The Adoption and Adaption of Open Innovation: Empirical Evidence from the Biotechnology Industry

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A thesis submitted in partial fulfillment of the requirements of London South Bank University for the degree of Doctor of Philosophy

February 2020

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In Memory of Papi and Marc. ✝

Abstract

The biotechnology sector is one of the most research and development intensive sectors in the healthcare industry. This thesis provides insights into the innovation management approaches and underlying processes to develop radical innovative technologies, products and services. Radical innovation usually does not come from Germany. Despite the history of high quality products, grounded in German engineering and the power of the so called Mittelstand (SMEs), the typical German innovation is essentially incremental, rather than radical. Therefore, this thesis aims to shed light on this myth, by studying the different stages of the founding process of a biotechnology spin-off, led by a serial entrepreneur. The in-depth, longitudinal case study provides a profound, fine grained inside view into the development of radical innovation in the German ecosystem. To broaden the view and be able to draw conclusions for the biotech sector, multiple cases from five successful, mature, biotech SMEs, based in Germany(4) and the Netherlands(1), are included in the study.

The theoretical framework proposed, is based on two complementary perspectives by firstly integrating the five key characteristic activities of the open innovation concept: R&D, Intellectual Property, Collaboration, Networking, and Entrepreneur- and Leadership, and secondly, the conceptual framework of open innovation, which covers the management of knowledge. The comprehensive data collection includes 11 interviews, observation and participant observation, as well as a rich, in-depth longitudinal data collection of 210 events that illustrates the different stages of founding the spin-off company. Extensive content analysis, coding and constant comparison, adapting grounded theory methods led to empirical themes for both case study types.

This empirical study embraces two different types of organizations to shed light on the innovation processes from multi-level perspectives. These perspectives covering the organizational, intra-organization and the inter-organizational level,

strengthened by the project and individual perspective. Therefore, the findings from this thesis filling a gap in the recent literature about open innovation.

The outcome of this research emphasizes, that radical innovation, like the Human-on-a-Chip technology are based on the vision of an experienced, serial *Entrepreneur*, who managed to find and motivate the *Right People* for this ambitious project. The open attitude and willingness to share knowledge at every stage of the newly founded biotech spin-off, is one of the pre-requisites for their success story. The biotech spin-off TissUse GmbH has created a *Beyond* open innovation business model.

The findings about the mature biotech SMEs suggesting, that at a later stage of business development, *Partnerships* are at the core of their innovation strategies. Even if three of the five participating CEOs and C-level managers did not know the term open innovation, they are brilliant examples for the adoption and adaption of the open innovation concept. Nevertheless, their demand for external knowledge is driven by their own in-house technology expertise. Findings also suggest, that in context with *Partnerships*, especially the collaboration with big pharmaceutical companies is shadowed by the different size and culture of these organizations. In summary, this thesis makes contributions to the body of knowledge in a multi-perspective way. Academics can profit from the in-depth, comprehensive findings about biotechnology organizations, practitioners and young potential founders can learn from TissUse' success story and the SMEs innovation journeys. Open innovation moved from a business *phenomenon* to a *real business world* concept!

Acknowledgements

I am grateful to all the people, who have supported me during this (long) journey of research.

I am deeply indebted to my dissertation supervisor and director of study, Prof. Bruce Lloyd. He helped me at every stage of the research study. He was always available, motivated me and truly believed in me. I have got so much different support, from links to recent literature, skype sessions on weekends, not to mention the huge packed of his edited books, and he has sent me to Germany. I could always count on his support. I enjoyed the visits in his LSBU office with walls out of books a lot. My thanks go to Leslie Gadman, who was there at the early stage of my research. I also would like to thank Robin John, my former Strategy Professor. Many years ago, when I did my MBA at LSBU, he inspired me for *international strategy*. Especially, his support at the final stage is exemplary. Both, Bruce and Robin made every effort to enable me to finish my dissertation.

I am very thankful to all the participants from different biotech SMEs. Without them, this dissertation would have been not possible at all. All professional partners here, did not questioning the purpose of studying innovation management, and open innovation in particular. They all supported me with their contributions during the interviews and discussions about their innovation strategies. I am thankful for their precious time.

My special thanks go to Dr. Uwe Marx, the founder and CEO of TissUse, the spin-off company, which is at the core of this dissertation. I never met a professional, who is such an open minded, down to earth and truly radical innovator. He always puts his team first and is leading by example. I have learned so much from him. All the data, he has shared with me are very rare, therefore this dissertation becomes something special. I thank Prof. Roland Lauster and his scientific team for the great collaboration, even in the years before. Silke Hoffmann, Reyk Horland and Gerd Lindner were always open to my questions and added a lot of value to this study. The input from SD, a life science management consultant from the US, was very helpful. I am thankful for his time and early thougths and recommendations for my study.

The international open innovation community was always important to me. The ISPIM and WOIC conferences, and the people I have met there inspired me constantly. Being a part of this community is a great honor. I am convinced that with this dissertation, I will give something back.

My warmest thank and appreciation goes to all my precious friends. They were there for me, even at the hardest moments of my PhD journey. Who to mention first? Without the constant motivation from Kate, Morgan, Tara, Uwe, Leila, Timo, Philine, Elena, Larsi, Sophia, Silly, Claus, Petra, Nick, Bine, Patrick, Klingel, Aniane, Usi, Gabi, Uwe, Gabi N., Dieter, Tom, Ivan, Holger, Ulf, Hannah, Alexis, Petra V., Kristina, Volker and the Ulmer crew, this piece of work would not have been possible They all supported me in different, mostly emotional ways. My special thanks go to Elena for her view on my data evaluation and our inspiring professional and spiritual discussions. I am very thankful to all of you!

I am lucky to have such a supporting family. I thank my nephew Philipp for not asking, “When will you become a PhD?" my father Winfried and Monic for being proud of me, and my sisters Ariane, Ricci and Sandra for their good wishes.

Finally, and most importantly, I thank my parents Ingrid and Sieghard. They always believe in me, no matter how ambitious my plans are. I dedicate this dissertation to my long gone grandparents, Margarete and Georg. For their generation education was luxury. I owe them a lot.

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List of Abbreviations

5 Key open innovation	Open innovation Activities R&D; IP; NET; COL; EL
Biotech	Biotechnology Industry
BMBF	Bundesministerium fuer Bildung and Forschung (Ferderal Ministry for Science and Education) -
BMWi	Bundesministerium fuer Wirtschaft und Energie (Federal Ministry for Economic Affairs and Energy)
CDA	Confidentiality Disclosure Agreement
CeBiTec	Center for Biotechnology (University Bielefeld)
CMO	Contract Manufacturing Organization
COL	Collaboration
COLIPA	The European Cosmetics Association
DNA	Desoxyribonucleic Acid
EC	European Commission
ECVAM	European Centre for the Validation of Alternative Methods
EFPIA	European Federation of Pharmaceutical Industries and Associations
EL	Entrepreneur & Leadership
EMA	European Medicines Agency
EPO	European Patent Office
FDA	US Food and Drug Administration
FTO	Freedom to operate
Gene	A linear sequence of nucleotides along a segment of the DNA
GO-Bio	Gruendungsoffensive Biotechnologie des Projektträger Jülich
HOC	Human-on-a-Chip
IP	Intellectual Property
ipal GmbH	Intermediary agency mainly for the Berlin universities (TUB, FUB, HUM, Charité, University of Applied Sciences, PEI etc.) founded in 2002 and closed in 2013.
IPR	Intellectual Property Rights
iPSCs	Induced pluripotent stem cells. These type of cells hold great potential in the field of regenerative medicine.
ISPIM	International Society for Professionals of Innovation Management
LOI	Letter of Intend
MBA	Master of Business Administration
Medbt	Medizinische Biotechnologie, Fakultät-Technische Universität Berlin, Partnerinstitut und Sitz des Spin-off TissUse GmbH bis 2016
MNC	Multinational Corporation
MNE	Multinational Enterprise
MOC	Multi-Organ-Chip
NDA	Non Disclosure Agreement
NET	Networking
NIFDC	National Institute for Food and Drug Control China (comparable to EMA and FDA)

NIH	Not Invented Here
NME	New Molecular Entities
NPD	New Product Development
NPV	Net Present Value, see also rNPV
OECD	Organization for Economic Co-operation and Development
open innovation	Open Innovation
OOC	Organ on a Chip
ORI	Open Radical Innovation
PET bio-recycling	Technology which can completely depolymerise all kind of polyethylene terephtalate (PET).
Pharma	Pharmaceutical Industry
PMDA	Pharmaceuticals and Medical Devices Agency, Japan
POC	Proof of Concept
R&D	Research and Development
ROI	Return on Investement
rNPV	Risk-adjusted Net Present Value
siRNA	Small interfering RNA, class of double strained RNA molecules. Besides other roles, it interferes with the expression of specific genes.
SMEs	Small and medium sized Enterprises
TIB MOLBIOL	Biotechnology company founded in 1990, with offices in IT, PO,USA ,SP and distributors in Asia and Africa.
TUB	Technical University Berlin
WHO	World Health Organization
WIPO	World Intellectual Property Organization
ZEBET	Zentralstelle zur Erfassung und Bewertung von Ersatz und Ergaenzungsmethoden zum Tierversuch
ZKBS	Zentrale Kommission für die Biologische Sicherheit

1 Introduction

"The philosophers have only interpreted the world, in various ways; the point, however, is to change it" (Karl Marx)

1.1 Motivation

In 2015 the time to develop a medicine, from the initial discovery, pre-clinical and clinical trials, getting FDA (Food and Drug Administration) approval and finally hit the market, was at least 10 years, but on average 13,5 years (Tufts CSDD, 2014). During this period of time each successful drug costs an estimate of US$ 2,6 billion. There is a likelihood of only 12% that a promising candidate component will make it to the patient (PhRMA, 2015). In this context the biopharmaceutical industry is represented by the top 50 worldwide active companies (Tufts CSDD, 2014). Despite all emphasis for the adoption of innovation at the different stages of the value chain of drug development, mentioning one important bottleneck is missing here. The huge gap between pre-clinical results from animal testing and living cell line testing and the next step: clinical tests in humans. Even if this discrepancy has led to the disastrous outcome of the TGN1412 case (Stebbings et al., 2012), where six healthy volunteers suffered from severe adverse reactions, the majority of pre-clinical tests are still conducted in animals (Attarwarwala, 2010; Marx et al., 2016). It is therefore surprising, that there seems to be no strong focus on this proven obstacle. Even if new disease models, i.e. animals, living cells and computer simulated models are under investigation, applying a human emulation approach before the first-in men (FIM) studies is very promising.

For the first time, not only the scientific research and development of such a radical innovation in biotechnology, but also the socio-economic framework for it, is under investigation and in the focus of this dissertation. Emulation the human biology in a "Multiorgan on-a-Chip" (MOC) system is a radical innovation, developed by an entrepreneurial German biotechnology spin- off organization. Because of the importance and relevance, not only for the pharma-and biotech industry, but also for the society and the academic world, this dissertation aims to add valuable new insights to the body of knowledge. To strengthen the chosen case study methodology, the single case is complemented with multiple cases from the biotech sector. The companies are at a later stage of development and have already proven their success.

Unfortunately, another clinical phase I disaster in France is supporting the urgent demand for more reliable, more humanlike pre-clinical tests. One healthy volunteer died, after being diagnosed brain dead as a result of participating in a clinical trial with an enzyme drug, BIA 10-2474 developed by Bial Portela & Ca. S.A., a Portugal based pharmaceutical company (Kroll, 2016). Additional five patients are hospitalized, three of them suffering from serious, irreversible health conditions. Several other news- and professional articles are discussing the risks and ethical aspects of clinical trials at this stage, but surprisingly none of the authors providing the recent status of research on emulating the human biology to close this fatal gap. The sad truth of the dead volunteer is one important motive to provide more insights about the scientific and socio-economic background of biotechnology driven innovations. The in-depth, longitudinal case study research about a newly founded biotechnology spin-off is at the core of this dissertation, backed up with insights from five mature biotech SMEs. The open innovation phenomenon was chosen as the theoretical framework for this study. The following paragraph is describing the background of the research framework more in detail.

1.2 Background to the Research

The term open innovation was coined and developed by Henry Chesbrough for the first time in 2003. In contrast to closed innovation, Chesbrough defined open innovation as follows:

> "Open innovation is a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as they look to advance their technology." (Chesbrough, 2006 p.1)

One of the early prime examples of introducing open innovation principles in the early-1980s is the US IT industry. Taking Xerox Corp. as an example, which has founding over 20 new start-up companies dealing with spin-off innovation (Chesbrough, 2003). Furthermore, Xerox re – invented itself in recent times by adopting a radically new business model founded on open innovation principles. Facing the challenges of competitors like Canon and other rivals with simpler and cheaper copiers, Xerox went into the classic story of the "Innovators Dilemma" (Christensen, 2011). By turning the business into becoming a service provider for banks and law firms, Xerox innovative, simple web-based document tools saved the company (Scott and Christensen, 2011). High-tech industries, especially those with very short innovation cycles, are most receptive to the flexible adoption of the open innovation concept. Other prominent examples of the early adoption of open innovation and, therefore, the switch from a closed innovation business model towards an open one are IBM, Intel, and Procter & Gamble (Chesbrough, 2003). These representative companies of different US industrial sectors are characterized by significant financial resources, traditionally readiness to assume risk and good internal incentive programmes to foster innovations.

The biotech industry was "born" in the USA in 1976 with the foundation of Genentech, the first company which used genetic engineering techniques to produce therapeutic proteins. The biotech industry, especially in the USA, is strongly aligned with the pharmaceutical industry (Harris and Lyle, 2009). In contrast to the IT sector, the US biotech industry has always been an innovator on behalf of the pharmaceutical industry. This fact has had significant impact on the innovation cycles and innovation approaches of the biotech industry. Drug development cycles of eight to twelve years from the invention to market and tremendous potential blockbuster value were significant drivers for completely closed pharmaceutical innovation systems (Ernst & Young, 2010).

This starting position changed significantly in the US and with global pharmaceutical companies at the end of the 1990s, when numerous executive positions were occupied by finance officers (MBAs) rather than chemists (natural scientists), and the paradigm of continuously growing return on investment (ROI) took over the paradigm of patient welfare, also called the "healthy outcome", for individuals, groups or populations (Ernst & Young, 2010).

Simultaneously, significant candidate failure rates, clinical trial mismanagement and "drug-disasters" (e.g. Thalidomide (Contagan), Vioxx, TGN 1248, BIA10-2474) have increased the risk awareness of regulatory bodies on both sides of the Atlantic since the mid-fifties (see Fig.1). Consequently, the worldwide pharmaceutical industry is facing large innovation crises. The research and development (R&D) spending is constantly increasing over the last twenty years, but the decreasing productivity and the numbers of approved drugs are evidence of the innovation deficit (Marx et al., 2016).

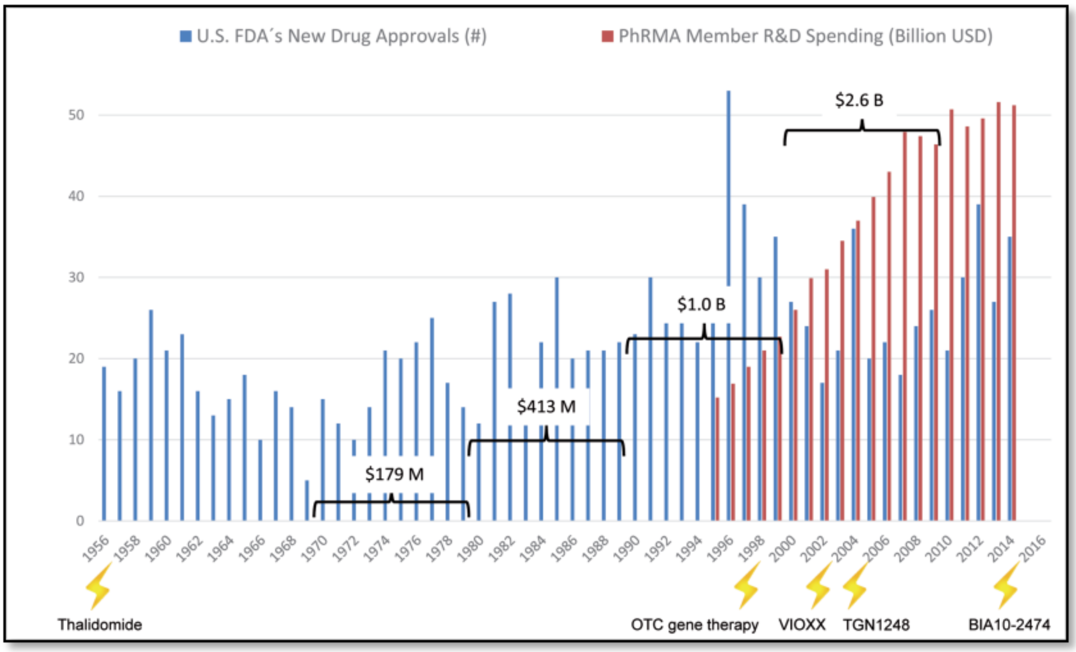

Figure 1: Changes in drug development over the last seventy years (Marx et al., 2016)

As illustrated in Figure 1, the pharmaceutical research and development (R&D) costs increased from $179 Million in the seventies to $ 2,6 Billion (in brackets) as of in 2016. The numbers of new drug approvals by the US FDA are plotted against the R&D spending. The disastrous drug and substance failures are highlighted below the graph.

