulting need for adaptation. This could be done by internal newsletters, trainings or informative talks at town hall meetings.
- Exchange with relevant industry associations and, as applicable, with other companies facing similar challenges.

This list of suggested activities is to be considered as a general recommendation and needs to be adapted to the specific needs of the company.

Another recommendation is to engage actively in lobbying. Companies should use their policy departments or other appropriate functions to constantly address any pain points or risks the company is facing related to Brexit and the upcoming changes of the drug regulatory framework. Collaboration with other affected companies and membership in industry associations has proven to be an effective way to make sure that the voice of the industry will not be missed in ongoing negotiations and political discussions. Many companies have been actively involved in forming the voice of the industry ever since the UK's withdrawal referendum, mainly through industry associations such as EFPIA, B.A.H. or vfa, in order to influence the political trends. However, for companies that used to be rather reserved and did not yet utilize their full potential in this field it is still not too late to start taking an active role and engage in shaping the industry's future.

4 Conclusions and Outlook

Brexit is surely amongst the biggest challenges for the pharma industry in the present age. In order to make estimations on the implications and recommendations for companies, careful evaluation of the political situation and regulatory framework is essential. In the first part of the master thesis three basic scenarios have been discussed related to the post-Brexit relationship between the EU and the UK: the EEA scenario, the EFTA scenario and the WTO/FTA scenario. The latter one is clearly considered to be the most likely basic scenario. However, the overall impact strongly varies between the sub scenarios which are subject to different kinds of free trade agreement options. The so-called 'hard' Brexit seems to be the most likely scenario considering the current state of affairs and the risk of a no-deal scenario is growing constantly as the exit date is coming closer. Most likely there will be a transition agreement covering the period from exit day until end of December 2020. However, considering the plenty of open problems to be solved and questions to be clarified, the risk remains high that the new exit date of new year's eve 2020 might still not be sufficient in order to ensure an orderly exit and to settle adequate agreements regarding the future relationship between the UK and the EU.

Some hope is still left that there might be some kind of free trade agreement in place at the day of Brexit paving the way for contractual arrangements of mutual recognition related to major drug regulatory aspects between the UK and the EU. However, the probability of occurrence for a no-deal hard Brexit seems to be dominating. Consequently, this is the scenario that the industry is recommended to prepare for, especially in order to mitigate risks for patients and public health.

The comprehensive evaluations of selected key areas of pharmaceutical law revealed that such a no-deal Brexit would severely impact multinational pharmaceutical companies operating in the UK. Such companies are usually affected in various ways and need to prepare accordingly.

Installing a Brexit Working Group or taskforce assessing the need for action and coordinating the resulting activities is considered to be a kind of best practice approach, at least for companies that need to deal with several adaptations and changes in parallel. Taking action proactively and sufficiently early is key in order to ensure adequate preparedness and to minimize any risk for non-compliances and resulting supply issues of pharmaceutical products.

At this stage of negotiations there are still many uncertainties. The different scenarios and their evaluation may be useful to understand the potential consequences and to prepare as good as possible for the expected changes of the regulatory framework. Yet, only the future will show the final impact of Brexit on the industry and public health. Without any doubt Brexit will serve as a gigantic case study. It would be interesting to review the evaluations and recommendations of this master thesis in some years and compare it to the actual events as part of the such a case study.

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Implementation of Measurable and Sustainable Actions to Improve Employee's Engagement and Business Performance: Global Medical Clinical & Regulatory Affairs (GMCRA) – A Role Model at Fresenius Kabi



Silke Baasner

Abstract The department *Global Medical, Clinical & Regulatory Affairs* (GMCRA) was founded in 2010 and is *Fresenius Kabi's* driving force and strategic unit for medical, scientific and regulatory affairs. This unit provides global standards to ensure the safety of products and patients. Since its foundation, the team as well as its tasks and responsibilities are continuously growing and the department has a clear understanding of how to develop further. The basis for this development process is an ambitious strategy, excellent operations and a strong high performance culture. To bring a high performance culture to life and to add value to the company the management of GMCRA has started the initiative *Excellence@GMCRA*. To evaluate the status regarding employee engagement a computer assisted web questionnaire on feedback culture at GMCRA, focusing on leadership behavior and staff development, was performed. In the following article the results are described as well as the actions the management decided to implement, namely:

- Onboarding program for new employees with a buddy concept
- Regular 1:1 meetings with superiors and employees
- Individual personal development plan (PDP) for each employee

At the end of the chapter a conclusion is drawn if the overall goal to increase job performance of employees within GMCRA has been reached and if this has a positive effect on business performance.

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1 Background

GMCRA is a globally acting department within the *Pharmaceuticals Division of Fresenius Kabi*. In the year 2014, the initiative *Excellence@GMCRA* was kicked off to shape the future of the department as well as to foster business performance. To observe the status quo regarding the satisfaction of employees and to figure out, which processes can be improved within GMCRA a first *Employee Online Survey* regarding “Feedback Culture at GMCRA” was performed. With every one of the 75 GMCRA employees participating in the survey, the commitment was extraordinarily high. The survey was performed as a computer assisted web interview, which was self-completed by the participants, managed and hosted by an independent international research company. All responses were handled strictly anonymously. In the present article, the first part of the survey with six questions dealing with the leadership behavior and staff development will be analyzed and discussed. The summary of results is depicted in Table 1.

In a nutshell, the results of the survey as well as the outcome of group work from a GMCRA *Excellence Conference* demonstrated that no strong feedback culture is established in the organization (only 64% agree on getting sufficient feedback from their superior) and many colleagues (~ 62%) felt a lack of personal development options and wanted more transparency about career progression. Additionally, GMCRA lacked a common guideline on the onboarding process of new employees. As a consequence, new team members often felt not being welcomed enough and had not developed a team spirit. Furthermore, tasks and competences were not communicated appropriately within the organization and team members felt hesitant to contact colleagues from other groups within GMCRA.

For the preparation of concepts to establish a sustainable feedback culture at GMCRA as regular part of the day-to-day work from the beginning, several working groups were formed. They consisted of team members from different management levels and met regularly during the course of the last years. This effort should enable

Table 1 Summary of results of employee online survey

Question	Agree [%]	Indifferent [%]	Disagree [%]
I get sufficient feedback from my direct superior?	64.0	32.0	4.0
I can understand and follow the feedback I receive from my direct superior?	82.7	16.0	1.3
I feel valued by my direct superior?	84.0	9.3	6.7
The work expectations of my direct superior are clear, understandable and comprehensible?	72.0	26.7	1.3
I can have a constructive and critical dialogue with my direct superior?	80.0	16.0	4.0
My direct superior points out specific strengths and development opportunities to me in regular employee feedback sessions?	37.3	41.3	21.3

Own representation based on the survey results

all team members working together much closer and to become even more effective. Furthermore, an atmosphere should be generated allowing that everybody can fearlessly and candidly address feedback, independently from hierarchies and departments. After alignment with the management team, the respective working groups suggested the following actions to be implemented at GMCRA:

- Onboarding program for new employees with a buddy concept
- Regular 1:1 meetings with superiors and employees
- Individual personal development plan (PDP) for each employee

2 Statement of Expectations

2.1 With Onboarding the Bond of Employees to the Company will be Increased

To generate a welcome atmosphere and to increase the team spirit from the beginning an onboarding program with a buddy concept was developed in close collaboration with colleagues from the *Talent Management* department of *Corporate Human Resources (CHR)* at *Fresenius SE*. The concept for onboarding at GMCRA is a systematic process with a personal touch and shall ensure a fast adaptation and identification of new employees with the department. The elaborated process proposal was introduced to all team members on a *GMCRA Excellence Conference*. After approval by the local works council of *Fresenius* according to German law (*Betriebsverfassungsgesetz*), it was set in force in July 2018. One important part of the program is the onboarding plan where different topics are covered: e.g. administrative aspects (work place and IT systems), social aspects (networking systems, teambuilding events and company related sport activities), professional aspects (trainings, webinars and mentoring program), cultural and legal aspects.

The onboarding is divided in different phases: before day 1, day 1, week 1, month 1–3 and month 4–6 and is completed after 6 months. During these phases several feedback sessions are recommended. Each new employee is supported by a buddy who is defined as a fellow employee providing advice and guidance. In general, the onboarding process should help to settle an outsider down to the workplace and to the respective company culture.

2.2 Regular Feedback Meetings with Superiors will Engage Employees

As a first step on the way to implement a strong feedback culture within GMCRA and true to the motto ‘Leadership is a language game’ (Van Quaquebeke and Felps 2018) a seminar was designed. The *Constructive Feedback & Criticism Workshop*

was conducted for all team members. In the theoretical introduction of the workshop definitions of feedback and criticism were given and the purpose and importance of feedback for individuals and organizations and the qualities of constructive feedback were explained. In the practical part exercises on giving and receiving of feedback were performed and ways to facilitate discussions were trained. Additionally, a proposal for the feedback practice in GMCRA including a guideline on expressing criticism clearly and constructive was worked out.

2.3 Personal Development Plans will Lead to Better Performance

The last expectation that PDPs will lead to better performance is due to my personal experiences. Since I have started my work in the department GMCRA 8 years ago, I have implemented PDPs for each member of my team. The preparation of the development plan is carried out on a voluntary basis and the level of maturity was individualized. After a management assessment and accompanied by colleagues from the *Talent Management* department of CHR at *Fresenius SE* training measures for professional knowledge as well as for soft skill development are discussed and agreed on with the respective employee. All activities are collected in a personal document and are constantly adapted to individual needs. Thereby, the personal development planning is a cyclical process according to the *Chartered Management Institute (CMI)* and consisting of seven steps (Managers.org.uk 2013). After defining the purpose for development of the employee the needs are defined and appropriate training or development opportunities are selected. The action plan is generated and the agreed actions are conducted. At the end of the cycle the outcome is evaluated and further directions are defined. The steps have to be adapted to changed goals or needs after each cycle round. This process needs a close collaboration and regular feedback between superior and employee leading to a deep relationship. In my point of view, this continuous caring is associated with an increase of engagement and therefore a better performance.

3 Managerial Implications

To improve performance and sustainability within an organization, mechanisms to track progress for meeting goals and executing strategies need to be transparent. Organizations, especially in the health care sector, have a responsibility to follow current market trends of lowering cost and simultaneously improving quality and patient satisfaction. Therefore, balance in managing the needs of various customers as for example patients, health care providers and insurance companies are important. Strategic goals can be monitored using a *Balanced Score Card* as a strategic

management tool as described in the publication of Kaplan and Norton (Kaplan and Norton 2007). As well as the classical financial and operational measures the management of employees has to be taken into account. A new area of “people management” has started and employees are defined as “human capital”. Recently, Ram Charan and co-authors published the book *Talent Wins—The New Playbook for Putting People First* (Charan et al. 2018). In particular, the book was written for top managers and leaders with the goal for teaching them, who and not what the key to the future of their company is. Each of the three authors is quite experienced in consulting board members of large, globally acting organizations and assisting them by generating value and becoming most competitive. They wrote this book after having recognized the tremendous shift in the importance of what is really driving the value of companies’ success, namely the talent management. By using real world examples and sharing best practice approaches from companies like *Amgen*, *General Electric* and *PepsiCo* they draw a clear picture, how to reshape human resources tasks and responsibilities and to create a talent-driven organization (Charan et al. 2018).

The press release regarding the *Gallup Engagement Index 2016* clearly accentuates the above mentioned facts. In this article the business numbers for Germany were published proving that the engagement of employees is directly connected to the performance of an organization. In the headline of the respective press release, the authors pointed out that ‘*Schlechte Chefs kosten deutsche Volkswirtschaft bis zu 105 Milliarden Euro jährlich*’ (Translation: Bad bosses cost the German economy up to 105 billion Euros per year). The results of the *Engagement Index* clearly showed that only 15% of employees in Germany are engaged, whereas 85% are not engaged or actively disengaged at work (Nink 2017). Most of the employees in Germany have no emotional bonding to their company resulting in competitiveness factors as rate of absence, reduced productivity and quality and customer loyalty. Additionally, this is associated with high turnover, and every third employee in Germany is looking for a new job. There is a large gap between wishes of employees and the reality regarding leadership skills of supervisors. Only 21% of employees are happy with and motivated by the behavior of their superior. The lack of feedback is a main issue for the employees dealing with their respective leaders in the day-to-day business. Only 14% of employees report a continuing feedback process over the year, and only 38% feel that the feedback they receive from the superior is helpful to improve their work outcome (Nink 2017).

A comparable percentage distribution of engaged versus not or disengaged employees worldwide is reported by Jim Harter (2017) in his recent *State of the Global Workplace* report. In this report, data from employees in 155 countries were assessed regarding the effectiveness of organizations fostering employee’s engagement. Worldwide the proportion of full-employed adults, who are enthusiastic and highly engaged about their work and workplace, is only 15%. According to Harter, this low number of engaged people limits organizations in the creation of a high performance culture. Companies with high engaged employees are 17% more productive and 21% more profitable in comparison to companies with a high number of disengaged people. The research of Harter and colleagues clearly shows that

engagement as well as performance can be fostered by the fulfillment of basic human needs (J. Harter 2017).

In my point of view, these numbers are alarming because they are on the same high level for more than a decade.

But luckily, the recently published survey results of the *Chartered Institute of Personnel and Development* (CIPD) showed the increasing awareness of organizations to invest in people or talent management activities, which is seen as a competition factor. Therefore, 54% of CEOs in the UK participating in the survey stated that talent management has a very high priority and the budget for employee development has increased (CIPD.com 2017).

For an organization it is highly important to optimize profitability as well as to balance short-time and long-time goals within the business model to guarantee sustainable success. This follows a very simple rule: For sustainable financial growth, customers have to keep being satisfied and therefore, products or services have to add value to the customers. To achieve the highest level of satisfaction for the customer, companies have to deliver excellent products. This is closely related to engaged people working within the companies. To assess how effective organizations are delivering products and services and on what level of excellence they are working, a holistic approach is needed. The *European Foundation for Quality Management* (EFQM) *Excellence Model* provides a framework that encourages the cooperation, collaboration and innovation and helps organizations to increase their effectiveness (EFQM.org 2017).

A practical application of the EFQM *Excellence Model* is described in the article of Miriam Garbarova (Garbarova 2017). According to Garbarova, every organization needs success and is trying to be successful. Thereby, the employee is a key factor to generate success. In her article Garbarova describes the EFQM *Excellence Model* as a beneficial tool for the improvement of human resources management. She concluded that the use of the EFQM *Excellence Model* can lead to increase companies' ability to compete and to satisfy their employees.

3.1 Implications on Fresenius Kabi

What can we, as managers, learn from these very positive examples? Beside the above described high impact of "people management" and the importance of "human capital" organizations like *Fresenius Kabi* have to meet requirements from several authorities, e.g. *European Medicines Agency* (EMA), *U.S. Food & Drug Administration* (FDA), *Federal Institute for Drugs and Medical Devices* (BfArM). Therefore, employees of healthcare companies have to follow strong rules and regulations. By the implementation of standards which are merged in a Quality Management System (QMS), the control of compliance is simplified. Typical standards for a QMS are published by the *International Organization for Standardization* (ISO), e.g. *ISO 9001* (iso.org).

From my point of view, it is strongly recommended to follow the example of other organizations like *Robert Bosch GmbH Blaichach Plant*, one of the three *Global EFQM Excellence Award* winners in 2017 (EFQM.org 2017), and to extend the QMS of *Fresenius Kabi* with aspects of the *EQFM Excellence Model*. Interestingly, *Vamed KMB*, a company belonging to *Fresenius SE* group and being in charge for the technical operation of the *Vienna General Hospital* was the *EFQM Excellence Award Prize Winner 2015* in the category “adding value to customer”. *Vamed KMB* is using the *EFQM Excellence Model* since 2003 and was awarded three times from 2010 to 2013 in different categories (Vamed.com).

Zinta S. Byrne (2014) proposed a very simplified model in her book about the understanding of employee engagement. According to this model, job engagement is based on three parts: The personal environment, the work environment and the person itself. In relation to the time the interaction of these three parts prognosed how engaged an individual will be. Thereby, the *Personal Environment* is defined as external regarding to the job (e.g. family, friends, house, health); the *Work Environment* defined as internal (e.g. organizational culture, leadership, internal resources, support and stability) and the *Person* itself (e.g. personality, identification and focus). The model consists of various cycles showing that the process of engagement is self-sustaining and engagement itself can stimulate more engagement over time.

As to my judgment, this model fits very well to the topic discussed within this chapter, and I tried to adapt the model accordingly in Fig. 1. The managerial actions, which will be implemented at GMCRA, are related to the work environment at GMCRA. An engaged team member, who has chosen to use these actions for further development will be motivated internally resulting in more engagement.

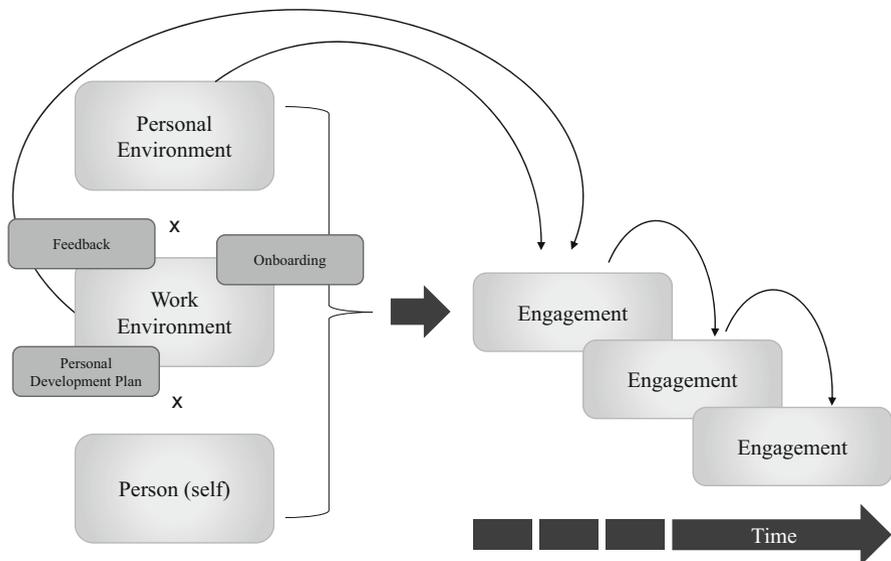


Fig. 1 Proposed model of employee engagement. Own interpretation based on Byrne (2014, 199)

The actions to increase employee's engagement, which can be fitted into this model, included but are not limited to onboarding, regular 1:1 meetings and PDP. Other measures are currently discussed within GMCRA, e.g. job rotation, mentoring program, flexible working times, international exchange program or attractive working space. The most advanced activity is the mentoring program, which is planned since 2 years and will be rolled out at *Fresenius Kabi* and *Fresenius SE* soon. With the help of mentors, ambitious employees can increase their self-reflection about opportunities and development possibilities at *Fresenius Kabi* based on the experiences of the mentors.

4 Direction for Future Research

The most obvious future research is to perform the second *Employee Online Survey* at GMCRA. This is recommended not earlier than 1 year after implementation of the described managerial actions. For further research, a larger group of *Fresenius Kabi* employees should be included in the survey, or the circle of participants should be spread out to appropriate departments within the *Pharmaceuticals Division* with approximately 5000 employees. In the meantime, the monitoring and evaluation framework of the initiative *Excellence@GMCRA* should be developed. The use of a planning tool, e.g. a *Planning Triangle*, could help to clarify what should be achieved and on the basis of the *Planning Triangle* a list of outputs and the respective output parameters can be defined. The outputs should be prioritized; measures set realistically and number of output indicators limited. Thereby, the planning of how to measure "soft" outcomes (e.g. engagement of employees) has to be done very carefully. Because the change of how people think or feel is impossible to assess directly, it could be useful to measure observable behavior changes. Therefore, appears to be helpful to set more targeted indicators such as participant's reactions to and satisfaction with training programs or employees changes in knowledge, skills and attitudes and lastly there modified on-the-job behavior. During the course of the research, the regular review and the adaptation of the prioritization of outcome indicators is needed. Survey questions, topics for focus groups and interview schedules can be defined according to the outcome indicators. In this context the publications by Stockmann (2006) as well as the consultancy of the *Center for Evaluation (CEVAL)* could be helpful (Stockmann 2006).

5 Conclusion

The purpose of this article was to describe the implementation of managerial actions like onboarding, regular 1:1 meetings and individual PDPs to improve employee's engagement and business performance at GMCRA. Furthermore, an attempt has

been made to figure out how the effects of the described actions can be measured and sustainability ensured.

In summary, the stated expectations could be verified by using literature data and first impressions of GMCRA employees as well as by setting the context in relationship to other organizations. By describing the combination of a QMS with an excellence model and by applying this to the circumstances at *Fresenius Kabi*, recommendations for managers were derived. Furthermore, a proposal for a model of employee engagement was adapted to the managerial actions implemented at *Fresenius Kabi*.

A take home message of this article is that “human capital” is of highest importance, and in times of shortage of skilled professionals, bonding of employees to their organization is a key performance factor.

Numerous studies and surveys performed by well-known researchers and management consultancies, e.g. Gallup, McKinsey or Deloitte, have shown that the emotional bonding of employees to their company is dramatically bad (Harter et al. 2016) and 85% of employees are not engaged with their work and workplace (Nink 2017). As a consequence thereof, it was predicted that 66% of the Millennials (Generation Y, born between early 1980 and early 2000) will leave their company by the year 2020 (Deloitte.com 2016).

Gary Hamel, one of the most famous American management experts, advised to change the most common way of thinking of leaders, who believe that the needs of the organization have to be put in front or on top of the individual needs. In this regard, the needs from an individual employee have to be put first, followed by the institutional needs. In an environment with less hierarchy and more autonomy, talents are able to grow and will be committed to high performance. Instead of being depleted and exhausted because of overloading activities like doing email communication, attending in unproductive meetings and preparing redundant presentations, good leaders should be a role model, should lead by example, should be transparent and thereby, should build trust (Hamel 2012).

GMCRA has started to put people first and to establish a convincing feedback culture. It can be expected that the first implemented actions will lead to increased engagement of employees and to an improved performance culture of GMCRA. With a continuing evaluation process, as described, and a regular adaptation on business needs, sustainability and long lasting success will be ensured. To get support on this journey, a membership in the non-profit organization EFQM is recommended. By combining the EFQM *Excellence Model* with the existing *ISO 9001-2015* standards at *Fresenius Kabi*, a high performance culture can be built up and competitiveness can be increased.

Currently, several departments within *Fresenius Kabi* are acting as a role model, and different actions regarding “people management” are established within the organization. Hopefully, these jigsaw pieces will be merged and a commitment for putting people first will be achieved in the whole organization in the near future. According to literature and following the experiences of large, global companies, e.g. *Bosch Group*, the business success will also be reflected in financial KPIs after a certain time.

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Leadership Models and Work Behavior: An Empirical Analysis of Consequences of Authentic and Transformational Leadership



Martin A. Lange and Alina Hernandez-Bark

“The greatest leader is not necessarily the one who does the greatest things. He is the one that gets the people to do the greatest things.” (Comment by Ronald Reagan, former U.S. President)

Abstract With increasing importance of organizational effectivity and efficiency measures like Balanced Scorecard and optimization of employee work behavior to achieve higher organizational efficiency, Human Resource activities concerning leadership development and academic leadership research are growing. Throughout the course of the twentieth century, a multitude of empirical studies show primarily positive relationships between different constructs of leadership models and desirable variables of organizational behavior. It becomes apparent, though, that in academic research the selection of analyzed leadership models and their consequences is very heterogeneous. This Master Thesis has the objective to contribute to Leadership Research by applying a comparative empirical study in the—until today—often neglected study population of in-house and sales personnel within the pharmaceutical industry. For this purpose, an online employee survey with $N = 137$ participants from a leading pharmaceutical company in Germany was conducted. Based on contemporary leadership theory, a range of Hypotheses regarding consequences of modern leadership models is empirically tested. The results of the study reconfirm Identification with Manager, Trust & Loyalty and Employee Satisfaction as consequences of Authentic as well as Transformational leadership. Work context as in-house vs. sales setting shows moderating effects on some of the leadership-consequences relationships. As the research involves multiple structurally different variables as well as constructs and compares feedback of different study populations, tangible management implications to boost desirable work attitudes and behaviors

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can be derived and appropriately adapted to match the respective work context. Ramifications for future scientific research are also presented.