The US biotech sector has been the prime and lead global biotech industry over the whole period until now. Biotech revenues in the US in 2016 were US $ 112.2 Billion (US 2015 = US $ 107.4 Billion) compared to the EU, with US $ 27.2 Billion (EU 2015 = US $ 22.8 Billion) (Ernst & Young, 2017) Ernst & Young. The biotech hype in Europe took place at the end of the 1990s, 15 years after the USA, and experienced a significant fall back in the first decade of this century.

Since that time, different open innovation approaches have been improved throughout many industries and large pharmaceutical organizations have tried to catch up to solve the R&D dilemma. One example is the open innovation platform, "Grants4targets", founded by the German pharmaceutical company Bayer HealthCare (Grants for Targets, 2011).This open innovation initiative has become successful over the years and resulted in two additional platforms, Grants4Apps and Grants4Leads, with the benefit for Bayer to identify new promising targets and increase their reputation in the scientific community (Dorsch et al., 2015).

In-house R&D is no longer the main resource for new medicines, such as molecular entities, vaccines and biologics. Pharma companies are forced to look outside of their own company boundaries for novel, innovative products. Therefore, starting more than a decade ago, collaborations, strategic alliances and partnerships between the pharma and biotech industries and academia are signs of a new era in worldwide healthcare product development (Deloitte, 2006). A collaborative framework is one of the drivers for adopting the open innovation concept. Knowledge sharing on a global basis will improve the innovation progress and productivity of the pharma and biotech industries significantly. Collaborations with research institutes and universities are important resources to fill the pipelines of the pharma and biotech companies. German biotech companies are collaborating with research institutes, other biotech companies, industrial partners, and other organizations (BIOCOM, 2011; BIOCOM, 2017). These collaborations are taking place across the entire value chain and almost every second industrial cooperation incorporates at least one international partner. To overcome the innovation deficit, the pharma and biotech industries have to focus on understanding how the human body functions on a molecular level, the knowledge of the pathophysiology of diseases, the use of new technologies to improve and speed up the research process and clinical development, and to open up their company boundaries for more collaboration with academia, regulatory authorities, healthcare providers, and governments (PricewaterhouseCooper, 2010).

In 2017 Germany had 646 dedicated biotech companies, with 21.860 employees, € 4,1 Billion sales, €1,1 Billion R&D investment and € 673 Million investments (BIOCOM, 2018). What makes Germany so different or special? According to the report of the German Commission of Experts for Research and Innovation (EFI, 2016), innovation activities in Germany will increasingly focus on high-value technologies (incremental innovations), rather than on cutting-edge technologies (radical innovations). This has led, and will continuously further lead, to a steady decrease of start-up rates in cutting-edge technologies (EFI, 2016). Nevertheless, the recent start-up development is more promising, since the number of 20 newly founded start-ups in 2016, doubled the number of 10 start-ups in 2015 (BIOCOM, 2017). These recent numbers and developments are strengthening especially the German biotech sector to become the backbone of the knowledge-based economy.

The Lisbon Strategy acknowledged biotechnology as the backbone of the knowledge-based economy (EuropaBio, 2011). A decade ago, the urgent demand for more cutting-edge technologies in Europe was correlated with the Lisbon Strategy:

> “The lack of the structural change towards more cutting-edge technology has contributed to the failure to achieve the three-percent target of the Lisbon Strategy.” (Frietsch et al., 2010)

In addition, at this time, German speaking countries in general, and Germany in particular, have historically developed a very special public sensitivity to biotechnology. Germany is the least optimistic country concerning biotechnology in Europe, according to the report of the European Commission on “Europeans and Biotechnology in 2010. Winds of change?" (European Commission, 2010). This was researched as a comparison of an index of optimism for biotechnology/genetic engineering among 32 European countries. Germany scored 12 in an index range from 0 to 100 in 2010. In the light of the fact that biotechnology/genetic engineering was the second less attractive technology out of six "next generation" technologies surveyed by the study, it can be concluded that the social/ethical/public environment for biotech/genetic engineering start-up activities in Germany was not supportive. Indeed, this trend can be substantiated by the German biotech performance data reported annually by different search organizations.

Therefore it can be concluded, that when the spin-off organization was founded in 2010, the social, ethical and political environment for this type of technology, namely biotechnology tissue engineering was not well accepted and not well supported.

1.3 Perspective of the Researcher

This paragraph aims to introduce the specific perspective of the researcher, who is motivated to conduct this study and dissertation in academic rigor, based on extensive practitioner's experiences in the life science sector. The scientific and engineering background, the relatively late accomplishment of an International MBA, and the more than 30 years of working experiences in the food, biotechnology, and diagnostic sector, followed by a position in managing technology transfer from university research into the industry, have positively influenced the researchers decision to study the open innovation phenomenon in theory and practise. The motivation was originated and driven by the question, what leads to innovation in general, and in particular, what makes radical biotech innovation feasible? The strong professional network and trustworthy relationship to the case study participants, enables the researches to provide a comprehensive, in-depth, longitudinal case study, backed up with multiple cases, of established biotech companies with strong innovative product records. Compared to most academic driven dissertations, with limited access and insight to specific industries, this study is based on long-term direct professional participation in the German life science ecosystem. Overall gain is to add new knowledge to the academic and business world. The following sections are focusing on the aim of the study with emphasis to the purpose, the framework of the open innovation concept, the research questions and the limitations of the study.

1.4 Purpose of the Research

The specific German background exhibiting significant hurdles for biotechnology in general and radical innovations in particular has stimulated the research concerning the question, whether cutting-edge technology start-ups and spin-offs are possible in Germany, and to what extent open innovation business models are improving their performance and survival rate in this particular sector. The overall theoretical framework for the research is the open innovation concept. This phenomenon has been well investigated and described in the literature since 2003, and many researchers have conducted studies via observation, industry analysis, surveys, and case studies (Chesbrough, 2003; Chesbrough 2006; Enkel et al., 2009; Chesbrough 2010; Chesbrough and Bogers, 2014, Bogers et al., 2017). However, most of the research identified focuses on established companies. Research-based start-ups are the drivers for innovation (Christensen, 1997). These start-ups and spin-offs are characterized by different starting conditions which lead to huge variations on the time to market of their first products (Heirman, 2004). Therefore, research about the business models of start-ups and spin-offs , and the evolution of their business models during the pre-foundation stage needs further in-depth investigation.

De Jong, Vanhaverbeke, Kalvet, and Chesbrough published "Policies for Open Innovation" in 2008. The sholars evaluated and established the key behavioural aspects of open innovation, which are characteristic for innovating enterprises based on their broad experiences with the open innovation concept. These identified five key characteristic activities in context with adapting the open innovation concept are:

1. Research and Development - **R&D**,
2. Intellectual Property Management - **IP**,
3. Networking - **NET**,
4. Collaboration - **COL**, and
5. Entrepreneurship and Leadership - **EL**.

Research by Lichtenthaler (2011) focused on developing a framework for knowledge generation on different levels, namely on the organizational level, the project level and the individual level in context with the open innovation phenomenon. These different levels are investigated from the internal and external perspective. Furthermore, Lichtenthaler (2011) emphasizes the need for future research on profitable business models which are able to create radically innovative products. The focus of this dissertation is, therefore, the evaluation and interpretation of the key characteristics of the open innovation concept based on De Jongs et al. (2008) by integrating them with Lichtenthaler's (2011) conceptual framework for open innovation.

The researcher decided to combine both concepts to create the model framework for this dissertation. The rationale was to find the right model framework to embrace the five key open innovation activities, R&D; IP; NET; COL, and EL, and their causality and interdependency on the organizational level, the project. and the individual level. The model framework will include the different types of capabilities on the organizational, project and individual level in connection with the knowledge creation process underlying the development of radical innovation. The dynamic capabilities of open innovation (Lichtenthaler, 2011; Lichtenthaler & Lichtenthaler, 2009; Teece, 2007) combined with the key characteristics of the company's behaviour adopting open innovation is under investigation for the first time. Embedded in the study design of an in-depth case study about a German biotech spin-off company, and backed up with multiple case studies from five mature biotech companies, this dissertation aims to fill the gap in the knowledge about the value creating business model for radical innovation, embedded in the German ecosystem. Furthermore, this dissertation aims to provide new insights into the transformation process of a project based research group into a commercial entity. The five open innovation activities, the research questions and objectives, and the case study design are described in the following section.

1.5 Research Objectives , Research Questions and Study Design

The aim of this dissertation is to investigate the challenge of the creation of radically innovative products and services in the highly competitive biotech sector. Giovannetti (2011) stated:

> "While the biotech industry's aggregate performance improved in 2010, there is now a widening gap between large, established companies and those at earlier stages for whom access to capital continues to be difficult."

Companies at earlier stages, such as start-ups and spin-offs, are facing the difficulties of gaining access to capital, while being, at the same time, the drivers and indicators for innovation (Braun-Thuermann, 2010; Spender et al., 2017). This type of early venture was chosen as the main source for the data collection focusing on the open innovation activities: R&D, IP, NET, COL, and EL. The open innovation activities were identified and evaluated during the first years of study with the aim to investigate the open innovation phenomenon in regard to the biotech sector. At this stage of the study the innovation process itself, regardless whether it leads to incremental or radical innovative products and/or services was studied. Later on, based on the data collection the focus was narrowed to radical innovation.

This research study qualifies for an empirical study, since the investigation is based on "real" data from the observed and investigated six biotech companies. Therefore, the following research objectives are guiding the overall study:

- To develop insights and knowledge about the successful development of radical innovation in the biotechnology sector.
- To provide an integrated picture of the adoption and adaption of open innovation in the biotechnology sector.
- To evaluate the interdependence and correlation between the five open innovation activities: Research & Development (R&D); Intellectual Property (IP), Collaboration (COL); Networking (NET) and Entrepreneur- and Leadership (EL).
- To analyse and evaluate theories for different types of business models, applicable to biotechnology spin-offs and SME`s.

The research questions, initiated by the researchers first publication "How do recent Trends in the Pharmaceutical and Biotech Industry influence Open Innovation Approaches?" (Kunz, 2009) and the comprehensive study of the innovation literature, led to the following three research questions:

RQ 1: Is the Open Innovation concept adopted by biotech companies?

RQ 2: Can Open innovation enable the development of radical biotech

innovations in a German ecosystem?

RQ 3: How does the evolving business model look like?

The causality and interdependency of the open innovation activities and the underlying variables were chosen in order to provide a holistic view of the adoption of the open innovation concept with regard to RQ1. RQ2 aims to identify the success factors for radical innovation in the specific German ecosystem setting. Answering research questions RQ1 and RQ2 will lead to answering RQ3, the identification and evaluation of the evolving business models in the biotechnology sector.

All three research questions are examined by utilizing the research methodology based on the case study approach. The specific case study design for this dissertation embraces two basic types of case studies: Firstly, the single-case design of a spin-off organization, and, secondly, the multiple-case design of five SMEs. Both designs are embedded with multiple units of analysis (Yin, 2009). The case study methodology was chosen in order to generate a rich collection of data in the context of a spin-off biotech company backed up by the additional data collection of multiple cases, namely established SMEs from the same sector.

In 2011, the European Medicines Agency (EMA) identified advanced therapies, such as cell therapy, gene therapy and tissue engineering, as the scientific progress drivers for change in the next five years (EMA, 2011). The main resource for the case study data collection is a biotech spin-off whose new product development is based on cutting-edge tissue engineering technologies. This case meets the requirements for an exemplary case study, since it is of general public interest and will play an important role from the national, German perspective (Yin, 2009). The general public interest can be linked with the EMA's perspective regarding new and emerging science. This case study is of great importance nationally from the German point of view, because the seed funding for the technology development has evolved from a German governmental funding program: *GO-Bio* initiated by the BMBF (Strey, 2015). However, even if this single case has its location and starting point in Germany, it is not limited to being an example which is only relevant on a national level. The international scientific and commercial network of the serial entrepreneurial founder of the new venture will allow conclusions and recommendations on an international level to be made.

To not limit the research study to only one organization, the multiple cases, the biotech SMEs will deliver profound data too and complete the picture. Nevertheless, the two types of analysis, the longitudinal single case and the multiple cases are investigated and developed separately. The structure, context and content of the dissertation are described in detail in the next paragraph.

1.6 Structure of the Dissertation

This dissertation covers six chapters. The main structure and contents of each chapter are illustrated in the following Figure 2:

Figure 2: Structure of the dissertation

1.7 Limitation of the Dissertation

This dissertation aims to answer the question whether radical innovation in the biotech sector in a German ecosystem is possible, and, if so, under which conditions? The chosen methodology of the case study research design has its advantages, but also some disadvantages - the limitations. Qualitative research methods, such as case studies, play an important role in socio-economic research to contribute to our knowledge of individual, group, organizational, social, and related phenomena (Yin, 2009). Forms of the research questions of this dissertation are "what" and "how". Schramm (1971, cited in Yin, 2009, p.17) emphasis his definition of a case study as the following:

> "The essence of a case study, the central tendency among all types of case study, is that it tries to illuminate a decision or set of decisions: why they were taken, how they were implemented, and with what result." (Yin, 2009, p.17)

In the context of this definition, other research methods, such as experiments, surveys, archival analysis, and history studies, are inappropriate to the scope of this dissertation (Yin, 2009). Even so, the chosen methodology faces some limitations. The main resource of the data collection is a single in-depth case study, backed up with five multiple case studies from established, mature biotech companies. In contrast to results from quantitative research, e.g. surveys, this is a relatively small number of samples. But all companies have in common, that they further developing and have developed technologies, evolving from university/research organizations. Therefore, the SMEs and the spin-off companies are comparable.

Flyvbjerk (2006) identified and discussed the common misunderstandings about case study research illustrated in Table 1.

Table 1: Five Misunderstandings about Case Study Research

Misunderstanding	Restatement
1. General knowledge is more valuable than context-specific knowledge.	Universals cannot be found in the study of human affairs. Context-dependent knowledge is more valuable.
2. One cannot generalize from a single case, so a single case does not add to scientific development.	Formal generalization is overvalued as a source of scientific development; the force of a single example is underestimated.
3. The case study is most useful in the first phase of a research process; used for generating hypotheses.	The case study is useful for both the generating and testing of hypotheses, but is not limited to these activities.
4. The case study confirms the researcher's preconceived notions.	There is no greater bias in case studies toward confirming preconceived notions than in other forms of research.
5. It is difficult to summarize case studies into general propositions and theories.	Difficulty in summarizing case studies is due to the properties of the reality studied, not the research method.

Source: Adapted from Flyvbjerg (2006), pp. 219-245.

The restatements are important arguments concerning the limitations of the research methodology. However, there are some limitations concerning the researcher's point of view, since the researcher acquires all the data, conducts the interviews and analyses and interprets the data collection. The threat of bias can be limited by taking an open-minded, neutral position towards all information acquired and adhering to the theoretical model framework for the study.

Another limitation of this dissertation is the richness of the data collection from the single case study which is investigated in regard to the open innovation activities (De Jong, 2008) and the conceptual framework of open innovation (Lichtenthaler, 2011). The data collection could additionally become the resource for other, new research questions outside the scope of this dissertation. To overcome this limitation, the researcher plans, to submit further publications based on the rich data collection. The scope of this dissertation and the underlying literature review is described in the following Chapter 2.

2 Literature Review

"Information is not knowledge." Albert Einstein

2.1 Introduction to the Innovation Literature

The aim of the literature review is to get an overview about what has been published about innovation and open innovation in general and the management of innovation in regard to the biotech sector in particular. Source material included books, publications, recent commercially available reports about the sector, and numerous additional valuable sources. Consequently, the research was streamlined to observe and identify open innovation specifically in connection with the European and German biotech industry. Pre-eminent resources in the literature are the highly cited publications in the area of innovation management, i.e. by Chesbrough and Vanhaverbeke. Chesbrough first described the open innovation phenomenon and the paradigm shift from closed innovation to open innovation in 2003 (Chesbrough, 2003). His research initially focuses on open innovation in large multinational enterprises (MNE), especially in the USA. Vanhaverbeke's research and his numerous publications provide deep insight into and knowledge about the adoption and adaption of open innovation in small and medium size enterprises (SMEs) (Vanhaverbeke et al., 2009; Brunswicker and Vanhaverbeke, 2010a,b; Vanhaverbeke et al., 2012; Vanhaverbeke, 2017), and the influential role of research organizations from a European perspective (Van de Vrande, 2008;, Brunswicker and van de Vrande, 2014).

Additionally, important resources include the annual proceedings of the International Society for Professional Innovation Management (ISPIM). This organization is a worldwide network of innovation management professionals from research, industry and intermediary organizations. The open innovation phenomenon is an important research objective to this international community.

This literature review will, therefore, focus on innovation literature, starting from a global perspective. In this context, the review will include and focus on literature about radical innovation versus incremental innovation. The relevant literature about the open innovation phenomenon across different industries and from a global perspective will be outlined in the following section. Furthermore, inside knowledge about the global characteristics of the pharma industry and literature about the specific German biotech environment and ecosystem will serve as a framework for the case study on a German biotech spin-off company. The scope of the literature will be analysed and evaluated in the critical review to identify gaps and represent the link to the research objectives of this dissertation. The following Figure 3 illustrates the scope of the dissertation in relation to the open innovation concept.