1 The Importance of Leadership for Corporate Success

Today's organizational and business environments become heavily disrupted by challenges stemming from political, economic, social or technological currents and trends. The pharmaceutical industry, for example, faces strains like global, regional or local pressures on product pricing, new Market Access hurdles, compliance guidelines and regulations, competition from innovative, generic or biosimilar companies as well as the advent of digital business models that put corporations under pressure to be effective and efficient. Human Resource (HR) departments evaluate how to best deal with one of the companies' most important resource: their employees. Therefore, leadership is key in organizations' strive for long-term success and financial performance. In order to contribute to leadership research and its positive outcomes for organizations' success, this work's main objective is to provide an overview of relevant leadership theories, to summarize current scientific literature on consequences of leadership and to empirically test relationships between leadership and defined work attitudes and behaviors. A secondary objective is to close research gaps regarding leadership in different work contexts, esp. with regards to pharmaceutical sales and in-house personnel.

2 The Concept of Leadership

Burns (1978) stated that "Leadership is one of the most observed, yet least understood, phenomena on earth" (p. 3). This indicates that both the scientific and managerial community operates with various definitions of leadership. Vecchiotti's (2018) chronological perspective of leadership definition development starts with a patriarchic view based on characteristics of men situated in positions of authority. Over time, the role of subordinates was recognized and leadership encourages implementers to contribute to achieve mutually agreed goals. A paradigm shift due to new aspects like collaboration, teamwork, work-life balance, continuous feedback and learning becomes apparent (Vecchiotti 2018). Consequently, the following definition best reflects the latest view: "Leadership is a long-term, value-based process that encourages leaders and implementers to initiate actions that contribute to achieving a common purpose, and to willingly make significant contributions in meeting mutually agreed to goals." (Vecchiotti 2011, p. 6). Leadership, by its processual character, is a construct that has to be considered ambiguous, polymorphic and multifaceted. Von Rostenstiel's Leadership Model (Fig. 1) comprehensively describes the various components and entry points for leadership theory and research (von Rosenstiel 2001).

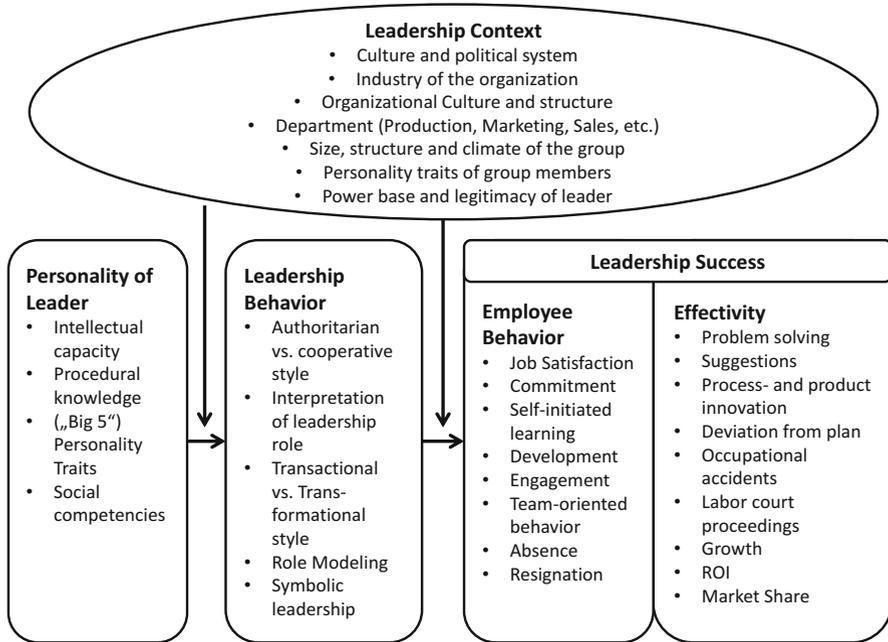


Fig. 1 Von Rosenstiel’s Leadership Model. Source: von Rosenstiel (2001)

Von Rosenstiel’s Model is an excellent stimulus to look into four different approaches widely discussed: trait approach, behavioral approach, contingency approach, as well as two contemporary approaches of positive leadership.

Historically, leaders were described by traits (Galton and Eysenck 1869). In the 1930s and 1940s, leadership research focused on personal characteristics of an individual and sought to identify personality, social, physical, or intellectual attributes that differentiate leaders from non-leaders. Trait theory was aiming at discovering a built-in set of traits that leaders possess, e.g. “aggressiveness”, “self-control”, “independence”, friendliness”, or “optimism” (Owens 1973). A famous example is the “Big 5” Personality Model with the five fundamental dimensions “extraversion”, “agreeableness”, “conscientiousness”, “emotional stability” and “openness to experience” (Costa and McCrae 1992; Norman 1963; Tupes and Christal 1961). Academic research describes “Extraversion” as the most predictive trait of leadership (Bass and Bass 2008).

Behavioral theory tries to identify the right things effective leaders do, e.g. how they communicate, motivate, delegate, plan, or handle meetings (Owens 1973). The most comprehensive example is the Ohio State Studies with the objective to identify independent dimensions of leadership behavior (Schriesheim and Bird 1979). Two key dimensions are “Initiating Structure” and “Consideration”. The former describes task-oriented behavior, e.g. putting high emphasis on work organization, work relationships, deadlines and goal attainment. The latter refers to people-oriented

behavior with a focus on mutual trust, respect for subordinates' ideas, and regard for their feelings (Fleishman and Peters 1962). One of the biggest contribution of behavioral theory is the introduction of five leadership styles: (1) the autocratic leader (who permits little or no freedom, relying on his or her position, knowledge or power to reward and punish), (2) the bureaucratic leader (who gives clear orders, relying on the organization's policies, procedures and rules), (3) the diplomatic leader (who provides limited freedom, relying on personal persuasion), (4) the participative leader (who gives a high degree of freedom and accepts group decisions and majority votes) and (5) the free-reign leader (who lets subordinates operate freely unless asked for invention) (Owens 1973).

Contingency approaches of leadership comprise three elements: (1) a dimension of leader behavior ("x"), (2) a criterion by which the effectiveness of the leader may be determined ("y"), (3) an environmental or situational variable ("z") (Korman 1972). The focus is on the environmental or situational impact "z", which influences the correlation between "x" and "y". In the 1960s, Fiedler's Contingency Model is looking for the proper match between a leader's style (i.e. task- vs. relationship-oriented) and the degree to which the situation gives the leader control. If the right match is achieved, effective group performance follows (Fiedler 1977). According to Fiedler's Model, a situation is assessed in terms of three situational dimensions: (1) leader-member relations, (2) task structure, (3) power situation. The combination of these dimensions leads to eight possible categories of leadership situations (Fiedler 1972). Fiedler's fundamental conclusion is to define two ways to improve leader effectiveness: (1) Change of the leader in order to fit the situation, or (2) Change the situation to fit the leader.

Today, two so-called "positive leadership styles" attract high scholarly and managerial attention: Transformational Leadership (TL) and Authentic Leadership (AL). Transformational leaders motivate and encourage others to outperform expectations (Podsakoff et al. 1990). The four components of TL are referred to as the "4 I's": Idealized influence/charismatic leadership, Inspirational motivation, Intellectual stimulation, and Individualized consideration. As TL is associated with performance beyond expectations, this model remains at the forefront of scholarly attention (Bass and Reggio 2006; Gardner et al. 2010; Yaslioglu and Erden 2018). At the beginning of the twenty-first century, authentic leadership gained high scholarly attention and is now among the most prominent leadership styles studied (Banks et al. 2016; Berkovich 2014; Celik et al. 2016; Walumbwa et al. 2008). Walumbwa et al. (2008) define AL as a composite of four dimensions: (1) self-awareness (including an understanding of one's strengths and weaknesses and being cognizant of one's impact on other people), (2) relational transparency (which means presenting one's authentic self to others, sharing information and expressing one's true thoughts and feelings), (3) balanced processing (which means to objectively analyze all relevant data before decision making including challenge deeply held positions), (4) internalized moral perspective (which refers to an integrated form of self-regulation guided by internal moral standards and values versus outside pressures) (Walumbwa et al. 2008). In sum, AL is a construct that incorporates traits, behaviors, styles and skills to promote ethical and honest behavior (Covelli and Mason 2017).

3 Constructs and Generation of Hypotheses

A recent meta-analytic review by Banks et al. (2016) indicates construct redundancy of TL and AL, claiming that none of the constructs adds palpable incremental validity beyond the other. Joo and Nimon (2014) though concluded that both leadership models are complementary, not substitutable (Joo and Nimon 2014). Consequently, it is hypothesized that TL and AL both contribute to the relationship of leadership with various dependent variables by explaining incremental variance.

In line with Zaccaro and Klimoski's (2002) view that different dimensions of organizations can moderate the nature of organizational leadership and its antecedents and consequences (Zaccaro and Klimoski 2002), scientific leadership research has been covering many of these aspects (Golden and Shriner 2017; Charbonnier-Voirin et al. 2010; Jensen 2013; Kulophas et al. 2015; Zubair and Kamal 2016). According to Antonakis and Atwater (2002), structural distance can be defined as physical structure (i.e., physical distance between leader and subordinate), organizational structure (e.g., hierarchical level, span of control), and supervision structure (i.e., frequency of leader-subordinate interaction). In this work, research participants' affiliation to a specific organizational setup (in-house vs. sales staff) of the collaborating pharmaceutical company is treated as context variable. Its moderating effect on various leadership-consequences relationships is analyzed. Especially the physical distance between leader and subordinate is structurally different in both work settings. When coming to TL's and AL's relationship with employee attitudinal and behavioral constructs, moderation analysis will be carried out on the basis of participants' affiliation with one of the two work contexts. Moderation hypotheses in this work have the structure presented in Fig. 2 below.

Social Identity Theory (SIT) postulates that individuals identify with social entities, e.g. individuals or organizations, to foster and maintain a positive self-concept (Tajfel and Turner 1986). Organizations offer employees a multitude of identification targets, so-called foci. These foci can be an organization as a whole, a team, or a manager (van Dick 2001). Positive leadership theories should be able to enhance subordinates' identification with manager (IM). With respect to the IM construct, it is expected that both leadership models will contribute to employees' Identification with Manager:

H_{1a}: Authentic Leadership will be a positive predictor of subordinates' Identification with Manager

H_{2a}: Transformational Leadership will be a positive predictor of subordinates' Identification with Manager

Moreover, it is hypothesized that the employees' work context (i.e. organizational unit: in-house staff vs. sales) will have a moderating effect on the AL/TL-IM relationship:

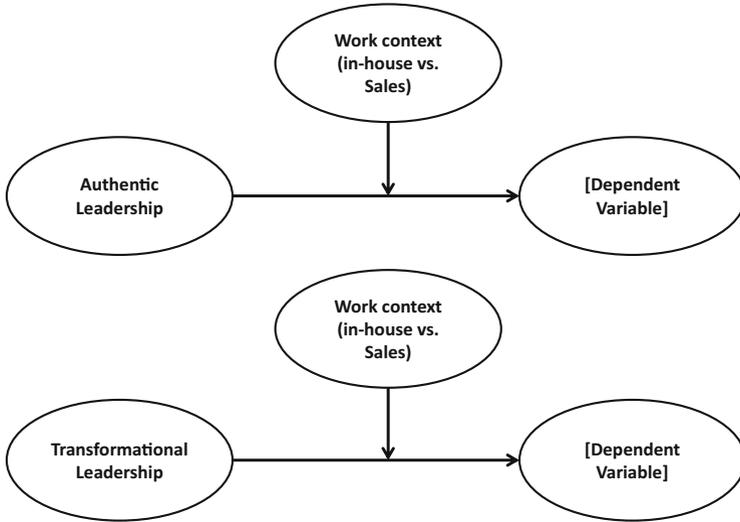


Fig. 2 Structure of hypothesized moderator effects. Source: Own representation

H_{1b}: The relationship between AL and IM will be moderated by employees' work context (in-house staff vs. sales)