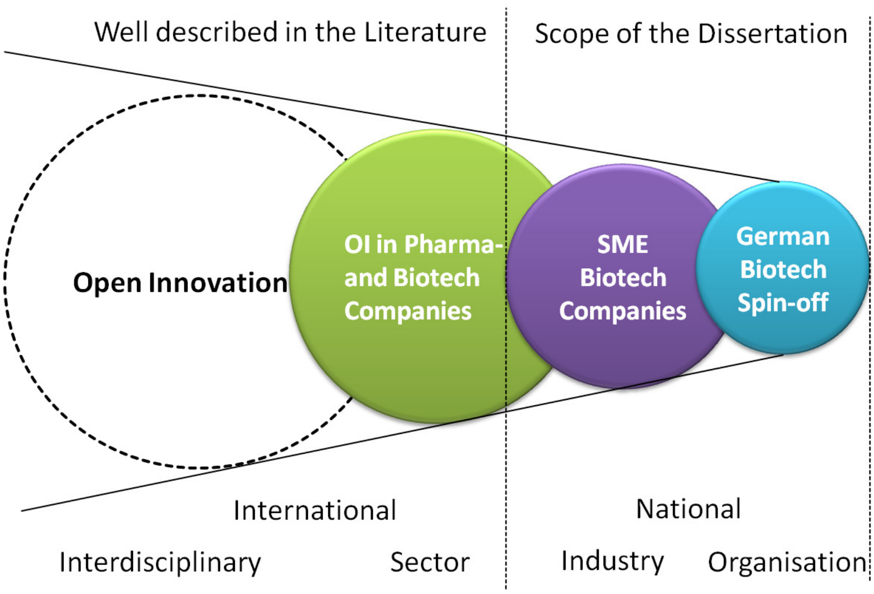

Figure 3: Scope of the Literature and Dissertation

2.2 Innovation in a Global Context

Innovation is a highly stressed term throughout all areas of our "Information Age" (Castell, 2001), and is characterized by sharing information on a global basis. Many publications focus on innovation management in a global, cross-sectorial, interdisciplinary context. Some authors, such as Berkun (2007), try to disclose the myth behind innovation. He went far back into history to identify the myth about innovation, while using examples from science, history, the arts, business, and politics. Innovation, from Berkun's perspective, can only happen due to persuasion and perseverance. The time of the lone inventor is long gone and has been replaced by two or more innovators working together in pursuit of their ideas (Berkun, 2007).

However, innovation is the "lifeblood" from the business perspective and a strategic priority, and, therefore, the driver of the global economies (Dyer et al., 2011). Chesbrough's vision goes further into knowledge-intensive infrastructure and product lines that evolve into "the engine of growth for the entire developed world" (Chesbrough, 2011). The company of the future will provide not only innovative products, but also service platforms and the opportunity for the consumers to experience and influence these products and services (Chesbrough, 2011). One of the early theories about innovation, "The Diffusion of Innovation", was developed by Rogers (1962). The theory indicates that the number of "real" innovators is relatively small in comparison to the early adopters, the early and late majority and the laggards. This leads to the characterization of the different groups with emphasis on the innovators. They are venturesome, educated and have access to multiple sources of information (Rogers, 1995). Innovators need the ability to understand and apply complex technological knowledge and financial resources, and the willingness to cope with the high degree of uncertainty of the innovation itself is mandatory. These abilities of innovators are under investigation in this research study, by focusing on a spin-off organization founded by a serial entrepreneur.

Despite the fact that there are numerous definitions of the term "innovation" available in the literature, Schumpeter (1934) coined a very complex definition which is applicable to different types of organizations. From his perspective, innovation is:

> "The introduction of new goods […], new methods of production […], the opening of new markets […], the conquest of new sources of supply […] and the carrying out of a new organization of any industry."

He went further with his definition of the drivers for capitalism, and emphasises that new consumer goods, the new methods of production or transportation, the new markets, and the new forms of industrial organizations created by capitalist enterprises are essential for the process of creative disruption (Schumpeter, 1947). There is a strong link connecting his theory of the numerous definitions of innovation to authors of our century. Von Hippel's (2005) research on innovation focuses on the power of the consumers and their influence on the new product development (NPD) process. From his perspective, the democratization of innovation is strongly influenced by the consumer and leads to innovative products, technologies and services. His "lead user approach" is optimally applicable to the consumer market, but has some limitations regarding the involvement of other external partners of an organization. However, his contribution to the theoretical knowledge and implementation of a user-driven innovation approach is tremendous (e.g. 1986, 1988, 2005, 2006, and 2013).

Drucker (1985) evaluated the link and interdependency between innovation and entrepreneurship by his defining of innovation as:

> "The specific instrument of entrepreneurship [...] the act that endows resources with a new capacity to create wealth."

His principles of innovation are summarized in a number of do's and don'ts, backed up by three important conditions. Firstly, innovation is hard work and requires knowledge and ingenuity. Secondly, innovators must build on their strengths and always look at opportunities that fit themselves and their company. Thirdly, innovation becomes an effect in the economy and society. Innovations, therefore, have to be close to the market and focused on the market; in other words, market-driven (Drucker, 1985).

Schumpeter's and Drucker's definitions from the academic and business perspective of this dissertation present a proper framework in regard to innovation in a global context. However, one decade later, Christensen (1997) analysed why and how leading companies fail in the innovation race. Christensen created the following new rules for managers and entrepreneurs focusing on disruptive technologies:

- "not to listen to customers at the right time,
- invest in lower - performance products, and
- pursue small markets at the expense of larger, lucrative ones."

There are many examples described in the innovation literature which illustrate established technologies and their disruptive counterparts (Christensen, 1997, p.xxix).

Table 2: Established and Disruptive Technologies

Established Technology	**Disruptive Technology**
Silver halide photographic film	Digital photography
Wireline telephony	Mobile telephony
Offset printing	Digital printing
Open surgery	Arthroscopic and endoscopic surgery

Source: Extract adapted from Christensen, 1997, p. xxix

More examples of disruptive innovations are the Apple iPod, which competes successfully the Sony Walkman, and Skype, which uses a free-of-charge strategy to beat AT&T and British Telecom (Dyer et al. et al., 2011).

Moore (2005) called disruptive innovation the "most dramatic" form of innovation and categorised four types of innovation from the market/product perspective. The following figure demonstrates the author's perspective on the link between the different types of innovation and the potential outcome: radical technologies, products and services, and incremental technologies, products and services.

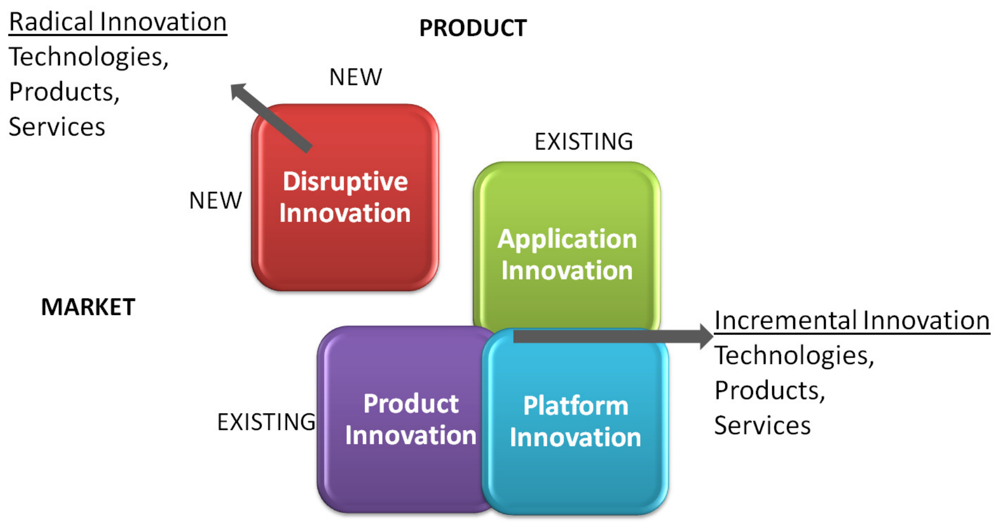

Figure 4: Radical Innovation Matrix based on Moore, 2005

While application, product and platform innovations are based on existing knowledge of established products and markets, disruptive innovations are characterised by being new to the market and creating novel, radical innovative products, technologies and services. The single case study of this research is addressing exactly this type of innovation, a disruptive technology which leads to radical innovative products and services.

Due to the fact that our century is characterized by a phenomenon called the "commodity trap" (Chesbrough, 2011), which means that highly innovative products eventually become commodities with nearly similar prices, there is a need for more radical rather than incremental innovation in all sectors.

This dissertation will focus on incremental and radical innovation in order to simplify the numerous definitions of innovation and its different types. The incremental/radical dichotomy is used by many authors, however, the terms and the resulting consequences for the strategic direction of an organization are defined early in the literature by Abernathy and Clark in 1985 and Tushman and Anderson in 1986. Two important dimensions have to be taken into account by separating an incremental from a radical innovation.

Incremental innovation builds upon existing knowledge and resources based on the internal capabilities of a company, which means it will be "competence-enhancing". In contrast, a radical innovation forces the company to acquire completely new knowledge and resources and will, therefore, be "competence-destroying".

Incremental innovation from the market perspective and the positioning of a company in the competitive environment involves minor technological changes, and only improvements and the existing products on the market will remain competitive. A radical innovation is characterized by large technological advancements; it delivers novel products, which are, for a certain period of time, non-competitive. Another important characteristic is that radical innovations can create completely new markets. Both incremental and radical technologies, products and services require a so-called "chameleon innovator" (Diligu, 2006). This type of innovator is able to handle both types of innovation while creating new products and markets, as well as maintaining their position in the established market incrementally.

Emerging markets, such as China and India, are changing the rules of innovation due to their unique market needs. India, for example, is one of the great new potential markets at the bottom of the economic pyramid: Low income consumers demanding high-tech products at affordable costs (Prahalad, 2006). Innovative global-acting companies are forced to leave their comfort zone, bounded by existing technologies and business models, and embrace radical innovation too. Diligu et al. (2006) challenges innovation executives to create an "innovation box" where radical and incremental innovations are integrated. In this model, radical innovation means that *invention is the mother of necessity*, and incremental innovations means that *necessity is the mother of invention.*

Innovation today is as important as it was more than 30 years ago, stated Drucker (1986, p.31): The only thing that matters is innovation!" He emphasizes further that four sources inside an organization can become opportunities to innovate:

- "The unexpected - the unexpected success, failure or outside event;
- The incongruity - between reality and reality as it assumed to be or as it 'ought to be';
- Innovation based on process need; and
- Changes in the industry structure or market structure that catch everyone unawares."

In addition, he identifies three sources from outside the organization:

- ″Demographics (population changes);
- Changes in perception, mood, and meaning; and
- New knowledge, both scientific and non-scientific."

All these early sources for radical innovation and the requirements from the academic and organizational perspectives are important to investigate to answer the question: What makes radical innovation feasible in the biotech sector? The role of the radical innovator, described by Gemuenden et al. (2007) has three dimensions. Innovators pursuing radical innovation have to master organizational changes, societal changes and changes in the competition.

Since all these challenges and opportunities come from both, inside and outside the organization's boundaries, accepting these challenges leads to the open innovation concept described in the next section. This part of the literature review will provide the theoretical perspective and aims to critically review the past, present and future of the open innovation phenomenon.

2.3 *Open Innovation*

Open innovation is a business phenomenon observed and described for the first time by Chesbrough in 2003, but it has its roots in the behaviour of companies which have to cope with competitors and the pressure from the market to deliver value, e.g. innovative products, technologies and services. The term was coined then, but the approach has a longer history (Rothwell, 1994). A decade ago, Trott and Hartmann (2009, p.517) criticized the open innovation concept simply as: "old wine in new bottles." In this context, the data collected from the multiple cases studies will provide insight into the practical, real world adoption of open innovation.

Numerous publications about open innovation are available in the form of books, articles in journals, conference proceedings, reports from international organizations, such as the OECD and the EU commission, as well as many reports and studies conducted by renowned global action consultancies. Chesbrough googled the phrase "open innovation" in 2003 and got only a couple of hundred links (Norton, 2011), but a decade later there are 66 Mio links (accessed on July 24, 2011). The term has become a buzzword in connection with innovation management and new product development.

From the perspective of this dissertation, the core literature provided by authors such as Chesbrough (2003, 2006a, 2006b, 2010, 2011, 2014, 2015); Vanhaverbeke (2005, 2006, 2008, 2014, 2017) West, Bogers, von Hippel, Enkel, Gassmann, Piller, Reichwald, and Lichtenthaler are important basic resources. Notwithstanding, additional authors are included in the ongoing literature research and review. A decade ago, Calida and Hester (2010) studied and analysed 91 articles containing the term open innovation published between 2009 and July 2010 to provide an overview of research gaps and emergent conceptual themes across the on-going open innovation research. In addition, the existing literature on open innovation at this point of time was summarized.

Fredberg, Elmquist and Ollila (2008) were additionally identified as having provided a summary of open innovation publications. Their study included interviews with internationally acknowledged open innovation researchers, such as Chesbrough, Piller and von Hippel, to name only three. The outcome of this study was that only 49 papers and books analysed open innovation by including the phrase in the title, abstract or keywords in 2008. Even though this analysis has its limitation, the finding that there is great potential in the further theoretical development in the open innovation field seems to persist until today (Gassmann et al., 2010; Chesbrough et al., 2014; Bogers et al., 2017; Yaghmaie and Vanhaverbeke, 2019). Looking back at the open innovation core literature over the last fifteen years, one important conclusion can be drawn: The open innovation model was created by observing the behaviour of organizations in their competitive environment. Therefore, the ecosystem around organizations in a global context has been the most influential factor for the switch from the closed innovation approach to open innovation.

2.3.1 Open Innovation – A Historical View

A historical view of Rothwell's (1994) five generations of innovation models was considered appropriate in order to analyse the evolution of the open innovation concept. The key features of every generation have to be taken into account to understand the paradigm shift from closed innovation to open innovation. The following table is adapted from Tidd (2006).

Table 3: Five Generations and the Innovation Approach

Generation	Key features	Time	Innovation Approach
First	The linear model - technology **push**	1950 to mid-1960s	Closed Innovation
Second	The linear model - market **pull**	Mid-1960s to early-1970s	
Third	Interaction between different elements and feedback loops between them - the **coupling model**	Mid-1970s to mid-1980s	↓
Fourth	The parallel lines model, **integration** within the firm, upstream with key suppliers and downstream with demanding and active customers, emphasis on linkages and alliances	Early-1980s to mid-1990s	Open innovation
Fifth	Systems integration and **extensive networking**, flexible and customized response, continuous innovation	From the 1990s onwards	

Source: Adapted by the author from Tidd (2006) p. 3

Rothwell evaluated in his research that each generation was influenced by changes in the ecosystem, such as economic growth, industrial expansion, more intense competition, inflation, stagflation, economic recovery, unemployment, and resource constraints. These factors are important indicators for an organization's innovation strategy. Combining Rothwell's theory with Chesbrough's observations, open innovation started, to some extent, when the fourth generation of innovation models was defined. Prominent examples are Chesbrough's (2003) case studies about Xerox and the transformation of IBM, which cover exactly this period of time, the 1980s to the mid-1990s.

Another perspective on the paradigm shift from closed innovation to open innovation focuses on the contrasting principles of an innovation approach on the level of an organization itself. The following scheme (Chesbrough, 2003) compares the underlying principles to each other.

Table 4: Closed Innovation versus Open innovation

Closed Innovation principles	Open innovation principles
The smart people in the field work for us.	Not all the smart people in the field work for us. We need to work with smart people inside and outside the company.
To profit from R&D, we must discover it, develop it and ship it ourselves.	External R&D can create significant value: Internal R&D is needed to claim some portion of that value.
If we discover it ourselves, we will get it to the market first.	We don't have to originate the research to profit from it.
The company that gets an innovation to the market first will win.	Building a better business model is better than getting to the market first.
If we create the most and the best ideas in the industry, we will win.	If we make the best use of internal and external ideas, we will win.
We should control our IP, so that our competitors don't profit from our ideas.	We should profit from others' use of our IP, and we should buy others' IP whenever it advances our business model.

Source: Chesbrough 2003, p. xxvi

As the open innovation principles indicate, organizations are forced to include the inside-out process, such as sharing knowledge and selling intellectual property via out-licensing with external partners and markets (Lichtenthaler, 2005), on one hand, and the outside-in process of sourcing outside knowledge into the organization (Gassmann and Enkel, 2004), on the other. The shift from closed to open innovation principles do not indicate at what stage of the value chain, e.g. new product development (NPD), an organization should completely adopt the open innovation and to what extent. Even if academics (e.g. Chesbrough, 2003, 2006a, 2006b, 2011; Laursen and Salter, 2006) and practitioners (e.g. Rivette and Kline, 2000; Huston and Sakkab, 2006) consider the open innovation concept as superior to the closed innovation model, the full adoption has its limitations (Torkkeli et al., 2009). With emphasis on the important role of absorptive capacities (Cohen and Levinthal, 1990), organizations which are acquiring and using external knowledge in their innovation process must establish in-house absorptive capabilities. These capabilities are necessary to exploit which competencies are in-house and what is supplemental and must be acquired from external partners. The following figure (Figure 5) illustrates the advantages of the open innovation business model compared with the closed business model. An organization will benefit from the open innovation model from the revenue perspective by generating new revenues due to sales and divestiture to new markets, new venture founding (spin-offs) and income from in- and out-licensing. On the cost side, organizations can benefit from cost and time savings due to leveraging external developments outside their organization's boundaries. This model was originated in 2006 and has the limitation that it is based on the findings of the adaption of open innovation at Procter and Gamble (Hutson and Sakkab, 2005). Notwithstanding that the cost and time savings are beneficial for established companies, even Chesbrough argued that Hutson and Sakkab's study did not demonstrate the real business benefit in figures, e.g. increased sales, increased profit and total return on investment (Chesbrough, 2006).

The literature about open innovation and its implementation in the innovation strategy of large, incumbent organizations has a longer history and, therefore, more sources. The open innovation business model in Figure 5 does not imply that it is applicable to any organization. It was chosen as an illustrative example to demonstrate the benefits of adapting open innovation as a business model. The real value of an innovation can only be achieved through the business model of the particular organization (Chesbrough and Rosenbloom, 2002), which can vary on many points. This indicates that when it comes to the single organization's level, researchers should refer to "firm x's business model" (Amit and Zott, 2001).

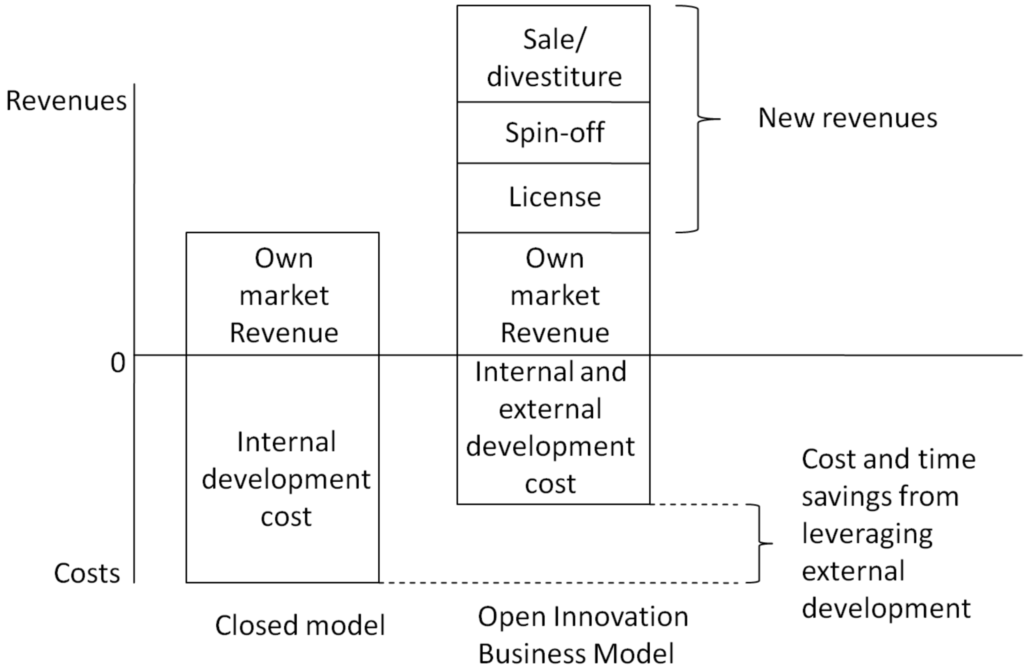

Figure 5: The new Business Model of Open Innovation (see Chesbrough, 2006a, p.17)

Insights in the innovation management strategies of organizations caused several debates in the literature as to what extent the open innovation concept is the favourable innovation strategy for an organization, and what kind and degree of openness is applicable (Brunswicker and Vanhaverbeke, 2010a). Still, only limited empirical research on open innovation and an external innovation search of small- and medium-sized enterprises (SMEs) is available (Chesbrough, 2006a; van de Vrande et al., 2009; Vanhaverbeke, 2017). A study of 1,489 European SMEs was conducted to conquer this limitation of the literature (Brunwicker and Vanhaverbeke, 2010b). The industrial sector of biotechnology/pharmaceuticals and chemicals incorporates a sample of 143 organizations. The research model was especially created in this context and measured the innovation performance (innovation success and income from innovation) in relation to the open and collaborative strategies (external innovation search, relationship and co-development) effected by mediating variables (innovation planning, innovation development process, innovation control, culture for innovation integrated in the investment into an innovation knowledge base).

The higher innovation success measured was positively influenced by indirect customers and, to a greater extent, by network partners. Indirect customers are defined as the distant downstream actors along the value chain (i.e. the car driver rather than the car manufacturer; Brunswicker and Vanhaverbeke, 2010b). Interestingly, the hypothesis: "Innovation search among universities has a negative effect on innovation performance" was confirmed, but managerial proficiency can mitigate the potential risk and negative performance effect. However, limitations and directions for future research provide the intention to investigate formal and informal managerial practices, sustainable network ties, in-depth case studies and observational research, search channels and "cross-functional" learning, and IP protection schemes (Brunswicker and Vanhaverbeke, 2010b).

Additional insight knowledge regarding the question: "When is Open innovation superior to closed innovation?" is provided by the formal simulated model by Amirall and Casadeus (2010), based on the NK fitness landscape model created by Kauffman and Weinberger (1989). Limitations of this model are that the value created for the organization is measured only by higher willingness to pay for the products. If the product development together with external partners do not lead to a higher willingness to pay, the companies are more likely to follow a closed innovation approach. Important factors, for example, the creation of a culture that fosters innovation and user adoption and network effects, were assumed away. Even if the studies by Brunswicker and Vanhaverbeke (2010b) and Amirall and Casadeus (2010) are not comparable because of the different methodologies, from the practitioner's perspective, the model and findings by Brunswicker and Vanhaverbeke (2010b) are more valuable in order to understand whether the closed or open innovation approach is applicable to an organization's innovation strategy.

However, open innovation moved in a new direction from the literature perspective. In Chesbrough's (2011) book, *"Open Service Innovation. Rethinking*

Your Business to Grow and Compete in a New Era.", the term closed innovation is only used to explain the differences in regard to open innovation. Open innovation is nowadays a well studied phenomenon; several open innovation scholars from different parts of the world have summarized a decade of open innovation research in the book *New Frontiers in Open Innovation* (edited by Chesbrough, Vanhaverbeke and West, 2014). This book is a representative example for how open innovation is practised in the research community. Scholars from different research organizations collaborated to provide a review of the innovation concept at different levels of analysis, and new fields of application, i.e. open social innovation (Chesbrough and Di Minin, 2014). The following paragraph is focusing on further, recent developments in the research field of open innovation and the relevance for this thesis.

2.3.2 Open Innovation - A multi-faceted Phenomenon

Present developments concerning the open innovation literature are covering the timeframe of the past five years (2014-2019). Here, reviews of the open innovation literature from a global perspective providing a holistic perspective on recent trends, main research objectives and gaps in the body of literature concerning the open innovation concept. Open innovation scholars argue that open innovation moved from being a phenomenon, observed at the organizational level to a multi-faceted phenomenon, with the need for more research on different levels of analysis (Bogers at al., 2017). These different levels of analysises are at the core of the longitudinal, single-case study, the biotech spin-off. As described in more detail in the methodology chapter (see 3.6.2, Figure 13), the data collection is covering three levels of analysis: first, the organizational level; second, the project level; and third, and the individual level. For the multiple cases, this research study is two-dimensional (see 3.6.3, Figure 14) from the level of analysis. The focus is here on the organizational level and the individual level - incorporating the participants perspectives. Therefore, this study will provide new insights on a multidimensional level about the adoption and adaption of open innovation in biotech organizations.

How well a specific scientific field is investigated can be analysed by co-citation analysis of the respective literature. Resulting from a study of 1,092 articles with the term "open innovation" in their title, keywords or abstracts, Fernandes et al. (2019) identified 5 publications with the largest number of citations in the timeframe from 2003 to 2016:

1) Chesbrough (2003) - 784 citations
2) Dahlander and Gann (2010) - 547 citations
3) Chesbrough and Crowther (2006) - 490 citations
4) van de Vrande et al. (2009) - 433 citations
5) Enkel et al. (2009) - 310 citations.

Further evaluations led to the identification of the six conceptual clusters: open innovation concept, open innovation and knowledge, open innovation and innovation spillovers, open innovation and technology, open innovation management and open innovation and networks. Thus, the open innovation phenomenon became one of the most important topics in innovation management research over the last decades (Fernandes et al., 2019). Therefore, this established innovation management concept provides a valuable theoretical framework for the study of the single case - the spin-off and the multiple cases, the biotech SMEs.

2.3.3 Open Innovation and Innovation Ecosystems

Every valuable systematic review of the literature provides conclusions and recommendations for a future research agenda, often in form of implications for research, practice and the society. This thesis aims to provide such new insights by investigating a longitudinal single case study, complemented by multiple cases from the biotech sector. Recent developments of innovation strategies, in particular to develop radical innovation, from a high-tech and R&D intensive sector will impact the common understanding about innovation strategies, not only on the level of a firm. Additionally, studies about the university - industry relations are relatively rare (Nambisan et al., 2018). Since the spin-off organization is created at Technical University Berlin (TUB), this study will provide more insights about the open innovation adoption based on university - industry relations. Nevertheless, there is still a need to study open innovation across multiple levels of analysis (Bogers et. al., 2017).

From a broader perspective, open innovation as far as the concept is understood by scholars, should not be seen as a standalone innovation phenomenon.

As formulated in RQ2: "Can open innovation enable the development of radical biotech innovations in a German ecosystem?" the ecosystem is the framework for this study. Yaghmaie and Vanhaverbeke (2019) argue in their systematic literature review, that there are gaps in the innovation ecosystem literature. They advocate to link innovation ecosystems not only with open innovation, but also with the underlying value creation and value capturing processes. These complex processes must be orchestrated properly (Yaghmaie and Vanhaverbeke, 2019). From these scholars perspective, at least three "unexplored research questions" need future investigation. Firstly, *how* actors create and capture value in the innovation ecosystem, secondly, *which roles* does these actors play (orchestrators and non-orchestrators), and thirdly, the *exploration* of these orchestration strategies with a clear understanding of the role of every partner in an innovation ecosystem (Yaghmaie and Vanhaverbeke, 2019). From the biotechnology industry perspective on innovation ecosystems, there are only two publications identified (Iansiti and Levien, 2004; Rampersad et at., 2010, cited in Yaghmaie and Vanhaverbeke, 2019). This implies that even in this R&D intensive high-tech sector, innovation ecosystems through the lens of open innovation need future research. In summary, from the body of literature perspective and trough a broader open innovation lens, this empirical research study about the creation of a biotech venture through a university spin-off will address the above mentioned gaps in the literature. The multiple case studies about the biotech SMEs will strengthen the industry perspective and add more new knowledge about innovation partnerships, embedded in an ecosystem. Multinational pharma organizations can be innovation partners to the SMEs, but can be also competitors. In context with this study, how and why biotech organizations implement open innovation strategies is investigated. Thus, even the pharma industry, with its blockbuster driven strategies from the past, is nowadays embracing the open innovation concept and rethinking their current business models. Insights into the global-acting pharma and biotech sector with regard to the adaption of open innovation and beyond are provided in the next section.

2.4 Introduction to Open Innovation in the Biotech – and Pharma Industry

After reviewing the literature about open innovation from a holistic perspective, the research was narrowed down to the level of adoption of open innovation concepts in the international pharma and biotech sector. The labelling of the pharma and biotech sector is used to include both types in a global context. Both industries are different, but strongly connected to each other. The core competence of pharma companies is drug development, covering the value chain from lead generation of pre-clinical and clinical trials to production and marketing of the drug. The biotech industry is more diverse, using biotechnological technologies for production, platform technologies and services. Pharma companies and biotech companies will be used, depending on their core business, for the terms biopharmaceutical, pharma and biotech industry, for the sake of clarity. The main resources are articles in journals, reports from the sector, white papers, proceedings from conferences, and corporate presentations supplemented with case studies from the core open innovation literature above mentioned. The author conducted an initial study of the literature in 2008 to answer the question: "How do recent trends in the Pharmaceutical and Biotech Industry influence Open Innovation Approaches?"

(Kunz, 2009, see Appendix A). The aim of this study was to identify trends in the biopharmaceutical industry focusing on the key characteristics of open innovation (De Jong et al., 2008). Based on the open innovation activities R&D, IP, NET, COL, and EL, the study involved examples from the pharma companies Novartis, Roche and Pfizer. The limitation of this study was that only one representative example for every key characteristic was investigated. The most significant outcome of this study was the need to further investigate the open innovation characteristics, including their causality and interdependency. Even if all five open innovation characteristics are well described and under investigation in the recent literature, no literature about the causality and interdependency between them could yet be identified. Therefore, this study will provide profound insights into the innovation strategies of biotech organizations on multiple levels of analysis (Bogers, 2017) based on the evaluation of the aforementioned interdependencies.

2.4.1 The Open Innovation Phenomenon and the Global Biotechnology and Pharma Industry

A decade ago, in 2008, Torphy stated that the pharma industry had to move forward with open innovation approaches to overcome their R&D productivity gap. In 2011, Burrill argued in an interview that the pharma industry went from research and development to "Search and Development", which is an observed phenomenon indicating the switch from a company's own R&D resources to a search outside the company's boundaries. This is characteristic for outside-in open innovation and the switch to an open business model (Vanhaverbeke and Chesbrough, 2014, p.54).

The level of adoption of the open innovation concept in the international pharma and biotech industry is currently not easy to measure. Innovation metrics (Collins and Smith, 1999; Kaplan, 2007; Erkens et al., 2014) are scarcely available and under on-going research and evaluation. Due to the fact that many factors influence the innovation process, for example, Rogers' stages-gate model: scoping, business case building, development, testing and validation, and market launch (Rogers, 1962; Cooper and Kleinschmidt, 1987), measurable variables are dependent on the industry sector. Pharma and biotech companies are built on strong IP rights, therefore the number of patent applications and patents granted are one measurable indicator. How much companies are spending on R&D in-house and due to external partners is also a measurable and comparable variable. Some researchers (Muller et al., 2005) have set frameworks or a "family of metrics", such as return on investment, organizational capability and leadership. Collins and Smith (1999) developed innovation metrics based on Arthur D. Little's High Performance Business model focusing on the interdependent elements: stakeholder strategy, process, resources and organization, and culture. Additionally, resources are available from the practitioners' viewpoint via websites and blogs. Recent literature suggests that innovation and the level of adopting open innovation in particular should be measurable, and thus implemented in the firm's overall strategy (Bogers et al., 2017).

The Fortune 1000 companies' possess innovation metrics and the most prevalent are the following (Kaplan, 2007):

- Annual R&D budget as a percentage of annual sales;
- Number of patents filed in the past year;
- Total R&D headcount or budget as a percentage of sales;
- Number of active projects;
- Number of ideas submitted by employees; and
- Percentage of sales from products introduced in the past X year(s).

The so-called top 20 pharma and top 10 biopharmaceutical companies were selected to provide an extensive overview of the recent innovation strategies of the pharma and biotech companies from a global perspective (Roth, 2011a, b). In each case, ten companies were included with their open innovation approach with regard to their 2010 revenues (Koch, 2011).

Other research resources dealing with open innovation as an innovative strategy for this sector are the annually published reports about recent innovation strategies, future trends and financial challenges in the pharma and biotech industry (Ernst & Young, 2008 - 2015). These reports are considered as applicable sources since the research methodology used and data presentation of IPO analysis, merger and acquisition (M&A) evaluations and opinion leader interviews are based on internationally acknowledged data suppliers, e.g. MedTrack, BioCentury, BioWorld, Venture Source, Windhover, NewsAnalyser, IMS Health, FDA, WHO, and the Biotechnology Industry Organization. In this context, the biotechnology firms are defined as companies that use modern biological techniques to develop products or services for human healthcare, animal healthcare, agriculture productivity, food processing, renewable resources, and industrial manufacturing of environmental management (Ernst & Young, 2009). Even if the term open innovation is not explicitly mentioned in the reports, the growing number of alliances in contrast to declining numbers in M&As (Ernst & Young, 2011 - 2015) is evidence for the growing importance of this innovation strategy. The industry has created its own currency to measure the financial value of strategic alliances, "biobucks", which summarize the total deal value including the up-front payments (Ernst & Young, 2011 - 2015).

The new positioning of established biotech companies observed on a global scale demonstrates that the recent business models are facing strong challenges. These challenges can be summarized by the need for innovations (Ernst & Young, 2009). One early example of the adoption of open innovation is the Bristol-Myers Squibbs (BMS) model, "string of pearls". This program includes interrelated acquisitions, licensing agreements and partnerships with biotech companies. These alliances are created to generate the greatest innovation and value for BMS (Ernst & Young, 2009) from external resources.