H_{2b}: The relationship between TL and IM will be moderated by employees' work context (in-house staff vs. sales)

According to West and Farr, Innovative Work Behavior (IWB) describes the intentional creation, introduction and application of new ideas within a work role, group or organization in order to benefit role performance, the group or the organization (West and Farr 1989). In line with previous research, it is expected that both leadership models contribute positively to employees' IWB:

H_{3a}: Authentic Leadership will be a positive predictor of subordinates' Innovative Work Behavior

H_{4a}: Transformational Leadership will be a positive predictor of subordinates' Innovative Work Behavior

Moreover, it is postulated that employees' work context, i.e. their affiliation to in-house vs. sales teams, will moderate the AL/TL-IWB relationship:

H_{3b}: The relationship between AL and IWB will be moderated by employees' work context (in-house staff vs. sales)

H_{4b}: The relationship between TL and IWB will be moderated by employees' work context (in-house staff vs. sales)

Rousseau et al. (1998) comprehensively describe the nature of the trust construct: “Trust is a psychological state comprising the intention to accept vulnerability based upon positive expectations of the intentions or behavior of another” (p. 394f). It comprises both exchange processes and an understanding of trust subjects and objects not limited to an individual. For the purpose of this research, focus is on the interpersonal aspect of trust between manager (trust subject) and subordinate (trust object). According to Bass’ expansion of Burns’ TL theory, loyalty is an outcome of TL, mediated by trust, honesty and further qualities of the leader. This connection is substantiated in recent studies (e.g. Monzani et al. 2016). Overall, both leadership models are hypothesized to positively contribute to employees’ Trust and Loyalty (T&L):

H_{5a}: Authentic Leadership will be a positive predictor of subordinates’ Trust and Loyalty

H_{6a}: Transformational Leadership will be a positive predictor of subordinates’ Trust and Loyalty

Again, employees’ work context (in-house staff vs. sales team) is expected to moderate the AL/TL-T&L relationship:

H_{5b}: The relationship between AL and T&L will be moderated by employees’ work context (in-house staff vs. sales)

H_{6b}: The relationship between TL and T&L will be moderated by employees’ work context (in-house staff vs. sales)

Employee satisfaction (ES) is a construct frequently correlated with leadership in empirical research. Wong and Laschinger (2013), for example, established a direct positive relationship between AL and ES. Yang et al. (2011) confirmed a positive relationship for TL and ES. In this work, a positive relationship between both leadership models and subordinates’ ES is postulated:

H_{7a}: Authentic Leadership will be a positive predictor of subordinates’ Employee Satisfaction

H_{8a}: Transformational Leadership will be a positive predictor of subordinates’ Employee Satisfaction

Employees’ work context (in-house staff vs. sales team) will have a moderating effect on the AL/TL-ES relationship:

H_{7b}: The relationship between AL and ES will be moderated by employees’ work context (in-house staff vs. sales)

H_{8b}: The relationship between TL and ES will be moderated by employees’ work context (in-house staff vs. sales)

4 Empirical Assessment of the Models

The statistical software IBM SPSS Statistics 21 including the macro PROCESS (Version 3.1) was used to test the hypotheses (Hayes 2013). In total, 5 hierarchical regression analyses were conducted, consisting out of subsequent, identical steps for each of the five dependent variables. PROCESS Matrix procedure was also chosen to define and analyze the models evaluating moderating effects. Tests of unconditional interactions between independent variables and conditional effects of focal predictors in accordance to values of the moderators are possible.

Data collection for this research project occurred through an online questionnaire activated from June 17th until/including July 15, 2018. Participating functions were employees and their first line managers from selected sales, marketing, market research, market access, medical management, patient care, human resources, communication and further business support teams. $N = 247$ employees, thereof $N = 34$ first line managers, were invited. To avoid respondents' overload, a maximum duration of 15 min per survey is recommended (Batinic and Bosnjak 2000). With an average residence time of a bit longer than 11 min this threshold level was met. $N = 143$ employees clicked through the entire questionnaire. After initial exploratory descriptive data analysis using SPSS, $N = 6$ respondents were excluded due to missing data for four or more constructs. All final data analysis is therefore based on $N = 137$ respondents. Consequently, the ratio of evaluable cases vs. invited employees ($N = 247$) is 55%. Of $N = 137$ participants, 79 (58%) are female, 58 (42%) are male. The online cohort should quite closely reflect the workforce structure of companies of the healthcare sector. Regarding age distribution, the online cohort matches the national distribution of the German working population very well. An important variable is the affiliation of employees to in-house vs. sales personnel. In our sample, respondents are almost equally split between in-house based ($N = 76$; 55%) and sales employees ($N = 61$; 45%).

For the operationalization of AL, the ALQ (Authentic Leadership Questionnaire) as a well-established, theory-driven and validated measurement scale was chosen (Walumbwa et al. 2008). For the purpose of this research, a German translation of the ALQ, validated by Peus et al. (2012), was used. The version for external assessment from employees' perspective was applied. Internal consistency alphas (Cronbach's α) for each of the four subscales and the overall scale were originally reported to be higher than 0.7 in a cross-cultural validation study (Walumbwa et al. 2008). In the present project, SPSS data analysis shows a high Cronbach's α of 0.94 for the overall ALQ construct. Responses were collected on a 5-point Likert scale with pre-determined answer options ranging from (1) "Does not apply at all" to (5) "Fully applies"; German translations were used, respectively.

TL is operationalized by the GTL (Global Transformational Leadership scale). This short measure was tested, validated and confirmed by many studies in various geographical and business contexts (Carless et al. 2000; van Beveren et al. 2017). In the present analysis, Cronbach's α of 0.90 confirms its internal consistency. As in the

original study, the response format was a 5-point Likert scale ranging from (1) “Does not apply at all” to (5) “Fully applies”.

Based on an instrument for Organizational Identification (OI) from Mael and Ashforth (1992), Ullrich et al. (2009) developed a short measure for IM consisting of three items. The original Cronbach’s α was .69 (Ullrich et al. 2009). Similar to organizations, teams or workgroups, managers can represent a social category with which employees identify themselves (Gautam et al. 2004). Therefore, the original OI instrument was amended to an IM scale. In the present research, a Cronbach’s α of 0.84 was reached. Consistent with the previous measurement constructs, a 5-point Likert scale with identical response options was used.

IWB is assessed by nine items derived from Scott and Bruce’s (1994) scale. It has also proven validity and reliability in the work of Janssen (2000). In accordance to the theoretical concept described earlier, three items each refer to the aspects of idea generation, idea promotion and idea realization. Again, a 5-point Likert scale was applied. Response options now ranged from (1) “Never” to (5) “Always”. Janssen (2000) reported a Cronbach’s α of 0.95 for this instrument. The present data set delivers a very acceptable Cronbach’s α of 0.90.

Trust in and loyalty to the leader is operationalized by use of a six item scale of Podsakoff et al. (1990). The first three items represent the trust component of the instrument. In turn, the remaining three items stand for employees’ sense of loyalty to their managers. Again, responses were collected on a 5-point Likert scale with answer options of (1) “Does not apply at all” to (5) “Fully applies”. In our data set a Cronbach’s α of 0.93 was reached, pointing to a very good internal consistency.

Additional constructs like Organizational Identification (OI) and Employee Satisfaction (ES) considered in the comprehensive work were operationalized by a validated 3-item scale from Mael and Ashforth (1992) and a five-item short instrument based on an original scale developed by Brayfield and Rothe (1951).

Hypotheses H_{1a} to H_{8a} are tested by application of regression analysis. Hierarchical Regression analysis is applied to evaluate the differential explanatory effect of both Leadership Models, AL vs. TL. Four three-step hierarchical regression analyses were run with the following dependent variables: IM, IWB, T&L and ES. At step one of each of the separate calculations, the demographic variables age and sex were entered to control for covariates. AL was entered at step two as first predictor of conceptual interest. The second predictor TL was entered at step three. The variables were introduced stepwise to see if they have an effect over and above covariates.

Table 1 shows the Means, Standard Deviations, Cronbach’s α for all constructs covered, as well as Intercorrelations.

Due to limited space, not all statistical analyses are presented in detail. Of course, all analyses and their results are available when contacting the authors. As age and gender might have effects on the dependent variables of interest, they were entered in the analyses as control variables.

TL explained additional variance above and beyond AL in Identification with the Manager, Trust and Loyalty in the leader, and Employee Satisfaction (confirmation of Hypotheses H_{1a} , H_{2a} , H_{5a} , H_{6a} , H_{7a} , H_{8a}). However, neither AL nor TL explained

Table 1 Means, standard deviation, intercorrelations, and reliability

Variable	Means	S. D.	S. α	1	2	3	4	5	6	7	8	9	10	11	12	13
1 AL	3914	.659	.935	1												
2 TL	4106	.759	.898	.868**	1											
3 IM	2796	.957	.842	.446**	.454**	1										
4 OI	3416	.810	.857	-.024	.434**	.434**	1									
5 IWB	3372	.622	.898	.137	.063	.105	.029	1								
6 T&L	4215	.747	.928	.732**	.717**	.535**	.077	.156	1							
7 ES	4340	.616	.859	.164	.156	.115	.137	.173*	.173*	1						
8 WE	4131	.605	.719	.145	.021	.105	.076	.457**	.159	.175*	1					
9 OCB	4377	.385	.524	.135	.129	.104	.155	.174**	.265**	.119	.186*	1				
10 CD	3981	.771	.835	.013	-.010	.149	.055	.046	.194**	.022	.080	.191*	1			
11 Age	-	-	-	.025	.134	-.167	-.216*	-.201*	.024	-.175*	-.174*	-.057	-.154	1		
12 Sex	-	-	-	-.074	-.013	-.024	.088	-.196*	-.102	-.078	-.328**	-.024	.001	.162	1	
13 OrgUnit	-	-	-	-.164	-.145	.028	.315**	-.089	-.172*	-.090	-.041	.129	.115	-.332**	-.005	1

AL Authentic Leadership, TL Transformational Leadership, IM Identification with Manager, OI Organizational Identification, IWB Innovative Work Behavior, T&L Trust & Loyalty, ES Employee Satisfaction, WE Work Engagement, OCB Organizational Citizenship Behavior, CD Cognitive Diversity, OrgUnit Organizational Unit (i.e. in-office staff vs. sales force), S.D. Standard Deviation; CB α Cronbach's α ;

** Correlation significant on 0.01 level (2-sided); * Correlation significant on 0.05 level (2-sided)

Source: Own representation based on SPSS analysis

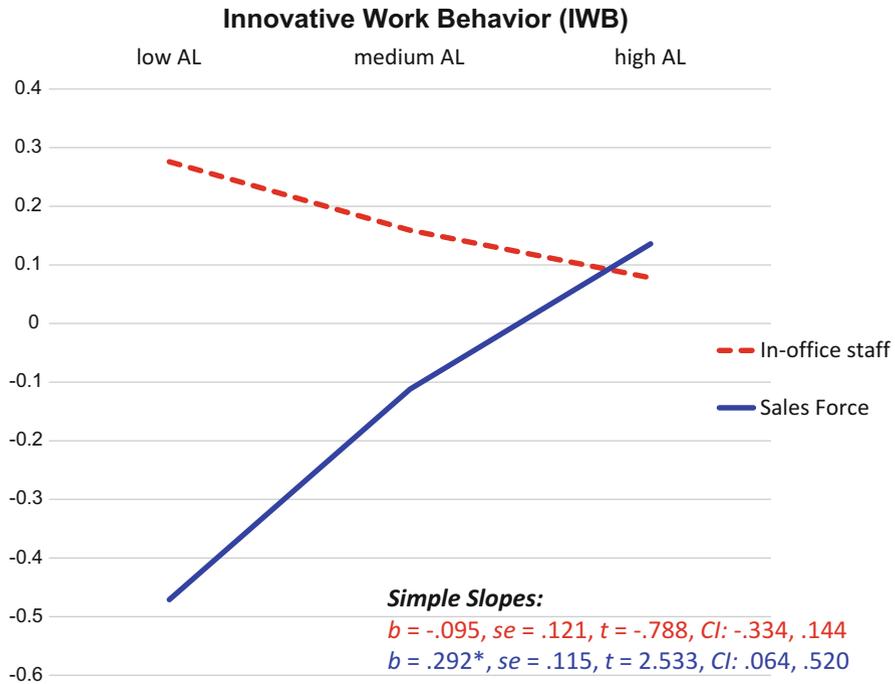


Fig. 3 The moderating influence of work context on the AL-IWB relationship. Source: Own representation based on SPSS analysis

significant variance in Innovative Work Behavior (rejection of Hypotheses H_{3a} , H_{4a}).