Another adopted open innovation principle was observed in Ernst & Youngs 2010 report "Beyond Borders". Licensing between pharma and biotech companies used to go only in one direction, IP in-licensing from biotech into pharma. This stands for the outside-in approach for external knowledge sourcing (Since most of the pharma companies have had to narrow their therapeutic focus, assets that they are unable to develop have now become free for out-licensing to biotech companies. This trend is explicit evidence for the open innovation concept; the need for more efficiency forces pharmas to move beyond their "not invented here" (NIH) syndrome. Japan, known as a global leader in patent productivity and technology progress, founded a unique public-private partnership, The Innovation Network Corporation of Japan, in 2009. This organization aims to advocate the open innovation concept by promoting collaborative thinking outside the walls of universities, start-ups and established organizations (Ernst & Young, 2010).

Two early examples, Pfizer, headquartered in the US, and GlaxoSmithKline (GSK), headquartered in the UK, will serve to describe open innovation concepts in the pharma industry. However, the innovation strategies and the level of adopting open innovation observed are differentiated from company to company.

The global-acting pharma company Pfizer was one of the early open innovation adopters (Chesbrough, 2003). Its announced "Center for Therapeutic Innovation" (CTI) (Allarakhia, 2011) will serve as an external resource for new drug entities. This early formation of networks with academic collaboration partners will follow a "venture capital-funded biotechnology start-up model". The University of California, San Francisco, is one of the first partners, receiving $ 85 Mio in research support and milestone payments over the next five years. Starting with CTIs in the US in 2012, centres in Europe and Asia followed. This open innovation concept includes funds for preclinical and clinical developments and offers IP rights, ownership rights and publication rights. Pfizer's' open innovation concept serves as an excellent early example since all six open innovation principles described under section 2.3, Table 4 are fully considered.

GSK is approaching open innovation from different directions. Their "Patent

Pool" is a resource of IP to external users, especially in the field of malaria drugs. ACE stands for the GSK - Singapore Academic Centre of Excellence; an initiative to create flexible partnerships with biotech companies and academia. Through these initiatives, GSK aims at greater flexibility around IP, new partnerships and access to new compounds. Their "open lab" at the Tres Cantos campus in Spain offers space for 60 scientists to develop drugs for developing countries. In partnership with the UK government and the Welcome Trust, GSK have created a global hub for the life science industry at the Stevenage Campus with scientists from all over the world. The "Innovation at GSK" website has expanded the access to new technologies on a global scale since 2007.

Both pharma companies have adopted the principles of open innovation caused by the challenge of dealing with expiring patents, "empty" pipelines and a decreasing number of blockbuster drugs

Even though the early adopters examples from this industry sector are a small sample, the key characteristics of open innovation (R&D, NET, COL, and IP) are at the core of these initiatives. In addition to building up small, excellent scientific teams, entrepreneurship and leadership (EL) are also mandatory.

The term "Pharma 3.0" was created in 2010 and was defined as the "healthy outcome ecosystem" (Ernst & Young, 2010,). The industry's long-standing vertically integrated blockbuster model (Pharma 1.0) moved to more diversified portfolios: Over the counter (OTC) products, branded generics, and consumer and/or animal health products (Pharma 2.0). Drivers of the change were trends, such as the patent cliff, decreasing R&D productivity, pricing pressure, globalization, and demographics. The pharma industry has been facing major transformations to the Pharma 3.0 model. New business models integrating non-traditional collaboration partners are now needed, influenced by healthcare reforms, demographics, health information technology (IT), and consumerism. These partners come from industries such as IT, retailers and financial services, and force the pharma industry to rethink and adapt their business models to compete with new entrents like Apple, Microsoft and Amazon (Dolata, 2017).

Evidence of the adoption of the open innovation concept, taking Johnson & Johnson as an example, is the declaration "The World is our Laboratory" (Ernst & Young, 2010). The next important step is to foster trust between pharma companies and the academic and scientific communities. Open innovation is commonly indentified as *the* creative way for a new outside-in approach embraced by the pharma industry.

"Pharma 3.0" claims to be the immediate future of the global pharma industry (Ernst & Young, 2011). Open innovation is clearly on the agenda. Anthony Rosenberg, Global Head of BD & Licensing, said:

> "I think we'll see more open innovation through alliances where we'll offer partners our strengths and assets (broadly defined) if they work with us on a new market offering in an open collaboration. Alliances with academia may be the best suited to this approach."

Another report further stated that:

> "Pharma 3.0 is really about co-creation-levering the insight and attributes of partners with different perspectives."

The perspective on innovation in this sector is based on radical collaboration and new multiple business models. In this context, active learning from other industries' changing business models and an *outside-in* approach to business model innovation is required. Following Procter & Gamble's (P&G) mantra, "only do what only we can do" (Ernst & Young, 2011), this enables pharma organizations to concentrate on their core competences and strengths while using external partners for everything else.

The global characteristics of the open innovation concept adopted by the pharma and biotech industry can be summarized as the following; Firstly, the adoption of open innovation is still under development; secondly, moving from open innovation in drug R&D the concept will be also applied to the development of new business models; and thirdly, radical collaboration and co-creation will involve academia, partners from other industrial sectors and patients. The challenging ecosystem of the sector forces the companies to innovate faster and rethink their traditional business models.

From this global of the sector, the further research was narrowed to the specific German innovation environment with emphasis on the German biotech industry.

2.4.2 The Open Innovation Phenomenon and the German Biotechnology Industry

The literature review regarding the innovation environment in Germany focuses on the biotech industry, notwithstanding that the innovation environment regarding cross-sectorial industries will serve as an introduction to the specific German ecosystem.

Researchers from the innovation community organized at ISPIM have published 26 proceedings which include "Biotechnology" in their title from their annual conferences between 2006 and 2011. Even if this is only a snap-shot and claims no representativeness, it indicates that more research about the biotech industry and innovation is needed. This was strengthening the motivation for the research focussing on the single and the multiple cases from the biotech sector.

Literature about the German innovation landscape as a whole is limited. The German Federal Ministry for Education and Research (BMBF) and the Federal Ministry for Economic Affairs and Energy (BMWi) has innovation on their agenda with emphasis on the translation of inventions and ideas from academia into innovative technologies, products and services.

The Federal Government of Germany is initiating studies about research, innovation and technological performance in Germany which are published by the commission of experts for research and innovation (EFI, 2010; EFI, 2011; EFI, 2016). Starting in 2010, this outstanding resource was identified as an excellent database to provide an overview of the German innovation landscape. The German knowledge economy is characterized by the following trends: a relatively low start-up rate (15%), high value technologies rather than cutting edge technologies (< 4%) and a closure rate in excess of 6%. The strongest industrial segments are automotive, with the "hot" topic of electro-mobility, the chemical industry, renewable energy sources, and knowledge consultancy. The knowledge-based medicinal products, processes and services cover a very small fraction of the German knowledge economy (EFI, 2010).

The research and innovation performance of the German research organizations are influenced by the internationally recognised "German Model". This model is unique because of the strong position of the non-university research organizations: e.g. the Max-Planck Society (MPG), Fraunhofer Society (FhG), Helmholtz Association (HGF), Leibnitz Association (WGL), and Federal Research Institutions (BFE). Germany did not play a leading role in the development of public research in an international comparison. However, the German R&D expenditures since 2004 have been constantly increasing above the average level of OECD countries (EFI, 2010; EFI, 2011; EFI, 2016).

The limited outcome of cutting-edge or radical innovations is caused by the absence of industrial utilisation opportunities. One well-known example is the MP3 player, the underlying technology of which was originated by Karlheinz Brandenburg at the Fraunhofer Gesellschaft (FhG) in 1995. Unfortunately, the German ecosystem for innovations was not ready for a radical innovation such as these new audio signals comprising technology at this point of time.

Germany cannot rely solely on high-value technologies and ignore cutting-edge technologies in the long term. Nevertheless, Germany has a strong drug pipeline, second after the UK, from the European perspective (Ernst & Young, 2011). Besides the traditional German pharma industry, the German biotech industry holds an important proportion in drug development (Ernst & Young, 2011).

In 201, the German biotech industry demonstrated a positive upwards trend in revenues and reduced losses. The industry listed 7 new company foundations. The biotech companies adapted their business model to sustain the funding crises. Trends such as increased outsourcing and new partnering opportunities with pharmas influenced the sector positively. The venture investments expanded three-fold with an amount of € 279 Mio to 2009 (Ernst & Young; 2011). Alternative funding sources, for example, from the government, became more relevant. Between 2006 and 2010, none of the German biotech companies has initiated an IPO. The interest of the capital market remains weak. Positive trends and signals for the step by step adoption of the open innovation concept are transactions and a growing number of alliances based on innovative technology platforms to generate products. German biotech firms are engaged in modern drug concepts, e.g. Antibodies (AB), proteins, RNA/DNA, and cell-derived medicines. The focus on oncology remains strong.

However, the major revenues are generated from marketed products, e.g. diagnostics, cell culture and research tools. In summary, the 400 private and public biotech companies earned € 1059 Mio in 2010, R&D expenditures were € 809 Mio and losses decreased about 8% compared to 2009, to € 451 Mio. The German biotech industry employed 10,043 people in 2010 (Ernst & Young, 2011). The Ernst and Young (2011) survey indicates that identifying alternative capital sources and adaptation of new business models are the key drivers of the German biotech industry. The classical venture capital model, developing therapeutical products with extremely high risk, long time-lines and high competition from pharma companies, has served its time. The increased need for innovation on the part of the pharma industry (described in 2.4) is another driver, since there is a trend towards more intensive collaboration along the whole value chain. The business models of the German biotech industry are based on, firstly, the service model, using platform technologies and research tools; secondly, the partnering model, based on alliances and nowadays option deals; and thirdly, the in-house product development and marketing is reserved for only a few very successful companies, which are more mature and have been through the first and second models (Ernst & Young, 2013). Some of the successful German companies which have managed the paradigm shift from one to another business model are Evotec, MorphoSys and Phenex Pharmaceuticals. The increasing outsourcing trend observed following "only do what only we can do" (Ernst & Young; 2011) offered companies the opportunity to become highly specialized service providers, e.g. Miltenyi Biotec in cell separation and Scienion in microarrays. The most successful products emanating from the German biotech industry are diagnostics (molecular, *in vitro,* biomarkers, microbial diagnostics, etc.), tools (markers, nucleotides, peptides, etc.) and cell culture equipment (media, factors, etc.).

Collaboration with external partners has always been a crucial business activity of biotech companies. The transformation of ideas and inventions from academia into innovation products and the co-development with commercial partners is a sign of the adopted open innovation concept. The growing number of alliances along all stages of the value chain is another indicator of open innovation. Lucrative alliances characterized by IP sharing, up-front, milestones, and royalty payments become alternative funding resources (Ernst & Young, 2011).

Over the last decade the life science industry gained growing importance by moving from blockbuster products to data-driven platforms (Ernst & Young, 2019). The German biotech sector in particular moved from a sector with a high demand for venture capital and other investments (biotechnologie.de, 2012), to a stabile sector, being "on the right tracks" to create new business models (Ernst & Young, 2013), towards constant economic growth (10% increase in sales), and better access to investments (biotechnologie.de, 2019). Thus, the adoption of open innovation approaches in the German biotech industry is visible, even though, from the author's observation of the industry over the last 30 years, some managers are not yet aware that they are instinctively following this concept, forced by the changing innovation ecosystem.

Evidence for the growing importance of the German biotechnology sector is summarized in a recent review of the last 20 years titled "From Biology to Innovation" (Ernst & Young, 2018). Interestingly, the number of new start-ups per year is only slightly increasing and seems to stagnate. On the other hand, the increasing sales figures (8% increase in 2017) are evidence for the economic success of the German biotech sector, despite divers obstacles. These obstacles are decreased R&D investments (3% decrease in 2017), and a reported lack of entrepreneurial spirit (Ernst & Young, 2018). The authors of the report are emphasising a" Mindset Change" in regard to the translation of research results into commercial success. Since, this dissertation is focusing on the commercialisation process of a radical innovation, based on profound applied research outcomes from universities and research organizations, these insights will add value to the need for the mindset change in the German biotechnology ecosystem. Another important recommendation from the 20 year review is targeting the start-up culture in Germany. Despite a strong start-up scene, forced by platform and IT solutions, the biotechnology sector is still facing a conservative development of newly founded biotech ventures (Ernst & Young, 2018). To overcome the risk-averse and security seeking mentality, which is the opposite to entrepreneurship, role models from the industry are important new drivers, e.g. Werner Lanthaler, CEO at Evotec; Simon Moroney, Founder and CEO at Morphosys (Ernst & Young, 2018). Hence, the participants from the multiple cases, the biotech SMEs remains anonymous, their statements and experiences are valuable resources to strengthen the envisioned innovative mindset in the sector. Three of the involved SMEs are public organizations and listed at the Frankfurt Stock Exchange, which demonstrates the relevance for the German economy. In summary, three main factors are mandatory to create a national and international recognised German biotechnology sector, first: translational research, second: entrepreneurial spirit, and third: access to capital (Ernst & Young, 2018). These factors are reflected by the content of this dissertation, which aims to investigate the innovation strategy of an entrepreneurial spin-off and the innovation ecosystem of established biotech SMEs. Therefore the outcome of this research study will add value to the understanding of the recent scientific and economic perspectives in regard to the German biotechnology sector.This part of the literature review aims to observe recent developments in the innovation literature with emphasis on the IO phenomenon in regard to the biotech and pharma sector, to provide the framework for this sector, nevertheless, comparable former studies, focusing on a newly founded spin-off organization could not be identified. This provides evidence, that more research on the adoption and adaption of the open innovation concept is demanded.

However, the study of the literature is not limited to the open innovation phenomenon, in order to not oversee new upcoming directions and potential paradigm shifts. Therefore, the above sections should provide the specifications of these sectors to envision the motivation for this study. The researcher observed this industry for 30 years as a practitioner in various positions. This prerequisite, combined with the academic curiosity is one of the motivations for this study. The next paragraph is moving back to the academic point of view by providing a critical review of the literature in context with the research questions and the research objectives.

2.5 Critical Review , Research Objectives and Questions

The function of the critical review of the literature is to summarize to what extent the revised literature shows limitations and gaps regarding the scope of the study. In addition to open innovation, vertical innovation, user innovation and cumulative innovation are described well in the literature (West et al., 2010). The following table summarises the underlying research questions, level of analysis and representative authors.

Table 5: Level of Analysis and representative Authors.

Type of Innovation	**Vertical Innovation**	**Open Innovation**	**User Innovation**	**Cumulative Innovation**
Research Question	How do firms control end-to-end innovation processes?	How can firms maximize innovation effectiveness?	When do users innovate? How can users be supported to become innovators?	How does technological progress take place?
Level of analysis	Firm	Firm	User	Society
Representative Works	Chandler (1977, 1990)	Chesbrough (2003, 2006)	Von Hippel (1988, 2005)	Allen (1983) Scotchmer (2004)

Source: Extract adapted from West et al., 2010, p. 7

As addressed by West et al. (2010), the firm as the level of analysis, provides insight in two types of innovation; vertical innovation and open innovation. From a practitioners perspective, these different innovation types should not be considered in silos. Recent innovation management strategies on the firm level have to involve the user as innovators and the society to cope with the fast technological progress (von Hippel, 2013).

The open innovation concept is the chosen framework within which to analyse the innovation effectiveness of an organization, but West et al. (2010) suggested including the role and importance of the three types of knowledge (Garud, 1997), know-why, know-what and know-how, for further research. Furthermore, the understanding about the interaction between internal absorptive capacity, external knowledge stores and the boundaries of a firm should be broadened through future research in this regard.

Lichtenthaler's (2011) research provided an overview of open innovation past research, current debates and future directions. He developed a conceptual framework which comprises the different types of knowledge generating in dependency from an internal and external view, and its implications at the organizational, project and individual levels (see Table 6).

Table 6: Lichtenthalers Conceptual Framework of Open innovation

		Knowledge exploration	**Knowledge retention**	**Knowledge exploitation**
Internal	Organizational level	Inventive capacity	Transformative capacity	Innovative capacity
	Project level	Make decision	Integrate decision	Keep decision
	Individual level	Not-invented-here attitude	Not-connected-here attitude	Not-sold-here attitude
External	Organizational level	Absorptive capacity	Connective capacity	Desorptive capacity
	Project level	Buy decision	Relate decision	Sell decision
	Individual level	By-in attitude	Relate-out attitude	Sell-out attitude

Source: Lichtenthaler, 2011, p. 80

This open innovation framework was identified to serve at all levels, namely on the organizational level, the project level and the individual level, as a suitable basis for the investigation of the German biotech spin-off company, as well as for the SMEs. The overall conceptual framework developed by the author will embrace the research objectives and will be presented in this chapter as a foundation of the research methodology.

Finally, Lichtenthaler emphasizes the identification of profitable open innovation business models and further research on the relationship of out-bound open innovation processes, and the creation of *radical product innovation* (Lichtenthaler, 2011). Gemuenden et al. (2007) concluded that, in the case of radical innovation, the innovator is faced by organizational and societal changes, as well as changes in competition. Therefore, *open innovators* are required in the worldwide open innovation arenas. This demonstrates the influential role of innovators with regard to radical innovations, which means in this context projects with a high degree of technological innovativeness.