Nevertheless, when context was included inside the model (moderator: in-house vs. sales), there was a positive relation between AL and innovative work behavior for sales, but not for in-house staff (see Fig. 3). Additionally, the moderator analyses revealed that the relation for both AL and TL and trust and loyalty towards the leader was stronger in sales than in in-house staff (see Figs. 4 and 5). Consequently, hypotheses H_{3b} , H_{5b} , H_{6b} are confirmed. Hypotheses H_{4b} , as well as H_{7b} and H_{8b} on moderating influences of context on the relationship between AL/TL and ES are rejected, though.

5 Summary, Implications and Outlook

Key objective of this work was to empirically test the relationship between leadership and its key consequences. By means of an online survey with 137 employees of a pharmaceutical company in Germany, the importance of positive leadership models—Authentic and Transformational leadership—for the occurrence of desirable



Fig. 4 The moderating influence of work context on the AL-T&L relationship. Source: Own representation based on SPSS analysis

work attitudes and behaviors like Identification with Manager, Trust and Loyalty, and Employee Satisfaction, was documented. This implies that in corporate practice a positive leadership culture is suitable to stimulate relevant employee actions that contribute significantly to corporate success.

Based on a comprehensive literature review, AL and TL were identified as the main contemporary leadership models of interest. Consequently, these approaches constituted the key independent variables entered both into multiple hierarchical regression as well as moderation analysis models. As a secondary objective, the empirical analysis shed light on the pharmaceutical industry sector and expanded scientific knowledge regarding consequences and potential moderating effects of work contexts.

Essences of the present empirical research are:

- Positive Leadership Behaviors (AL and TL) are positive predictors of critical employee attitudes and business targets like Identification with Manager, subordinates' Trust and Loyalty, and Employee Satisfaction.
- The empirical research results confirm construct validity and conceptual independence of both positive leadership theories, AL and TL.



Fig. 5 The moderating influence of work context on the TL-T&L relationship. Source: Own representation based on SPSS analysis

- Work context, operationalized as in-house vs. sales personnel, significantly impact some leadership-consequences relationships, i.e. leadership’s relationship with Trust and Loyalty is significantly moderated by work context (with a stronger effect in the study population of sales force); for the AL-IWB relationship, a significant moderating effect for sales personnel was also confirmed.

Although an often stated need for quantification of positive leadership behavior in corporate financial success and target figures was not subject of this investigation, the confirmed relationships between positive leadership and most of the desirable work attitudes and behaviors indicate that AL and TL contribute positively to operating profit.

In addition to the above mentioned financial aspects, hints on positive aspects of employee behavior, namely Innovative Work Behavior, could be derived. As this was especially accentuated in the context of customer facing sales personnel, one could infer that high AL in sales contexts can have a halo effect on sales reps customer interactions.

In order to achieve corporate goals, a recommendation to pharmaceutical companies is to establish a corporate culture that fosters positive leadership behavior.

Leader recruitment, leadership training and development should take the “4 I’s” of TL and the four aspects of AL as a reference. Specific examples for HR departments can be to provide platforms and trainings for people managers to develop capabilities as mentors, coaches and active listeners. In order to be able to act as a positive role model for employees, leaders should be clear about ethical and moral standards, also with regards to the specifics of the pharmaceutical industry. Moreover, tools to foster leaders’ and employees’ self-awareness, a culture that supports transparency and one of error tolerance would be very beneficial to establish the desirable leadership styles, hence positive employee attitudes and behaviors.

Although this research shows promising results, a few limitations need to be mentioned. First, this study has a cross-sectional design. Therefore, longitudinal investigations could be of interest in order to evaluate intrapersonal developments over time and if and how they impact job attitudes and behavior. Second, due to requirements of the collaborating company’s works council in order to ensure anonymity and maximum data protection, a dyadic approach to collect and analyze data based on team structures was not allowed. It would be advisable for future research to collect and use this information in order to enhance data quality and model reliability by reducing a potentially high amount of additional variance. Similarly, the actual duration of individual leader-subordinate relationships could actively be controlled for, as interpersonal relationships including the development of trust tend to evolve over time. Third, all outcome variables are solely based on employee self-assessment. This potential for common source bias could be reduced in future studies if additional sources of feedback and information can be taken into account, e.g. supervisors’ evaluations of employees’ behavior or secondary data from more objective performance evaluations. Fourth, the present moderation analysis is purely based on self-reported organizational allocation to in-house vs. sales departments. This was used as a surrogate for work context, primarily reflecting physical distance to the supervisor, which in turn was supposed to impact frequency and quality of communication. However, quality of leader-subordinate interaction might be perceived quite differently on a personal level. In future studies, analysis could therefore be controlled for effective communication frequency and/or perceived quality of communication channel and content of leader-subordinate exchange.

Despite these limitations and implications for future research, the study provided various important insights. It seems to be first research project to systematically analyze the two contemporary positive leadership models Authentic Leadership and Transformational Leadership in a comparative context of in-house staff and sales representatives of a single pharmaceutical company in Germany.

In order to build on the current outcomes, the following direction for future research can be proposed. First, a longitudinal study design could be chosen to be able to track the development of interpersonal leader-subordinate relationships over time. Second, recourse to potentially more objective multi-source data to substantiate the expressed employee attitudes and behaviors might be beneficial. Third, the study could be run in or across different companies and industries to detect significant differences or communalities. Similarly, the study could be replicated by

inclusion of different hierarchy levels within companies to assess if team size or span of control impacts the relationship of leadership and its consequences. Fourth, the evaluation of antecedents of AL and TL could be added to the research design to potentially derive implications for people management and personnel development.

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Alliance Management at Merck: Establishing an Operational 100-Day Plan for Alliance Launches and Management



Elmar Hörner

Abstract Pharmaceutical industry faced many challenges in the past 20 years that led to a change in business models which is still ongoing. One of the adaptations is the increase in importance and number of strategic alliances.

This thesis looks at the launch phase of an alliance and proposes an operational 100-day plan for the use during different sub-phases. This plan is validated by a survey with alliance managers at Merck KGaA. The survey evaluates specifically their perception on timely involvement into the transition activities from business development to alliance management, the governance structure and metrics of alliances and collects feedback on the proposed 100-day plan.

The contents of the plan are considered as useful for the launch of an alliance by the survey participants and their feedback shows opportunities to further improve the best practices at the alliance management department as a follow-up after completion of the thesis.

1 Introduction

The past two decades have seen a shift in how and where medicines are being discovered, developed and marketed. Factors like

- reduced efficiency of the research and development (R&D) process
- increased competition while major blockbusters lost their IP protection
- cost pressure from payers including the need to show efficacy in relatively small patient sub-populations
- new technological possibilities with the long-term goal of personalized healthcare and healing instead of live-long treatment
- higher transparency in global market access and pricing processes

and many more led to the need for changed business models of pharmaceutical companies.

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One of the adaptations is the increased importance and number of alliances. When not managed properly right from the start, the risk is high for failure in meeting the objectives. The alliance management plays a critical role in the setting of the alliance governance model and the continuous supervision of the processes and results of the partnership.

This study provides an overview on the different aspects of alliances with focus on the role and skills of Alliance Management (AM) during the lifecycle of the partnership. Especially during and after the transition phase from negotiation to alliance launch the important tasks are the setup of governance structure and the definition and continuous evaluation of the metrics.

A checklist is proposed that can be used by the Alliance Managers (AMs) for the planning of steps and decisions during the first 100 days of an alliance. This 100-day plan was improved and confirmed by feedback of the alliance managers at Merck KGaA.

After this short introduction, the following Sect. 2 discusses the already mentioned need for alliances and their importance in pharmaceutical industry more in detail. Thereafter, the nature and types of interfirm cooperations with focus on strategic alliances are shown in Sect. 3, together with the role of the alliance management department and manager.

A short history of Merck KGaA and its alliance management with recent examples explain in Sect. 4 the framework in which the main outcome of this thesis—the operational 100-day plan as shown in Sect. 5—shall be applied. This kind of checklist is then assessed and the results of the survey with alliance managers are discussed in Sect. 6. A conclusion and the further outlook finalize this thesis with Sect. 7.

The focus of the work was directed towards the practical aspects of alliance management and the theoretical backgrounds and motivations for alliance formation, various governance configuration models, economical theories (e.g. transaction cost economics or resource-based view), partner fit etc. have not or only in short been discussed.

Furthermore, the studies focus on the initial phase of an alliance. Other phases like partner selection, extension or termination are not discussed except for the general lifecycle of an alliance as mentioned in Sect. 3.2.

2 The Importance of Alliances for the Pharmaceutical Industry

2.1 The Problem “Productivity Paradox”

The pharmaceutical industry is a highly innovation-driven business which used to have an average sales growth rate of 11% per year from 1970 until 2004. Since then, the annual growth was reported by members of the Pharmaceutical Research and

Manufacturers of America (PhRMA) association always below 8% or even negative (–6.2% in 2012). The R&D costs increased from below 15% of sales before 1990 to more than 21% in 2017 (all data from PhRMA 2018)

The so-called “productivity paradox” describes the situation that despite rising R&D costs the pipeline output of pharmaceutical industry is low and declining. The annual statistics of US Food and Drug Administration (FDA) about the number of approvals of new molecular entities (NMEs) was slightly above 20 per year throughout 1980s, raised above 30 during 1990s with the highest number of approvals (51) in 1996. This was connected with some legislative changes which allowed FDA a significant increase in personnel and a reduction in backlog of pending registrations. Since then and during the 2000s the average number of yearly approvals fell again back to 20–25. While the numbers raised again during the 2010s to an average of slightly above 30 like in 1990s (2013: 27; 2014: 41, the highest number since 1996), these numbers have to be regarded in comparison to the steadily raise in R&D costs and the breakdown to the rate of successful companies.

Munos (2009) assessed the drugs that have been registered at US FDA over a period of 60 years (1950–2008). One of the findings was that the number of approvals of NMEs per year was the same at the end of this period as it was at the beginning. No company was able to achieve the approval of two or three NMEs per year which is the estimated number for meeting own growth objectives of big pharmaceutical companies. On average, one NME was approved every 6 years. In parallel, the costs per NME increased exponentially at an annual rate of more than 13%. Munos concludes that the “R&D model [. . .] is showing signs of fatigue: costs are skyrocketing, breakthrough innovation is ebbing, competition is intense and sales growth is flattening. This cluster of symptoms has often foretold major disruption in other industries”.

Scannell et al. (2012) evaluated the pharmaceutical R&D efficiency in a period from 1950 to 2010. The comparison of R&D budget vs. NME approvals showed that the number of approvals per \$1 billion budget declined almost every 9 years by half. The rate of decline was shown as quite constant over different 10-year periods in the overall 60-year period.