At the beginning of the extensive literature study for this dissertation, "Policies for Open innovation: Theory, Framework and Cases" by De Jong et al. (2008) was identified as one of the core pieces of literature aiming to provide internationally applicable guidelines for the adoption of open innovation. The report involves case studies from the Netherlands, Belgium and Estonia. At this time, five years after the term open innovation was coined and first mentioned (Chesbrough, 2003), this report provided a valuable resource. Chesbrough and Vanhaverbeke, as co-authors, delivered the definition of the key characteristics of open innovation. The underlying question was what are companies doing when they practice open innovation? The researchers (De Jong et al., 2008) distinguished five "Enterprise behaviours"; which are characteristic open innovation activities:

- Research and Development - **R&D**
- IP Management - **IP**
- Networking - **NET**
- Collaboration - **COL**
- Corporate Entrepreneurship and Leadership - **EL**

These five key characteristics of open innovation were chosen as research framework, notwithstanding, that this framework is based on a concept and not a theory per se (Bogers et al., 2017). The review of the open innovation literature and the identification of opportunities for further research resulted in the verification of one important gap. To the best knowledge of the researcher, no literature has been identified where the *causality, interaction, interdependency*, and *interrelation* of **all** five open innovation characteristics has been analysed in detail, and on multiple levels of analysis (Randhawa et al., 2016; Bogers et al., 2017). This dissertation will focus on these open innovation activities within the framework of an embedded case study design. Based on multiple units of analysis according to Yin (2009), the research is covering the combination of a longitudinal, in-depth single case study of a German biotech spin-off company and multiple case studies of mature biotech SMEs from Germany (4) and the

Netherlands (1). Since the longitudinal study about the spin-off organization is focusing on all open innovation activities, even before the company was founded, in a multidimensional manner, rare insights about the transformation process of the R&D project into a value creating business are provided. This engagement in a broader perspective will shed more light on open innovation mechanisms as factors for success or failure of innovation strategies (Yaghmaie and Vanhaverbeke, 2019).

2.5.1 Open innovation activities and External Conditions

The following section will discuss and explain the open innovation activities in correlation with their definitions from the literature in the context of the open innovation phenomenon. Based on De Jong et al. (2008) in addition the external conditions of the open innovation concept are evaluated and described.

2.5.1.1 Research and Development (R&D)

According to the OECD (1993, p.13), R&D can be defined as follows:

> "Research and development is a term covering three activities: basic research, applied research and experimental development."

The R&D activities of companies in the context of open innovation can be evaluated as absorptive capacity, which is defined as an organization's ability to value, assimilate and apply new knowledge (De Jong et al., 2008;). In contrast to the closed approach, this means that companies have to open up their boundaries at the early stage of value creation: The R&D phase of the value chain. This is only manageable when internal R&D capabilities enable the organization to identify complementary new ideas and knowledge from outside. Chesbrough (2006stated in this context:

> "You cannot be an informed consumer of external ideas and technology if you don't have some very sharp people working in your own organization. Not all the smart people work for you, but you still need your own smart people to identify, recognize, and leverage the work of others outside your company."

Internal R&D teams bring in prior-based knowledge, communication skills and the ability to identify and absorb external knowledge (Zahra and George, 2002. Sources for this external knowledge are potential collaboration partners, which are accessed by MNEs due to setting up their R&D laboratories near universities and public and private research organizations on a global scale. Research by De Jong, Braaksma and Jansen (2007) indicated that small enterprises tend to search for collaboration partners at a close geographical distance.

The core activity to evaluate the grade of adoption of the open innovation phenomenon at the R&D stage is **Absorptive Capacity (Cohen and Levinthal, 1990)**: The valuation, assimilation and application of **new knowledge** inside and outside of the organization (Zahra and George, 2002). West and Bogers (2014) argue that there is a question to be answered, whether the internal R&D spending leads to complementary or substitute knowledge seeking outside of the organization. In context with this research study, biotech organizations are characterized by intensive R&D spending and long R&D timeframes, nevertheless, they are seeking for complementary external innovations (Spithoven et al., 2010).

2.5.1.2 Intellectual Property (IP)

The management of Intellectual Property (IP) plays an important role in regard to open innovation (Chesbrough, 2003, 2006a). IP rights are valuable, intangible assets for individuals and organizations, no matter if they are of public or private nature. Inventions are the the first step towards novel technologies, products and services. But without protecting the invention by IP rights (IPR), i.e. patents, the potential commercialization could become difficult. The following requirements have to be fulfilled to gain patent protection (WIPO, 2011):

- It is new (novelty requirement);
- it involves an inventive step or is non-obvious (inventive step or non-obviousness requirement);
- it is capable of industrial application or useful (industrial applicability or utility requirement); and
- it is disclosed in the patent application in a clear and complete manner (disclosure requirement).

IP can be obtained due to patents, copyright and trademarks. The management of IP in context with the open innovation phenomenon is one crucial indicator to what extent an organization has adapted to and is practicing open innovation. De Jong et al. (2008, p.20) defined the following:

> "In the open model, enterprises manage their IP proactively. They need to access external IP to speed up and nurture their own research engine. At the same time, they also profit from their own, unused IP when other enterprises with different business models find profitable, external paths to the market for ideas".

Due to the possible in-flow and out-flow of knowledge, ideas and IP, the IP rights gain additional market potential. IP is no longer restricted to the primary owner; external partners, even competitors, can benefit from access via licensing contracts. The proactive IP management stands for in-licensing and out-licensing, and indicates that IP can be traded on a regular basis (Chesbrough, 2006). According to Anand and Khanna (2000), licensing is concentrated in specific industries, e.g. chemicals and pharmaceuticals, electronics and electrical equipment, industrial machinery, equipment, and computer industries technology. In the biotechnology sector IPR are important assets and often the foundation of a newly founded venture. For the value creation of the single case and the multiple cases, IP was and is one of the most important assets, based on their R&D intensive knowledge creation inside the organization and by collaborating with external partners (Toma et al., 2017). Studying the management of IPRs in the framework of this research study will provide insights into the value creation and value capturing process of biotech organizations (Pisano and Teece, 2007).

The core activity to evaluate the grade of adoption of the open innovation phenomenon in regard to IP is therefore **Proactive IP Management**, which covers the patenting process (filing of new IP, enforcement of IP) and the in-, out-, and cross-licensing of IPRs. The process of in-licensing technologies via patents is related to the outside-in process, the out-licensing is related to the inside-out, and the cross-licensing is a typical activity for the coupled open innovation approach (Gassmann and Enkel, 2004).

2.5.1.3 Networking (NET)

We are living in the information age, and social networks, e.g. Facebook, LinkedIn, and twitter, to name only a few are accommodating and connecting millions of users worldwide. Besides the social media, networking plays an important role in the evolution of the open innovation phenomenon. Networking, in this context, is the source of new knowledge from outside an organization (outside-in) and a channel to commercialize internal knowledge to external partners (inside-out) (OECD, 2008a; Chesbrough, Vanhaverbeke and West, 2006). According to De Jong et al. (2008, p. 17), networking can be summarized by the following:

> "Networking includes all activities to acquire and maintain connections with external sources of social capital, including individuals and organizations."

In this context, the ties between innovative companies with external partners are characteristic for the adoption of open innovation. Partners in these networks are customers, competitors, suppliers, consultants, engineers, industrial associations, universities and other public research organizations, governments, and non-profit intermediary organizations (De Jong and Hulsink, 2005, cited in De Jong et al., 2008). Thus, networks enable the company to complement specific knowledge needs without spending time and money to develop this specific knowledge internally. Another advantage is the identification of potential new business partners for a company's own technologies which do not fit into its business model through network partners.

The following enumeration summarizes the benefits of networking from the perspective of an organization in the context of open innovation (De Jong et al., 2008); networks enable a company to:

- discover opportunities,
- obtain new knowledge or resources,
- develop and absorb new technologies,
- commercialize new products,
- simply stay in touch with future potential commercial partners,
- create customer value, and
- evolve into formal cooperation.

Companies need to combine deep and wide ties with their external partners to utilise all these advantages. The following table exhibits the benefits of both types of ties.

Table 7: Deep Ties and Wide Ties

Deep Ties	Wide Ties
▪ enable enterprises to capitalize on its existing knowledge and resources, ▪ are results of an organization's strong network position, and ▪ allowing the tapping into key resources for innovation.	▪ enable enterprises to find yet untapped opportunities, knowledge and resources, and ▪ enable enterprises to explore.

Source: Adapted from De Jong et al., 2008.

Von Hippel (2005) stresses the early involvement of users in the entire innovation process. Users as networking partners are valuable sources to meet the requirements of the innovation design of new products before they are commercialized (Cooper, 2003, cited in De Jong et al., 2008).

The core elements to evaluate the grade of adoption of the open innovation phenomenon with regard to NET are the combination of **Deep** and **Wide Ties** in the company's external relations, the inter-organizational network (Vanhaverbeke, 2006).

Networking can be distinguished from cooperation but, to some extent, collaboration starts with a networking relationship. The more formal nature and link to the open innovation phenomenon is described in the next section.

2.5.1.4 Collaboration (COL)

The concept of collaboration provides a broader framework for the open innovation activity *cooperation* (De Jong et al., 2008). Collaboration is the behaviour of companies which is an essential element of the open innovation approach. SMEs, especially, have a long tradition in collaboration when it comes to the development of innovative technologies, products and services.

According to Chen and Vanhaverbeke (2019) the concept of collaborative innovation is a macroscopic concept. For this research study collaboration is evaluated on its full level, by including the government, industries, academia and research organizations. In contrast the definition of cooperation according to De Jongs et al. (2008, p. 17) more formal:

> "We consider cooperation to be more of a formal nature, i.e. more systematic, profound, and focused on specific purposes such as innovation projects, the latest technological or market developments."

External collaboration projects, especially in multinational, large companies (MNEs), are of growing importance in order to stay competitive and innovative (Chesbrough, 2003; OECD, 2008a). The evolving R&D alliances have become a popular framework within which the organizations get access to external expertise and share developmental costs and risks, and even competitors are becoming partners. In addition, these collaborations are formed, in a growing number, by public research institutes and universities. The number of privately, industry-funded COL projects at universities is increasing. The benefits for the companies include knowledge sharing and knowledge spillovers (Colyvas, Crow, Gelijns, Richard, Nelson, Rosenberg and Sampat, 2002, cited by De Jong et al, 2008).

The input from academic research influences the realisation and time to market of innovations positively. Due to the access to scientific research outcomes and results, companies gain increased sales, higher own research productivity and increasing patenting activities as an outcome from COL (Cohen, Florida, Randazzese and Walsh, 1998, cited in De Jong et al., 2008).

Again, as described in connection with NET, the user involvement in COL has to be taken into account. Von Hippel's (1986, 2005, 2013) research focuses on the impact of the influence of the *Lead Users* in the innovation process: COL with users. The following benefits are expected by involving users as COL partners, as conventional market research methods are considered not to work well for industrial goods and services (von Hippel, 2005):

- Providing missing external inputs into the learning process,
- co-developing products or technologies (e.g. open source software),
- decreasing the need to generate and evaluate ideas or concepts,
- reducing R&D and commercialization costs, and
- accelerating the involvement of customers in their own NPD and commercialization process.

Centres of excellence around the world became external innovation partners for larger companies (OECD, 2008b). The open markets and differences in location factors on a global scale, including costs and human capital, are forcing the MNEs to become more mobile and to shift their innovation activities across borders.

The core activity to evaluate the grade of adoption of the open innovation phenomenon with regard to COL is the involvement of *R&D collaborations* with public and private research organizations and companies, as well as the engagement with *users* and *competitors*. Another criterion for the evaluation of COL activities is the distinction whether they are "national" or "international".

By investigating how, when and with whom the spin-off and the SMEs are collaborating will provide insights into their innovation strategy from a multidimensional perspective (Bogers et al., 2017). The *how* will allow conclusions for establishing a collaborative network with external partners, the *when* will lead to a better understanding at what stage of value creation and value capturing partners are needed, and, the *with whom* will complete the picture about collaborative innovation in context with open innovation.

2.5.1.5 Entrepreneurship and Leadership (EL)

The term corporate entrepreneurship was adapted by the author into entrepreneur and leadership (EL). This was decided based on the background of the main source of the data collection, the in-depth, longitudinal single case study. Since the overall study focuses on the pre-founding and start-up phases of a spin-off, backed up with retrospective multiple cases, the term corporate entrepreneurship was narrowed to entrepreneurship and extended to leadership. Leadership can be summarized as a process of social influence (Chemers, 1997). In context with this dissertation and the strong link to the biotech sector, Alan Keith's view on leadership (Kouzes and Posner, 2007), he was the former CFO of Genentech, was identified as the best suitable source:

> "Leadership is ultimately about creating a way for people to contribute to making something extraordinary happen."

However, this was a conscious adaption according to the five key open innovation activities described by De Jong et al. (2008). The involvement of leadership was a conscious decision with the purpose of including the so-called *External Conditions* according to De Jong et al. (2008), described hereafter under 2.5.1.6.

Nevertheless, Chesbrough's (2003) definition of corporate entrepreneurship in context with the open innovation phenomenon is basic to this key characteristic:

> "Corporate entrepreneurial activities include corporate venturing, intrapreneurship. Corporate venturing is usually done by large companies; they invest in start-ups to ensure the development of innovations that do not fit into their current business model (Chesbrough, 2003, p 135).

Intrapreneurship is an important activity inside organizations to realise and foster innovations and organizational success (Van de Ven, 1986, cited in De Jong et al., 2008). Therefore, intrapreneurship can be promoted in the following ways:

- Investing in employees' ideas and initiatives,
- creating autonomous teams with dedicated innovation budgets,
- stimulating employees' external work contacts in order to enhance opportunity exploration, and
- promoting idea boxes and internal competition.

There are a growing number of companies which are commercializing their internal knowledge outside the boundaries of their organizations (OECD, 2008a). The foundation of spin-off or spin-out companies is, especially in the high-tech industry, a valuable source for new businesses. Another opportunity is to sell the new business to a third party and gain additional revenues. As described by Chesbrough (2003), Xerox was able to double their market value by spinning-out eleven new companies, mostly led by former employees. Even smaller companies are investing in setting up new organizations to pursue innovative projects (De Jong, 2006).

The core activities to evaluate the grade of adoption of the open innovation phenomenon in regard to EL are *intrapreneurship*, *spin-off or spin-out* and all *leadership* related activities. All these activities are resonating well with the single case study, but it will be interesting to investigate and analyze these activities due to the multiple cases, the SME perspective.

The new insight about entrepreneur- and leadership activities will provide valuable information about the grade of openness and knowledge flows from the inbound and outbound perspective on the open innovation concept (Nambisan et al., 2018).

2.5.1.6 External Conditions

This dissertation is focussing on the innovation strategies of a newly founded venture and established biotech SMEs. These organizations are at the core of the study, nevertheless, the external environment and conditions are essential for the success or failure of these organizations. In addition to the 5 key characteristics, De Jong et al. (2008) identified the key sources of capital, defined as external conditions. They include:

- A large stock of basic knowledge,
- a highly-educated and mobile labour force, and

- good access to finance.

These conditions are important and crucial to start a new venture. Even if they do not explicitly become research objectives, they are part of the investigation embedded in the rich, in-depth, longitudinal case study, as well as the multiple cases data collection. Since these external conditions are basic to the open innovation approach, it is expected that they are feasible at the starting point of the single case data collection.

A large stock of *basic knowledge* is one important internal and external source for adopting the open innovation concept. Universities and public research organizations provide research findings, experimental materials, cutting-edge research techniques, and the access to excellently trained human capital (Cohen et al., 2002). This implies that less basic research is done by companies and, therefore, investment in basic, fundamental knowledge is increasing (Chesbrough, 2006). Nevertheless, understanding the knowledge-capital, defined by Laperche and Lui (2012; p.2), as a set of scientific and technical knowledge and information produced, acquired, combined and systematized by firms, will contribute to answer the research questions.

Practicing open innovation becomes obsolete without a highly educated and mobile *labour force*. This major condition strengthens the absorptive capacity of organizations, and, on the other hand, allows knowledge to spill over to other organizations (Cohen and Levinthal, 1990; Zahra and George, 2002). The individual stock of knowledge, experience, skills, and connections that new employees bring into an organization at the time of hiring is fundamental to practicing open innovation (West, 2006). The tacit knowledge which employees bring with them from their former organizations is one important source of innovation (Polanyi, 1967; Boschma, 2005, cited in De Jong et al., 2008). Nowadays, the availability of highly qualified human resources has become more and more a global phenomenon (OECD, 2008a). Innovations must be financed in advance according to Tidd, Bessant and Pavitt (2001). External financing can include equity investment, debt financing, asset-based financing, and also grants from the government and non-profit organizations (De Jong et al. 2008). The sources of capital can range from friends, relatives, business angels, banks, venture capitalists, to governments and public stock markets (Shane, 2003). Even if the access to finance is difficult, especially for innovative projects which are characterized by uncertainty and often an asymmetry of information at the starting point, a profound financial base is a key requirement for the open innovation approach (De Jong et al., 2008). It is often helpful to scale down the size and develop the project in particular quantities (e.g. get the R&D financed until the proof of concept is reached in a fixed time frame of two-three years). The financial perspective of the involved biotech organizations is not explicitly at the core of this study. Hence, from the business perspective the measurement of success and failure are strongly correlated with the financial performance of firms.