Some reasons for the decline of R&D productivity and potential solutions have been discussed by Kramer (2016). He sees the challenges in the

- Raising R&D costs due to increasing scientific and regulatory requirements for the approval of new drugs, including the data on safety
- High attrition rate of drug candidates in phase II/III clinical trials
- Increasing competition by generics and biosimilars and between companies for attractive targets in human metabolism
- Increasing cost pressure of health organizations and healthcare providers
- Increasing pressure from public health for evidence on significant improvements compared to existing therapies
- Shortened time to regain R&D costs prior to the expiry of patent protection due to longer development times

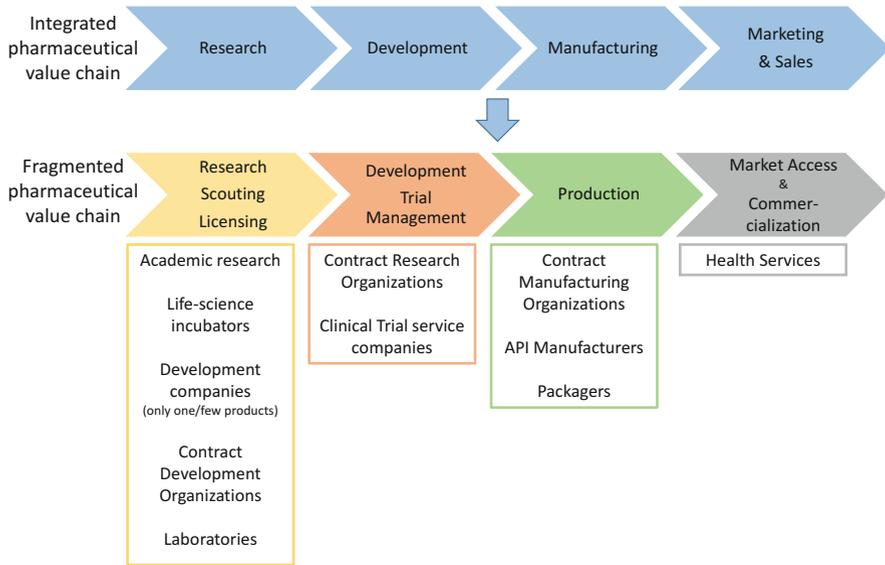


Fig. 1 The fragmented pharmaceutical value chain. Adapted from Capo et al. (2014) and IMAP (2012). API: Active Pharmaceutical Ingredient

Capo et al. (2014) see in addition to the above-mentioned stringent approval requirements the R&D cost driver in the “orientation of research towards increasingly complex pathologies, [that] have implied larger, more costly and internationally based R&D activities”. These challenges have led on the one hand to a consolidation of the industry via M&A activities, but also to a cultural change over last 20 years. The scientific R&D process and the subsequent value chain within one pharmaceutical company was disrupted into the orchestration of specialized contributors to specific parts of the chain as shown in Fig. 1.

2.2 Cooperation as a Potential Solution

The fragmentation of the pharmaceutical value chain as one potential solution to the paradigm shift (other solutions would be e.g. focus on niche markets or cost cuts in R&D which shall not be discussed here further) can be accomplished only with strong and multi-faceted interfirm cooperation. With such cooperation, companies can

- share skills, risks, costs and rewards
- bundle and complement resources
- create synergetic effects
- enter new and additional markets
- increase their (combined) competitiveness vs. others on the same market.

The interfirm cooperation has some benefits but brings also some risks. While scientific and commercial failure is not specific to cooperation but common to all R&D projects, Thong (2016, pp. 45–52) identifies two (elevated) risks and a general consequence when two or more partners have to coordinate:

Execution risk: Thong defines this as “the risk arising from being unable to resolve unanticipated problems [...] over the course of the project’s execution”. Like scientific and commercial risk that is partly applying to all R&D projects, but with more complex communication, problem-solving and decision-making processes higher than for internal projects. Inflexible project management (adherence to preset deliverables and timelines) and narrow project goals can further increase the execution risk.

Collaboration risk: These are added complications due to the work with one or more external partners. Fundamental differences in “organizational missions, processes, and culture [...] create confusion and tension”. Different needs and expected outcomes from a project can lead to a higher risk for project failure.

Collaboration tax: The elevated execution risk and the additional collaboration risk is called the collaboration tax by Thong (other authors use also the terms partnering or alliance tax). Before entering into an interfirm cooperation, each partner shall understand and evaluate the related collaboration tax. One mitigation is the assignment of a dedicated alliance management (AM) department within the company and of an alliance manager role within each project to minimize the number of issues or allow their early resolution as discussed in Sect. 3.3.

The specifics of (strategic) alliances as one form of interfirm cooperation, its differences to other forms and the lifecycle shall be shown in the following. Also the role and capabilities of the alliance management function and manager will be presented as well as general alliance structures and the evaluation of alliances.

3 The Nature of Alliances

3.1 Definitions and Types of Alliances

The terms interfirm cooperation and alliance are diffusely used in literature. Sometimes alliance is used as an overall term, sometimes only as a specific form of cooperation.

A more general definition is used by Stafford (1994): “Strategic alliances are long-term co-operative partnerships involving vendor, customer, competitor, or industry-related firms and are used to achieve some competitive advantage. They may include joint ventures, supplier and distributor agreements, licensing arrangements, just-in-time systems, and research consortia, to name just a few.”

Albers (2005, p. 9) defines every cooperative interorganizational relationship as “an alliance if a formal agreement exists between the actors that specifies the activities which are the subject of cooperation. Thus, not all cooperative relationships among firms are alliances, but all alliances span cooperative relationships

among firms.” He lists as characteristics of an alliance the voluntariness, fixation by agreement, exchange and/or pooling of resources and the sharing of benefit and control.

A more restricted view by Yoshino and Rangan (1995, p. 4–5) defines “a strategic alliance as possessing simultaneously the following three necessary and sufficient characteristics”: Two or more firms remain independent, share benefits and control and “contribute to a continuing basis in one or more key strategic areas”.

Suen (2005) combines this definition with the specifics by Gomes-Casseres (1999, p. 34): Each partner has only limited control and the cooperation is based on “an incomplete contract”. “Because the partners remain separate firms, there is no automatic convergence in their interest and actions. As a result, to deal with unforeseen contingencies the partners need to make decisions jointly.”

DePamphilis (2018, p. 553) uses the overall term of “Business Alliances” which covers a variety of partnerships (Joint Venture, Strategic Alliances, Equity Partnerships, Licensing, Franchising, Network Alliances, Exclusive Agreements) with different characteristics but “the common goal of the partners are the sharing of risks, rewards and control”.

The Association of Strategic Alliance Professionals (ASAP) says about the motivation for partnering: “Typically, strategic alliances have a broad and long-term impact on corporate performance and valuation. Often, strategic alliances are formed to create a competitive advantage for the partners in their respective markets” (https://www.strategic-alliances.org/page/alliance_definitions).

Merger and Acquisitions (M&A) activities are closely related to alliances and often seen as a kind of definitive, non-temporary alliance with a high level of control. The main differences are a higher investment, interest of controlling, less flexibility and the joint organizations become either one or belong to the same corporate parent (Gomes et al. 2011, p. 7f.).

The range of strategic alliances from pure contractual, non-equity based alliances like market transactions to equity-based alliances with its most definitive form of an acquisition is shown in Fig. 2.

There are three main types of alliances which can be assigned to the three main stages of the pharmaceutical value chain as shown in Fig. 1. Austin (2008, p. 166) differentiates accordingly:

- *Research alliances* for discovery, target and lead molecule identification, for assays, mechanisms etc.

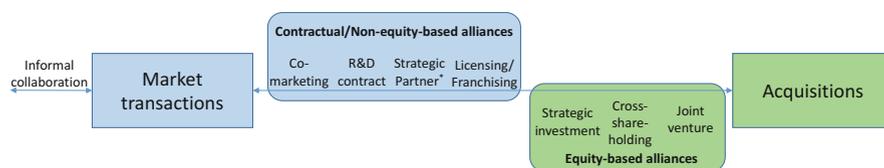


Fig. 2 Range of alliances from market transactions to acquisitions. Adapted from (Peng 2014, p. 213) and (Herrmann and Dressel 2014). *E.g. strategic supplier, distributor, service provider

- *Development alliances* for the formulation, chemistry and manufacturing processes of pharmaceutical products
- *Commercial alliances* for co-promotion and in the form of joint ventures

The alliance type can also be defined by the underlying business model and activities for which the partner agree the sharing:

- *In-licensing*: A company (licensee) acquires intellectual property from another company (licensor) to produce and/or market a product or to use a technology, platform or software for research and production activities.
- *Out-licensing*: Licensor commercializes the internal research results by giving licenses to another company for further development or commercialization in markets or market segments that are not of interest or not accessible by the licensor.
- *Co-Development*: Mutual development by companies that complement their available technologies, molecules, products and know-how.
- *Co-marketing or -promotion*: Two partners share their commercial activities for a product or range of products, but usually in different markets/countries.

3.2 The Lifecycle of Alliances

Each alliance undergoes usually several stages from its initialization to its termination as shown in Fig. 3.

The different phases are a synthesis of the ones proposed by (Thong 2016) and (Tjemkes et al. 2018). Steinhilber (2008, p. 18) uses the terms Evaluating, Forming, Incubating, Operating, Transitioning and Retiring to describe the lifecycle of an alliance. Beside the different naming of the phases, some overlaps or sub-division which results in a slightly higher number of steps, the general lifecycle model of alliances is well aligned between the scholars.

The first steps include the search for and evaluation of potential partners. Once such a partner was identified and first negotiations were successful, a due diligence (DD) is conducted to evaluate the partner's suitability and the asset which is in scope of the alliance. These steps and the negotiations about the contract are led by Business Development (BD) department. The AM department gets involved only



Fig. 3 Typical stages of an alliance. Adapted from (Thong 2016) and (Tjemkes et al. 2018)

during the late-stage of contract negotiations and takes over completely for preparation of alliance launch. BD's involvement is simultaneously decreasing during this period.

This transitional phase as indicated with the red arrow in Fig. 3 is critical for the success of an alliance. Not only the handover from the BD to the AM responsible is needed to ensure a complete knowledge transfer and seamless launch, but also the transition from the DD team to the operational team will minimize the risk of failure.

And that risk of failure is still high: There are numerous studies and it seems that with all differences in research approaches a failure rate of 50% is not exaggerated (Man 2005; Duysters et al. 2012). Tjemkes et al. (2018, p. 7f.) address three key findings:

- Each development stage of an alliance requires attention to different questions and decisions.
- Underestimation of challenges by different alliance objectives by the partners or diverging company characteristics/culture
- Institutionalization of the alliance know-how and know-what in a company (“alliance capabilities”) increases the probability of success.

3.3 The Role of the Alliance Management

The partners must invest continuous efforts and adjustments to make an alliance successful (Bamford et al. 2003, p. 5). The establishment of a dedicated AM function as proposed by Tjemkes was identified as a key advantage in different studies. Their focus is more on the internal operations of alliance partners than on the relationship between the partner companies. “[. . .] The experience a company has with alliances and the quality of alliance management are key success factors, which increase alliance success” (Man 2005).

(Alliance) Capabilities can be built by developing “mechanisms or routines that are purposefully designed to accumulate, store, integrate, and diffuse relevant organizational knowledge acquired through individual and organizational experience” (Kale et al. 2002). This study comes to the conclusion that companies increase their alliance success rates by investing into “a dedicated alliance function designed to capture and apply the know-how from its alliance experience [. . .]”.

According to Dyer et al. (2001, p. 39), the dedicated alliance function has the role to provide

- knowledge management and learning
- external visibility and support
- internal coordination and legitimacy
- alliance assessment and intervention to fix problems.
- With these activities, the function creates value by
- improving alliance success rates
- higher probability for stock-market gains
- enlarging the ability to form more alliances and to attract better partners.

The mechanisms for effective alliance capabilities are proposed in six categories (adapted from Heimeriks et al. (2009); Heimeriks and Duysters (2007)): Dedicated alliance function on an adequate hierarchy level, specific alliance training (e.g. negotiation, cultural competences), alliance managers (tasks and skills as below), tools (e.g. databases, templates, decision trees, Key Performance Indicators [KPIs]), processes (e.g. knowledge exchange, metrics, bonus system) and support by external parties (e.g. consultants, financial and legal experts, mediators).

The tasks of an alliance manager are identified by Thong (2016, p. 165f.) as follows:

Contract management: Monitoring the contractual obligations like milestone payments, resolving issues in case of different interpretation of the contract.

Monitoring the progress: Defining and reporting of KPIs and leading periodic health checks.

Process management: Establishing smooth operation, preparation of governance meetings and decision-making.

Acting as ambassador of the alliance at the partner and within the own organization.

Alignment and relationship management: Leading efforts for increased mutual understanding and trust.

Strategic value and risk management: Identifying and focusing on value drivers as well as identifying and mitigating key risks.

Change management: Anticipating changes and manage transitions smoothly.

An ideal AM should have strong communication and networking skills, high credibility, is curious but has also courage and does not shy away from conflicts (Thong 2016, p. 181f.). ASAP developed skill trainings in *context competencies* (not exclusive to AM, e.g. communication, time management, conflict resolution, contract negotiation, project management, change management, leadership), *core competencies* (AM-specific in the areas of alliance capabilities [governance structure, alliance cycle, conflict resolution], skills development [e.g. alignment, launch, governance, metrics, termination], collaboration) and *business/industry knowledge* (e.g. financial analysis, business sector knowledge, sales processes) (ASAP 2016; Nevin 2016, p. 271ff.).

4 Merck KGaA and Its Alliances

4.1 History of Merck KGaA

To understand the environment for which this thesis generates a launch plan of strategic alliances, this chapter shall give a short introduction about the history of Merck KGaA and its business units. A very detailed and complete history of Merck can be found in the recently published book for the 350-year anniversary by Scholtyseck et al. (2018).

Merck sees itself as “a leading science and technology company in healthcare, life science and performance materials” and the “world’s oldest pharmaceutical and chemical company”. The company was founded in 1668 by Friedrich Jacob Merck in Darmstadt, Germany. In 1827, Emanuel Merck conducted research in the chemistry of natural plant substances and prepared alkaloids which he offered under the name “Cabinet of Novelties” as the first kind of chemically standardized and relatively pure pharmaceutical substances. This allowed the expansion of the business to a global and industrial level.

The commercialization for the first technical applications of liquid crystals in 1968 under the brand *licristal*[®] for the first technical solutions built the start of today’s business unit Performance Materials which includes pigments and other functional materials. Around 70% of all liquid crystals worldwide are currently produced by Merck.

The production of chemicals, culture media and reagents for the R&D activities in academic and commercial laboratories was also an early business. This was strengthened by the takeovers of the competitors Millipore Corporation in 2010 (Merck KGaA 2010) and Sigma-Aldrich in 2015 (Merck KGaA 2015) and resulted in the business unit Life Sciences. A range of around 300,000 products covers laboratory water systems, gene editing tools, antibodies, cell lines and many more.

Merck acquired in 2007 the Swiss company Serono S.A. (Merck KGaA 2007) for its Healthcare business which was a significant transformation of the previous portfolio of small molecules into the field of biotechnological products. Today, Healthcare is the biggest of the three business units of Merck and contributes with 45% and almost €7 billion net sales to the total net sales. The activities for biosimilars were divested in 2017 to Fresenius Kabi (Merck KGaA 2017a) and the consumer health business in 2018 to Procter & Gamble (Merck KGaA 2018c).

Healthcare at Merck consists of a portfolio in the therapeutic areas of fertility, general medicines (diabetes, thyroids, cardiovascular), neurodegenerative diseases (mainly Multiple Sclerosis) and oncology. The distinct focus of current R&D activities lies in the areas of oncology (therapies against e.g. solid tumors and hepatocellular cancer), immunology (therapies against e.g. psoriasis, osteoarthritis, rheumatoid arthritis) and immuno-oncology (therapies against e.g. gastric, ovarian, colorectal or lung cancer).

Almost 53,000 employees in 66 countries generated in 2017 total net sales of € 15.3 billion in all three business units of Merck. The R&D budget was about €1.2 billion, with 68% or €1.6 billion of it for the healthcare business (Merck KGaA 2018a).

4.2 Significant Biopharma Alliances of Merck

Merck has a long history on alliances on both local and global level, on different activities (research, development, commercial), business models (in-, out-licensing,

co-development, co-marketing) with a variety of different partners. Currently more than 100 alliances are managed by the responsible team as detailed in Sect. 4.3.

According to Merck's website, the company is looking to "source new compounds, gain access to the latest technology platforms and develop novel therapeutics for patients. Our goal is to craft a pipeline that is a mix of both internal and externally sourced assets that are in line with the company's growth goals and strategically fit with both commercial and developmental strengths" (<https://www.merckgroup.com/en/company/partnering/collaboration/collaboration-in-healthcare/strategic-focus-and-partnerships.html>).

The most important strategic alliance was entered in 2014 with Pfizer Inc. for the co-development and later co-commercialization of a class of specific immunoncological compounds (anti-PD-[L]1) from both partners, in the meantime registered as Bavencio[®] (Avelumab). The contract included up to 20 immunoncology clinical development programs. Merck received an upfront payment of \$850 million—the biggest upfront deal payment in pharmaceutical industry at this time—and could receive regulatory and commercial milestone payments of up to \$2 billion Merck KGaA (2014). As an additional part of the contract, Merck received the right to co-promote Pfizer's oncological product Xalkori[®] (crizotinib) for the treatment of lung cancer in the US, Canada, Japan and other key markets.

Table 1 gives an overview about the different types of exemplary alliances which were entered between 2010 and 2018. The reference to the related press release with more background on the scope of the alliance is given below the table.

Table 1 Type and business models of Merck's selected alliances

Type of alliance	Business model of alliance			
	In-licensing	Out-licensing	Co-development	Co-promotion
Research	Vertex (2017a, b) ICR (2018)			
Development	Lupin (2014)	Newron (2011)	BeiGene (2014) Pfizer (2014) CheckMate (2018) Leap (2018) Vyriad (2018)	
Commercial	Xian Janssen (2018a, b, c)	Recordati (2010) BMS (2013)		Pfizer (2014)

Recordati S.p.A (2010); Newron Pharmaceuticals S.p.A. (2011); BeiGene (2014); BMS: The Pharma Letter (2013); Lupin: Merck KGaA (2014); Vertex: Merck KGaA (2017b); ICR: Cancer Research UK (2018); Checkmate Pharmaceuticals (2018); Leap Therapeutics (2018); Vyriad Inc. (2018); Xian Janssen: Merck KGaA (2018b)

4.3 *Alliance Management at Merck*

The advantage of a dedicated AM function within a company has been mentioned in Sect. 3.3. Such a department is established at Merck which shall—according to its own mission statement—“guide Merck to be recognized as preferred partner of choice in biopharma industry, maximizing the value of the partnerships.” The goal is to “maximize short and long term value creation by increasing the effectiveness of a project via an efficient governance structure, driving transparent decision making, anticipating risks and leading the resolution of issues” (all information in this chapter is derived from Merck-internal material and presentations). The partnerships shall “deliver more, at higher quality, in time, at lower cost.”

The department consists currently of ten AMs, based at sites in Germany, US and Latin America. That size is in the medium range: A study with 47 companies—representing two-thirds of all companies that are members of the Biopharma Council of ASAP—found that 42% have departments with less than five people and another 42% consist of more than ten people (Twombly and Shuman 2010). Number and scope of alliances in the portfolio of each AM were part of the general statistics section in the survey (please refer to Sect. 6.1).

The main activities of AM per phase of the alliance lifecycle according to the department’s handbook are as follows:

Prior to Deal Closure: Collaboration with BD; Input on contract sections regarding termination, governance, AM role, issues resolution; Nominate JSC members; Prepare KOM;

Alliance launch: Take lead from BD; Lead joint KOM; Communicate their roles and responsibilities (R&R) to JSC members and project team; Align plans and joint objectives with partner;

Alliance Management: Lead JSC preparation meetings; Facilitate JSC meetings and drive decision making; Manage intra- and inter-company alignment;

Issue resolution: Recognize early signs of problems and address issues in advance; Lead issue resolution and act as single point of contact in resolving disputes;

Refreshing or Leveraging: Drive continuous improvement of the alliance; Re-negotiate and amendments of the contract; Enhance and redesign governance

Termination: Lead termination agreement negotiations; Prepare and drive wind-down plan;

The AM department measures the long-term success with some KPIs to identify areas or alliances that need improvement. Seven KPIs have been identified as crucial for evaluation of success:

Effective Decision Making: Number of decisions made in the joint governance meetings, compared to total number of decisions asked to JSC.

Joint Objectives: Number of alliances with aligned joint objectives, compared to total number of alliances.

Alliance opportunities identified: Opportunities (extension of territory or products/molecules in scope) identified with the existing partner and/or with the network of partners that became a BD project in the later stage.

Value creation: Incremental Net Present Value (NPV) created with all alliances.

Planned Termination: Execution of termination in accordance to the proposed plan.

First 100 days onboarding: Align and execution of 100-day plan. Qualitative deviations from initial plan are measured.

Alliance Management survey: Merck performance on Alliance Management (see also below). One KPI for all alliances in total. Merck conducts a survey with all its partners every 2–3 years. Feedback is collected on the perceived performance of governance, operations and alliance management. The results showed constant improvement of the alliances since 2008 in all areas.

5 The Operational 100-Day Plan

Based on the available literature about alliance management, an operational 100-day plan for alliance launch has been created as the main practical outcome of this thesis (see Appendix 1, available as online resource). This kind of checklist allows to formalize and harmonize the steps around the launch of an alliance and separates the whole period into five different phases as shown in Table 2.

The tasks of *Phase I—Preparation of Alliance Launch* include the first involvement of AM into the ongoing negotiations between BD and the partner to get first insights into partner's culture and strategic motivation, identify the stakeholders of both parties and establish relationship, gain knowledge about scope and strategy of the alliance, allow the first evaluation on suitable collaboration platforms and first alignment on governance and decision-making model and communication plans, prepare internal and joint Kick-off meetings (KOMs).

All these activities contribute to a successful knowledge transfer and allow a seamless and early launch of the alliance while avoiding unnecessary surprises. The timing of this phase should start early enough but also not too early. As long as there is significant uncertainty on the terms and probability of the deal, the involvement of Alliance Management is blocking resources without benefit. A shared risk-based

Table 2 Phases of an alliance launch as used in the operational 100-day plan

Phase	Name	Timing
I	Preparation of alliance launch	Day -30 ^a – 0
II	Alliance launch/develop alliance strategy	Day 0–14
III	Execute alliance strategy	Day 15–89
IV	Evaluate alliance strategy	Day 90–100
V	Managing the alliance	Day 100+

^aThe start of this phase could differ and depends on e.g. the PoS for successful deal closure

decision should be made by the BD and AM departments regarding the best time to start with AM involvement. According to Bamford et al. (2003, pp. 111–112) “Expert opinions differ on whether those who will run the alliance should be included on the negotiation team. [. . .] Firms would be wise to choose a potential alliance manager to include on the deal team, after the initial partner screening and discussions of interest have taken place. [. . .] Including them on the negotiating team can only improve the odds of success.”

The *Phase II—Alliance Launch/Develop Alliance Strategy* starts with a distinct milestone—Day 0—when the contract is finally signed by both parties and the related communication and press release (if applicable) are circulated. Around this day, the common platforms need to be initialized and internal KOMs of both parties arranged to align on company position and first steps. The discussions of Phase I regarding governance model, meeting formats and frequencies and other details have to be finally aligned.

The most important and critical step during this phase is the conduct of the joint KOM with the relevant stakeholders. Depending on the governance structure there could be several KOMs of each committee, decision body or working group. A reasonable order of such KOMs should be aligned. There could be reasons to start from top-down and hold the JSC first, or to clarify first things on a more operational level in the different groups and get endorsement by JSC only later. The KOM is preferably done as a workshop with physical presence and depending on the complexity of the alliance a few days might be required.

During *Phase III—Execute Alliance Strategy* the metrics of the alliance is established with regular quality reviews and KPIs. An alliance charter can be used to document the framework including background, scope, vision, metrics, milestones, infrastructure, governance structure and other aspects. With this setup the operational work can start for all contributors and the AM needs to keep an oversight in the early days of an alliance: To manage the internal alignment, to anticipate issues and to resolve them. The AM has to participate in most of the relevant meetings to stay in close contact. In addition, the facilitation of JSC meetings is of importance especially in the launch phase. But also the development of alternative options—the potential exit and termination—is not of minor interest even when everything looks promising. Robert Thong (2016, pp. 143–146) calls this phase the “honeymoon period”, “when the activities are straightforward, the outcomes are predictable, and the inevitable personal frictions have not yet developed”. This phase shall be used to “build the foundations of success, taking advantage of the positive feelings and goodwill on both sides to establish strong communication channels and foster trust”.