2.5.2 Research Questions and Evolving Business Model

The researchers motivation for this dissertation is based on her longstanding involvement in the biotechnology sector. The overarching question, what makes technology transfer successful and what are the specific organisational modes for it, has led to study the open innovation phenomenon. As Bianchi et al. (2011) concluded in their study about how the bio-pharmaceutical industry is implementing open innovation, their study was one of the first attempts to study this industry. In contrast to their study, which is investigating the perspective of the so called *bio-pharmaceutical* industry, smaller biotechnology firms are important partners along the phases of the drug discovery and development process (Bianchi et al., 2011). One limitation of this scholars study is that only large firms are involved (the top 20 worldwide industry players). Therefore, this dissertation, with the focus on a spin-off and SMEs from the same sector, will contribute to the body of knowledge concerning the adaption and adoption of open innovation in the biotech industry.

The research was set up the answer the three research questions:

> **RQ 1:** Is the open innovation concept adopted by biotech companies?
>
> **RQ 2:** Can open innovation enable the development of radical biotech innovation in a German ecosystem?
>
> **RQ 3:** How does the evolving business model look like?

As described in Chapter 1, answering the RQ 1 and RQ2 will lead to a fine grained picture of how the evolving business model looks like. Radical biotech innovation is at the core of RQ2. The recent literature does not provide comparable research studies from the same sector, nevertheless Bahemia et al., (2018; p.2069) combines open innovation with the profit from innovation framework (Teece, 1986), to investigate a radical innovation project in the automotive industry. Outcome of this study suggests that in a radical innovation project, there is a switch from a closed model of innovation (Idea Generation; Business and Technical Assessment) to an open model of innovation (Concept Design and Prototype; Production; Ramp up for Production). Since there are similarities in radical innovation projects, it might be interesting, to compare the outcome of this investigation with what Bahemia and scholars have concluded.

Since the five open innovation activities are characteristics of the phenomenon with regard to the behaviour of organizations, the expected evolving business model could be an open business model. Not to anticipate any outcome from the study, a very broad definition should be the basic concept. Since this dissertation focuses on radical innovation, Osterwalder and Pigneur’s (2010, p.14) definition of business model was identified as the best definition:

> “Business model innovation is about new ways of creating, delivering and capturing value.”

Furthermore, Osterwalder and Pigneur's research on business models led to the conclusion that companies must "rejuvenate" their business models to stay competitive and innovative. Even if understanding the evolving business model is the core objective of RQ 3, the theoretical framework is set by investigating the adaption of the open innovation phenomenon based on De Jong et al. (2008) and Lichtenthaler (2011). Value creation and value capturing is at the core of every business model. This is the intra-organisational perspective. To investigate the open innovation phenomenon, it is mandatory to broaden this perspective to a multidimensional one (Bogers et al., 2017). Yaghmaie and Vanhaverbeke (2019) argue that the innovation ecosystem is a form of open innovation. Similar to the purpose of a business model, at the core of the innovation ecosystem is value creation and value capturing due to the collaboration of the involved organizations. Therefore, this research study will provide insights into the innovation ecosystems of a newly founded venture and mature SMEs in the biotechnology sector. On the macro-level of this study, value creation from different perspectives sets the framework. As part and outcome of this literature review and with the purpose to provide a conceptual framework for this study, in the following section the Value Chain for Open Innovation (VCOI) is presented. Again, with the purpose to evaluate how value is created and captured from the macro-level perspective, which is expected to support the pathway to answer the three research questions.

2.5.3 Conceptual, Theoretical Framework

Based on the comprehensive literature review and the researchers practical experiences in innovation management, the open innovation phenomenon was selected to serve as a conceptual framework, even though, that this is more a broad concept, than a theory itself (Bogers et al, 2017). Two, from the researchers perspective, core publications were identified, evaluated and selected to support answering the research questions (De Jong et al., 2008; Lichtenthaler, 2011).

The evolving five activities are covering the key behaviors of organizations, which are practicing open innovation (De Jong, et al. 2008). Nevertheless, these activities can be found in any value creating entity. This publication was identified as an outstanding source, since it was one of the first collaborative works, developing international applicable policy guidelines for the adoption of the open innovation concept. Collaborative in this context means, that the so called "father of open innovation", Henry Chesbrough and the European open innovation renowned researcher, Wim Vanhaverbeke were part of the authors team.

Lichtenthaler[1](2011) created an open innovation framework from the perspective of knowledge management at the different stages of the innovation process, including the internal and external perspectives of organizations, projects and individuals. The chosen case study design of the combination of a longitudinal in-depth single case study, backed up with multiple cases from the same sector, is focusing on the degree, adaption and adoption of the open innovation concept. The outcomes are innovative technologies, products and services, which are adding value to the organizations itself, the economy and the society.

Aim of this dissertation is to shed light on the innovation processes in the biotech sector, with emphasis on the pre-founding, founding and start-up phases of a spin-off organization and as well as, mature, successful biotech SMEs. The evolving insights from the data analysis of the qualitative, embedded case studies covering the different processes and perspectives on value creation with the goal of developing innovative technologies, products and services. From the perspective of this dissertation, the key activities: R&D, IP, COL, NET, EL are the

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[1] Some of Lichtenthalers publications were rejected after the public criticism of self-plagiarism in 2012. Notwithstanding, the cited publications are not subject to rejection. The publication in the highly recognized Journal Academy of Management was a selection criteria for the quality of Lichtenthalers publication in 2011.

chosen building blocks of the business model of an organization, focusing on the perspective of the adaption and adoption of the open innovation phenomenon.

The term "business model" was coined in the 1990 (Bucherer et al., 2012), but the concept is still evolving from being simply the "logic of a firm" or a "way of doing business" to a conceptual tool of different building blocks (Osterwalder and Pigneur, 2010). Osterwalders tool, including the four main elements: value proposition, operational model, financial model and customer relations is applicable to the different development stages of an organization, but for this dissertation a new perspective and a new, own conceptual framework is developed.

In addition, this framework is a result of the first data evaluation and the evolving demand for a visual tool to demonstrate the complex inter-relationship and causality between the five key open innovation activities.

2.5.3.1 Porters Value Chain

Three decades ago Michael E. Porter developed the conceptual model of the value chain (Porter, 1985). This model was identified as a valuable source for combining the open innovation phenomenon with the value creation process within organizations. The researcher decided to use the value chain model as a template, notwithstanding, in full honors of Porters past and recent work in the field of competitive advantage. There is a strong link between the scope of this dissertation and Porters view on analyzing the sources of competitive advantage (1985, p.33):

> "A systematic way of examining all the activities a firm performs and how they interact is necessary for analyzing the sources of competitive advantage."

The competitive advantage in regard to this research study is innovation and, in particular radical innovation. Specified for the single case study, the study is focusing on radical, disruptive innovations, in the multiple case studies we look at innovative technologies, products and services.

Surprisingly, at the time, when Porter created his value chain model, the term 'innovation' was referred to 'technological change' (Porter, 1985; p. 549), which is demonstrating the economic development at this time. Taken Rothwell's (1994) five generations of innovation models into account, this period of industrial development fits into the third generation from mid 1970s to mid 1980s (see Table 3). Nevertheless, Porters value chain model, especially the implemented technology change and technology strategy was considered as a valuable theoretical model and useful template.

Porter's model was amended and transformed into the theoretical, conceptual framework for this dissertation, by connecting and melting the concept of the open innovation phenomenon into a value chain for innovation. The following paragraph will highlight the strong connection between Porter's Value Chain (1985) and the arguments for the transformation into the Value Chain for Open Innovation (VCOI). This conceptual framework is based on the iterative process of the data evaluation, first data analysis in strong correlation with the ongoing literature review. The complexity of the research and the rich, comprehensive data collection from the single, in-depth, longitudinal and the multiple case studies, leads to the imperative for the creation of a visual model, displaying the interrelation and connection of the research objectives in the framework of the open innovation phenomenon. In addition, for every single open innovation activity: R&D, IP. COL, NET and EL (De Jong et al., 2008) an individual diagram was created to envision and summarize the characteristic processes in correlation with the open innovation phenomenon. To complete the picture of the holistic study approach, the multilevel perspective on the concept of open innovation, developed by Lichtenhtaler (2011) is envisioned by adapting his framework of knowledge management processes. Here, the concept of knowledge exploration, knowledge retention and knowledge exploitation on the organizational level is the basic model. Aim of the visualization of this dissertations study focus is the illustration of the conceptual framework for an integrative view on organizations innovation management activities. The conceptual model and the diagrams are useful tools for demonstrating the theoretical principals in the first instance and the second step, demonstrating and visualizing the results of the embedded case study analysis.

2.5.3.2 The Value Chain for Open Innovation (VCOI)

The value chain is a model focusing on the value creation process of firms to gain competitive advantage (Porter, 1985). It is an established model for the value creation of companies in correlation with their competitive environment. For this dissertation the model is changed into a theoretical conceptual framework, since several similarities and interrelations accursed. Johnson and Scholes (2002; p. 160) defined the value chain as followed:

> "The value chain describes the activities within and around an organization which together create a product or service."

Porter (1985) distinguishes the value activities (see Figure 6) in ***primary activities:*** inbound logistics, operations, outbound logistics, marketing & sales, services from the ***support activities:*** procurement, technology development, human resource management and firm infrastructure. The primary activities are involved in the physical creation, the sales and services of and for the product. The support activities are supporting all primary activities which are reflected by the dotted lines. The firm infrastructure is not directly connected with the primary activities, but supports the entire chain. All activities are the building blocks of competitive advantage, which leads to the ***margin***.

The link to the scope of this dissertation is the fact that the research is focusing on the five key activities of companies, to evaluate if they are practicing or following the open innovation concept. These activities are the foundation for developing innovative technologies, services and products. The transformation of Porters value chain into the Value Chain for Open Innovation evolved from the need, to visualize all five activities, their connection, inter-relationship and dependence from each other. The model of Porters value chain functioned as a template and a blueprint at the same time. Some of the elements were identified to embrace similarities, some were simply exchanged. Nevertheless the whole model was considered as bearing many similarities and in addition aiming to provide practitioners with a holistic concept of the innovation process. Figure 6 is illustrating Porters Value Chain and the transformation into the new structure and elements of the VCOI.

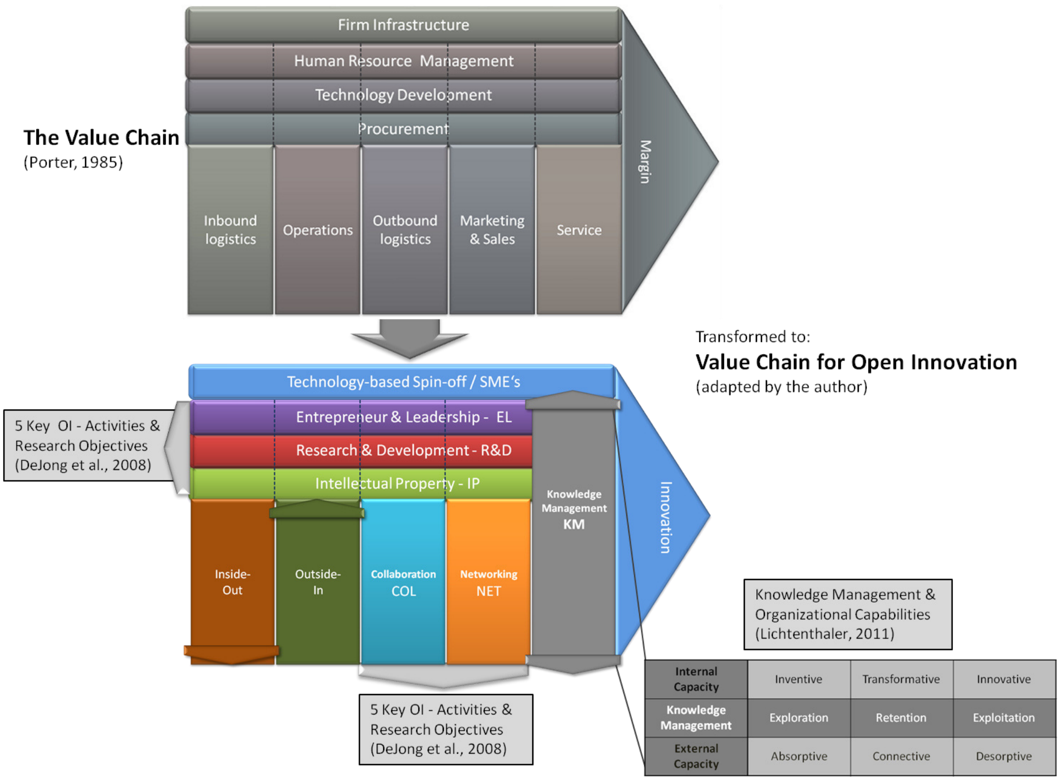

Figure 6: The Transformation of Porters Value Chain to the Value Chain for Open Innovation

Source: Adapted by the author, based on Porter (1985), De Jong et al.(2008), Lichtenthaler (2011)

This conceptual, theoretical framework is in addition fulfilling the demand for triangulation in the research methodology and study design. The theoretical concept is based, but not limited to the work of Porter (1985), De Jong et al. (2008), and Lichtentahler (2011). This implies the view from different perspectives, namely: firstly, Porters model of value creation in the context of competitive advantage, secondly, De Jong et al. comprehensive study with the outcome of 21 policy guidelines for the application of open innovation, and thirdly, Lichtenthalers knowledge management concept, based on the complex open innovation literature from a decade of open innovation research.

The following paragraph is devoted to the transformation arguments and logic implications of implementing the research objectives, embedded in the case study research design, supported by the characteristics of the open innovation phenomenon. The bold headings are representing Porters elements of the value chain, followed by a short description how and why the elements were changed.

Firm Infrastructure

This element was replaced by ***Technology based Spin off and SMEs*** companies, reflecting the multiple case study design. The similarity can be argued by the fact, that a company's infrastructure is including general management and the specific structure of an organization. The strong link is given, since that all cases studied, are based on technology driven product-and service development.

Human Resource Management

Human resource management is covering recruiting, hiring, training, development and compensation of personnel. This element was replaced by ***Entrepreneur and Leadership*** (EL), since there is a very strong link to the function and activities guided by an entrepreneur, in many cases the founder of a start-up company. Figure 7 is illustrating the characteristics of EL in context with the open innovation phenomenon.

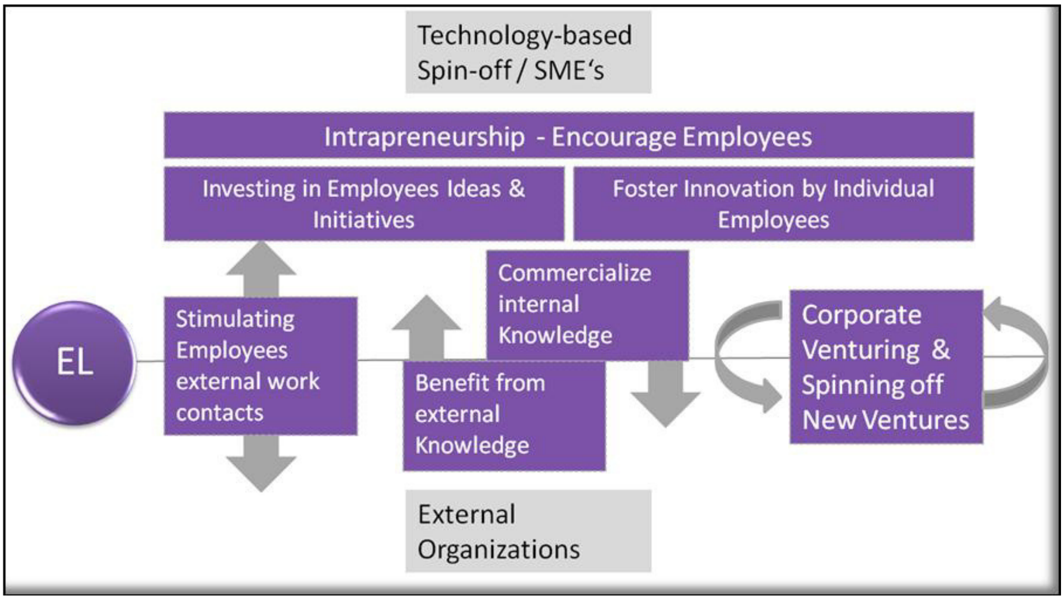

Figure 7: Entrepreneur and Leadership

Source: Created by the author, based on De Jong et al. (2008), Lichtenthaler (2011)

Technology Development

All activities connected with ***Research and Development*** (R&D) falls under the broader term technology development. Since the Biotech sector is per se (in itself) technology driven and dependent from scientific research achievements, there is a strong link between technology development and R&D.