At the end of the launch period in *Phase IV—Evaluate Alliance Strategy*, the time has come to run a self-assessment survey (or potentially even conduct a deeper gap analysis) on different levels (JSC and JPT) of the alliance and at both partners. Several aspects are usually evaluated by Merck’s AM like

- the quality of presentations
- meeting preparation and conduct

- discussion and escalation culture
- quality of decision-making
- overall satisfaction of the stakeholders
- suggestions for further improvement.

The results have to be thoroughly reviewed with focus on the areas of misalignment. The AM has to propose potential actions to close the gaps, document risks and issues and work on mitigation strategies.

The launch phase of the alliance is transferred after 100 days with this first evaluation round to *Phase V—Managing the Alliance Strategy*. Sharing the lessons learned during this phase with other AMs as well as with BD colleagues will improve the PoS for upcoming alliances.

For the running alliance the regular and ongoing tasks like

- facilitation of governance processes
- regular contact with project team
- long-term success metrics with e.g. surveys every 2 years
- resolution of issues
- contract amendments
- reporting and communication
- remain as vital tasks to ensure the achievement of alliance's objectives.

6 The Online Survey on the 100-Day Plan

To evaluate, validate and further improve the content of this checklist, an online survey was designed. The questionnaire consists of 24 questions which cover general statistics about the portfolio of each AM, the view of each AM on the alliance launch phase, questions on governance aspects, on evaluation of alliances and the feedback on the proposed 100-day plan. The online survey was sent to ten Merck Alliance Managers, of which nine contributed. In parallel they were provided with the 100-day plan to collect their feedback on it. The results are shown and discussed in the following, percentages may not add up to 100% due to rounding.

6.1 General Statistics

The different portfolio sizes of each AM are almost equally distributed: Two AMs each (22 percent) manage 1–5, 6–10 and more than 20 alliances, respectively. Three AMs (33%) have 11–15 alliances in their portfolio. That is quite a big variety which can be explained by the differences in scope, size and priority of the alliances. A research alliance with multiple clinical trials, which is complemented by additional alliances for combination therapies with molecules from other partners, requires more attention than commercial alliances with a limited product and geographical

scope. But there is also one AM with 1–5 alliances which were all commercial. On the other hand, one AM with more than 20 alliances has 70% with development activities.

According to the study “Practice of Alliance Management in the Biopharmaceutical Industry” by Twombly and Shuman (2010, p. 18) around 65% of all respondents in mature AM departments (established longer than 5 years) manage one to five alliances. Compared to this result, the portfolios are much bigger for Merck’s AMs. As already mentioned in Sect. 3.3, Merck’s AM department is bigger than the ones in 50% of the 47 companies that participated in this study. One of their finding—that fits to the survey results—was that there is a tendency for bigger portfolios of each AM when alliance groups are larger. The mixed portfolio of the survey participants should allow the coverage of many possible scenarios with one single 100-day plan, once it has been revised in accordance with the collected feedback.

21% of the managed alliances are related to research, 26% to development activities. The majority of almost 43% are commercial alliances which can have a limited product and geographical scope as already mentioned. As the other three types of alliances have also relevant numbers, the proposed design of the 100-day plan needs to fit to all types and their specific needs.

The majority of 61% are alliances where Merck licenses a technology, molecule, product or trademark from a partner. The alliances where Merck is giving a license to a partner or is co-developing products with a partner are almost equally distributed with 15 and 18 percent, respectively. Commercial (co-promotion or co-marketing) activities are not that common with only 6%. The business model can depend also on the lifecycle of an alliance: Research and development projects can be transferred to commercial alliances after successful launch or the resulting product can be out-licensed to one of the partners or a third party.

The question whether the AMs have sufficient time for each partner and the internal team was answered quite indifferent: In the 44% group (four AMs) with sufficient time, there are AMs which have only a few alliances but also one with the highest number. The situation is the same for the other 56% (five AMs). Therefore, the number of alliances in the AM portfolio cannot be seen as the decisive factor. But it seems that there is also no correlation between the alliance types or business models and the answer to this question. AMs with mainly R&D alliances gave both possible answers. And AMs with pure or mainly commercial alliances did the same. Finally, also the age of alliances in the portfolio (please refer to question 1.5) is not relevant for the kind of answer. Further evaluation on this question should be considered in order to find a root cause and show options to improve efficiency of AM work and their relation to partners and joint teams while reducing potential stress levels.

Regarding the age of alliances in each portfolio there is a big variety. The oldest alliances have been established already more than 30 years ago and are still active, the youngest was signed only seven months ago. The average age ranges from 1 to 14 years. Four AMs have quite young alliances with an average age of around 3 years.

6.2 *Alliance Launch Phase*

The average time from contract signature to KOM is almost 5 weeks in a range from less than 1 week to 8 weeks. The AMs were involved on an average 9 weeks before signature of the contract.

The study by Twombly and Shuman (2010, p. 20) showed that 67% of AMs from 47 companies were part of the DD team, including the role as advisors. They also were able to provide input into contract content. That fits in general to the actual results.

Five AMs (56%) are now involved earlier than they used to be, four AMs (44%) are not. The majority of six AMs (67%) would prefer to become involved even earlier into the negotiations of the deal, three AMs (33%) are fine with the current timing of involvement.

The quality of knowledge transfer from BD to AM was rated by one participant (11%) only with 3 out of 10 points. Two AMs each (22 percent) score with 6 and 7 points, respectively. Four AMs (44%) consider the quality of transfer with 8 points. That leads to an average rating of 6.8 out of 10 points which can be considered as acceptable, but leaves room for improvement.

6.3 *Governance of Alliances*

The number of alliances with and without JSC/JPT structures are almost equal. Four AMs have no alliances at all with JSC/JPT, one AM with almost only commercial alliances reported a low rate of 27% of them with JSC/JPT. The number of alliances four other AMs with JSC/JPT range from 43 to 80%. The four AMs which manage alliances without any JSC/JPT gave the following explanations: The alliances are only of low complexity, supply agreements or patent licenses or an out-licensing agreement where the partner is responsible exclusively for decision-making. The five AMs with a mixed feedback provided the following statements on the reasons for not having JSC/JPT for some of their alliances: They are either too small or quite mature, concern only supply agreements, in-licensing or distribution agreements with low complexity, more transactional/vendor type relationships, in a discovery phase or pure research technology licenses.

Only three of the AMs (33%) have an alliance charter or manual in place for at least one of their alliance, the majority of six AMs (67%) have not. Two of the three AMs with alliance charter or manual manage portfolios of 11–15 and more than 20 alliances, respectively. More than 90% are commercial partnerships in both cases. It has to be highlighted that from the survey data it cannot be concluded that the charters or manuals are established for a commercial alliance. The third AM with alliance charter manages a portfolio of 6–10 alliances, with 29% commercial and 14% research alliances. Three AMs (33%) have a regular communication to the joint

committees or other stakeholders of at least one of their alliances, six AMs (67%) have not.

The average satisfaction about the current governance effectiveness was rated by each three AMs with 8 and 9 out of 10 points (38% each). Two AMs scored with 6 points (25%). This results in an average rating of the governance effectiveness with 7.9 points which can be considered as quite good.

6.4 Evaluation of Alliances

Six AMs (67%) have regular evaluations in addition to Merck's general AM survey every 2–3 years as mentioned in chapter 0, three AMs (33%) have not. The additional evaluations happen every 3, 6, 12 months or at every JSC (frequency not mentioned, most likely either 3 or 6 months). As explanations for missing evaluations are provided: “really hands-off alliance”, “not yet implemented, JSC members not absolutely in favor” and “no formal evaluation, but we have the feedback from Merck JSC members”.

As commonly measured KPIs “decision making” was provided six times. “Opportunities identified” and “joint/established objectives” was given as response three times, “follow up on action items/deliverables” twice. JSC/JPT member's individual feedback is collected in at least one of the alliances of one AM. The adherence to the timelines of dossier submission to regulatory authorities is measured in at least one of the alliances of another AM. One AM measures the value creation. The frequently mentioned KPIs are quite similar to the ones of the regular Merck Alliance Management survey as listed in Sect. 4.3. Three AMs would not introduce any additional KPIs, one “as few as possible”. The others proposed adherence to budget and time, effective decision making, key milestones met or exceeded, alignment between internal and external goals, first 100 days onboarding and planned termination.

6.5 Feedback on the 100-Day Plan

Five AMs (56%) have already some kind of a 100-day plan for alliance launch in use, four AMs (44%) have not. As the three most important steps were mentioned mainly the very first steps:

- Arrange KOM (2 days with all project members, incl. definition of JPT)
- Appoint JSC and JPT members
- Alignment/good relationship with partner AM
- Align on joint objectives/operational plan for year one
- Ensure knowledge transfer from due diligence to operational team
- Align on governance and decision-making model

- In addition, some general rules and principles are seen as the most important steps like
- Documentation of roles and responsibilities
- Development of a project plan and communication matrix
- Empowerment of project teams for decision-making

Five AMs do not consider any of the content in the proposed 100-day plan as less important than others. One AM sees “celebrations, motivational training and cross-cultural analysis” as not so important. Another AM considers “IT infrastructure, alliance charter and sharepoints” (for exchange of data and documents, similar than IT infrastructure) as not so relevant. Both AMs are in charge of either “more transactional and vendor-type” alliances or commercial supply agreements which might not have relevant data exchange over a longer period of time compared to e.g. co-development alliances. One AM is of the opinion that “newsletter, survey with both partners at that point of time and lessons learned at that point of time” are not that relevant.

The survey results show that the proposed 100-day plan mainly lists relevant and important steps and was not including steps of low importance in the eyes of most of the survey participants. Six AMs do not have to add anything. One AM misses “full accountability”, another AM wants to see the 100-day plan established at the beginning of an alliance: AM function shall therefore become involved earlier during due diligence and prior to deal closure. One AM prefers an early appointment of project leader/manager and its/their involvement into the activities prior to contract signature.

Overall the feedback by eight experienced practitioners shows that the proposed 100-day plan already includes most of relevant steps and information.

7 Conclusion and Outlook

Some of the conclusions were already made directly in the analysis of the single results in the previous chapter. Therefore, only some general conclusions shall be presented here.

The elaborated 100-day plan has been well accepted by the AMs and their participation in the survey—both in terms of the 90% response rate as well as engagement and proposals—was excellent and above expectations. Due to its limited sample size and the focus on Merck with its specific framework and type of alliances, the result might be used in different environments and companies only with some adaptations. But for the situation at Merck not many things have been identified as missing or incorrect and the contents of the plan are considered as useful for the launch of an alliance.

After usage for a few upcoming kick-offs and launch phases of alliances, a review and further improvement in a workshop together with the relevant AMs should be considered as a next step.

Additional effort could be spent on the creation of an excel-based decision tool that would provide the specific tasks and best decision-making and governance approach in dependence of the type of alliance/business model and the current stage of the lifecycle (please refer also to Sect. 3.2). That would allow newcomers to Merck and/or other the AM department a quick and easy guidance. But also of value for experienced AMs if they enter into an alliance type or structure which they have not managed some time ago.

Another area of interest could be the further improvement of KPIs used for the regular AM survey by Merck but also the self-assessments in some of the alliances. For the knowledge transfer (from BD to AM/PL, from the DD team to the operational project team or also for newcomers to the alliance team in a later phase), the elaboration of a checklist on the required data, its structure and storage could be considered.

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Appendix 1: Operational 100-Day Plan for Alliance Launch

The appendix is available under http://www.goethe-business-school.de/fileadmin/user_upload/Files/07_Master_of_Pharma_Business_Administration/MPBA2018_PublicationHoerner-Appendix1-_00-DayPlan.pdf

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