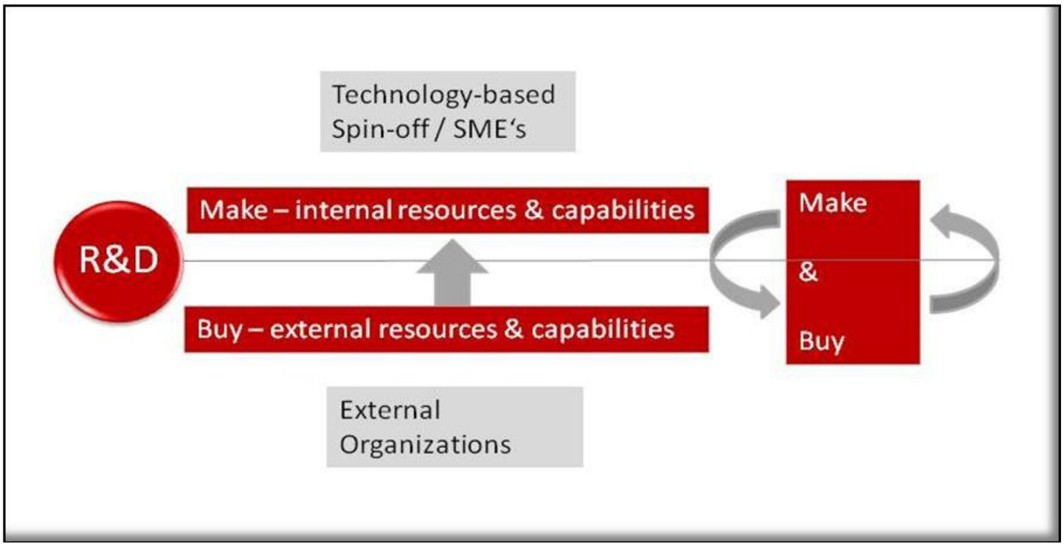

Figure 8: Research & Development

Source: Created by the author, based on De Jong et al. (2008), Lichtenthaler (2011)

Procurement

In Porters value chain, procurement is defined as the function of purchasing inputs. Assets are part of these purchased inputs. ***Intellectual Property*** (IP) is referred to intangible assets. The replacement of procurement by IP, gives this activity additional dimensions, since IP management in the context of the open innovation phenomenon, means patenting own inventions, and collaborative inventions, as well as in-and out-licensing of technologies.

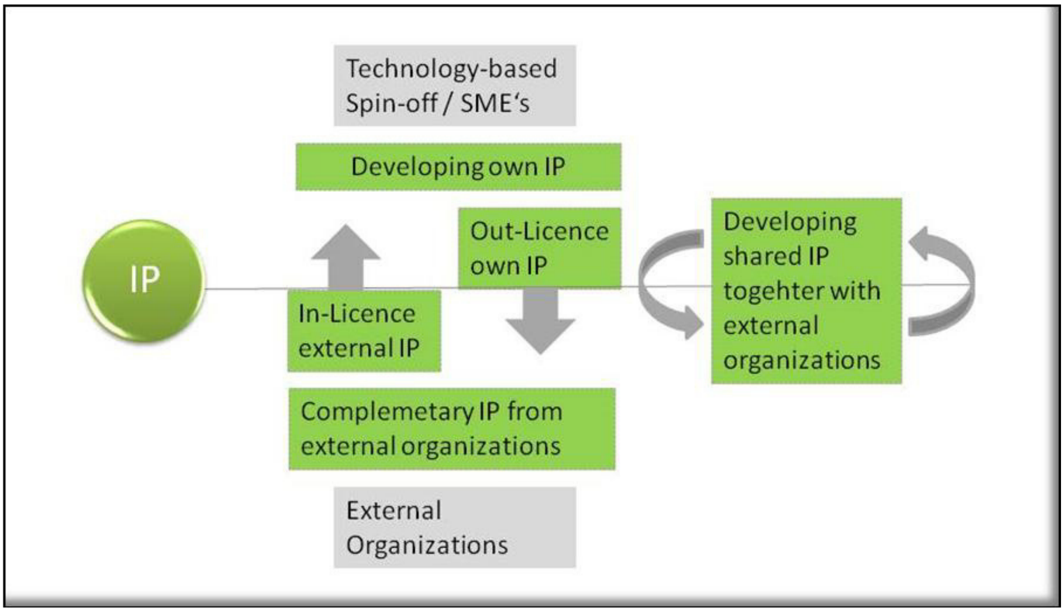

Figure 9: Intellectual Property

Source: Created by the author, based on De Jong et al. (2008), Lichtenthaler (2011)

According to Porters model the above are all support activities in the value chain. For the VCOI the five key activities are related to the research objectives, where EL, R&D and IP are devoted to the question "what" are organizations doing, to create innovation and the research objectives COL and NET are concerned to the question "how". In the following paragraph, the activities and processes focusing on the question "how" do organizations create value resulting in innovation. The positions of the categories were changed in order to illustrate the open innovation concept.

Operations

According to Porter, operations are all activities related to the transformation of inputs to the final product. The key activity ***Collaboration*** (COL) does include also activities, i.e. academic collaborations or strategic alliances, which are important requirements to be able to create innovative technologies, products and services under the open innovation concept.

Marketing and Sales

This category was replaced by ***Networking*** (NET), even if there is no direct link between marketing and sales activities related to advertising, promotion, sales force, distribution channels and pricing. In the framework of the open innovation concept networking is basic to collaboration and vice versa. Both research objectives are therefore combined in one diagram.

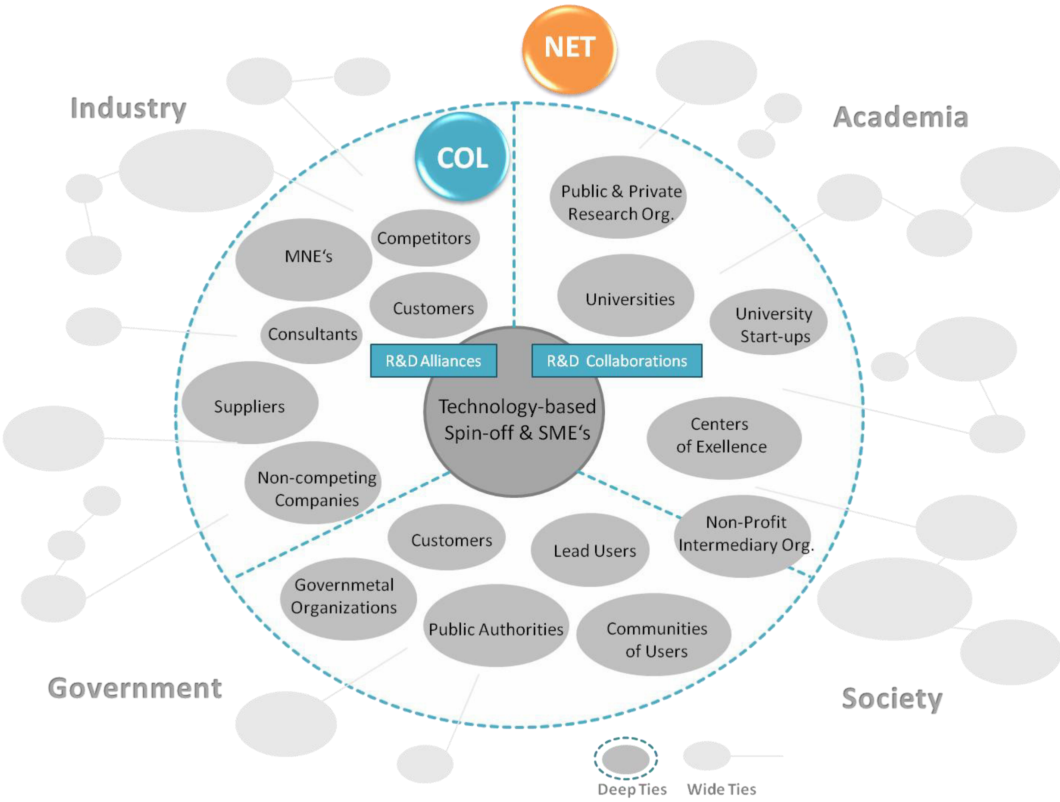

Figure 10: Networking and Collaboration

Source: Created by the author, based on De Jong et al. (2008), Lichtenthaler (2011), EY & Lily and Company (2010)

Inbound Logistics

Inbound logistics are activities associated with receiving and storing, i.e. material for the products. This is comparable to the ***Outside-in process***, which is characteristic for the open innovation phenomenon. For example the in-licensing of complementary IP from external partners.

Outbound Logistics

The ***Inside-out process***, i.e. selling or out-licensing technologies to external partners. These and other outwards related activities are strongly connected to the outbound logistics, were activities like physically distributing the product to the buyer are associated.

Service

The service activities in context to Porters value chain are provided to enhance or maintain the quality, respective the value of the product. Taken into account, that Porters model was developed nearly 3 decades ago, there is an ongoing swift from the economy based on production to a service driven economy. Today services cover approximately 80% of the economic activities in the US according to the OECD (Chesbrough, 2011). Thus, economic growth is emerging from the knowledge intensive service sector. Based on these facts, and recent economic developments, service was transferred into ***Knowledge Management*** (KM).

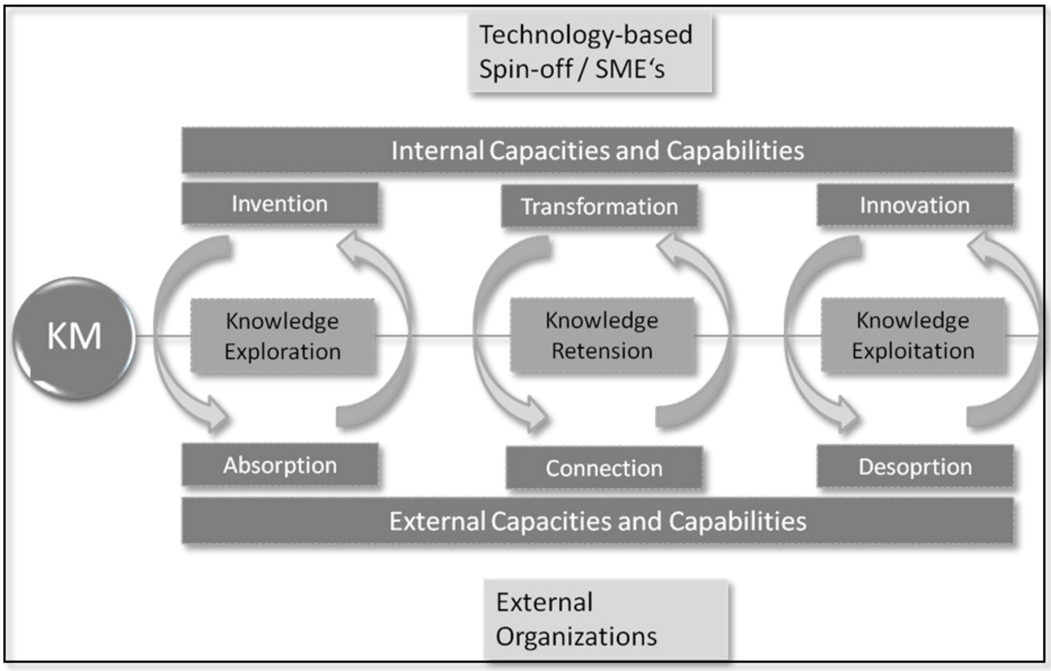

Figure 11: Knowledge Management

Source: Created by the author, based on Lichtenthaler (2011)

This conceptual theoretical framework of the Value Chain for Open Innovation meets the requirements according to Miles and Huber (1994, p. 18) who defined it as a visual or written product that

> "explains, either graphically or in narrative form, the main things to be studied - the key factors, concepts, or variables - and the presumed relationship among them."

Another requirement for a conceptual framework is the demand that it has to be created and build by the researcher him or herself, based on the comprehensive literature review, practical implications and the structure of the research study design. This framework was developed with the purposes to make the research findings meaningful and to establish orderly connections between the study observations and facts.

One of the prerequisites of the open innovation concept is the fact that it stems from observing the innovation practices in companies (Chesbrough, 2003). Nearly two decades later, it is an important task for innovation scholars and practitioners to link open innovation to different theories of a firm (Vanhaverbeke and Cloodt, 2014). For this dissertation, the researcher decided to develop a new framework by adapting Porters value chain (1985) on the macro-level framework and implementing the five open innovation activities (De Jong et al., 2008) and the concept of knowledge management (Lichtenthaler, 2011) on the micro-level perspective. Since the five open innovation activities are under investigation in this study, they were also guiding the ongoing literature review. In the next section, the identified gaps in the literature are leading to the envisioned contribution of this study to the body of knowledge about innovation management in the German biotechnology industry.

2.6 Conclusions from the Literature Review

2.6.1 Gaps in the Literature

The function of the critical review of the literature is to summarize to what extent the revised literature shows limitations and gaps regarding the scope of this study. In addition to open innovation, vertical innovation, user innovation and cumulative innovation are well described in the literature (Chesbrough 2003, 2006a, 2006b; von Hippel, 2005; West et al., 2010). The open innovation concept is the best framework within which to analyse the innovation effectiveness of an organization, but West et al. suggested including the role and importance of the three types of knowledge (Garud, 1997), know-why, know-what and know-how, for further research. Furthermore, the understanding about the interaction between internal absorptive capacity, external knowledge stores and the boundaries of a firm should be broadened through future research in this regard (Lichtenthaler and Lichtenthaler, 2009; Spithoven et al., 2010; West and Bogers, 2014).

Lichtenthaler's (2011) research provided an overview of open innovation past research, current debates and future directions. He developed a conceptual framework which comprises the different types of knowledge generating in dependency from an internal and external view, and its implications at the organizational, project and individual level.

Lichtenthaler emphasises the identification of profitable open innovation business models, and further research on the relationship of outbound open innovation processes and the creation of radical product innovation (Lichtenthaler, 2011). Gemuenden et al. (2007) concluded that, in the case of radical innovation, the innovator is faced by organisational and societal changes, as well as changes in competition. Therefore, so called open innovators (i.e. researchers, practitioners, policy makers) are required in the worldwide open innovation arenas. This demonstrates the influential role of open innovators with regard to radical innovations, which means, in this context, projects with a high degree of technological innovativeness on one hand, but also complexity and uncertainty on the other hand. Even if these gaps in the literature were motivating the researcher at the beginning of this research study, these gaps are still relevant as of today.

To the best knowledge of the researcher, there are actually five main areas in the research landscape of open innovation, which are still in demand for more attention by the academic innovation community (WOIC, 2019). These areas are in the focus of the upcoming 6th Annual World Open Innovation Conference (WOIC) with the theme: *Opening Up for Managing Business and Societal Challenges.* From the academic perspective, open innovation still needs more research from a multi-level perspective (Bogers et al., 2017) in the following research categories: behavior and cognition; strategy and design; communities and users; ecosystems and open policies and governance.

This dissertation will contribute to these three selected themes, demonstrating recent gaps in the open innovation literature (Bogers et al., 2017):

- Open innovation behavior and cognition
- Open innovation strategy and design
- Open Innovation ecosystems

Recent research about open innovation is addressing the causality of open innovation, knowledge sharing, innovation strategy and innovation performance (Bagherzadeh et al., 2019). These open innovation scholars argue in their conclusions that the *internal* organization of open innovation is the forgotten dimension (Bagherzadeh et al., 2019, p.12). The longitudinal case study about the formation of the biotech spin-off is addressing their suggestions for future research by developing longitudinal and/or experimental designs. Both dimensions, the internal organization and the longitudinal design are addressing also Bogners et al. (2017) declared need for more multi-dimensional level analysis in the field of open innovation.

This dissertation is focusing on the biotechnology sector, which is and will be one of the driving forces in providing solutions for societal challenges, like life expectancy, food ecologies and climate change. The following quote from a recent European Commission Horizon 2020 report is evidence for the growing role of biotechnology in context with openness (European Commission, 2019, p.8):

> "Openness to the world will be reflected in three flagships addressing: nanosafety; global health care; and biotechnology for the environment. "

Therefore the insights of this study will not only address the challenges of the German innovation ecosystems, but will also provide a better understanding of how to develop radical innovation in the field of biotechnology.

2.6.2 Expected Contributions

The comprehensive literature review illustrates the gaps and the potential for a future open innovation research agenda. The insights from the innovation literature over the last years of study, combined with the practitioner's view on the global biotech sector over the last three decades, has motivated the researcher to answer the question, what makes radical biotechnology innovation possible? In addition, there are limited sources in the open innovation literature about startups (Spender et al., 2017), respectively organizations at the very early stage of founding, or the pre-founding stage. The researcher is able to provide a fine-grained picture about a high-tech spin-off biotech company, by a longitudinal study, and in addition, complementing this study due to multiple case studies about five representative, mature, successful biotech SMEs. Bagherzadeh et al. (2019) argues that it is difficult to obtain longitudinal data from senior managers, due to their busy schedules. Therefore the longitudinal data collection of the spin-off organization with a serial entrepreneur and senior manager at its core provides a rare and valuable set of data. To gain also insights in the open innovation strategy of established biotech SMEs, this is complemented by the participation of five senior managers (i.e. CEOs, Vice President of BD) in the multiple case studies.

From the more general perspective the outcome of the study will contribute to the body of knowledge in three dimensions: Firstly, to our knowledge about what enables early ventures to develop radical innovations from the business perspective; secondly, to what extent is the open innovation phenomenon adapted, avoided or resolved from the academic perspective; and thirdly, what implications and suggestions can be given to the policymakers, with the goal to support applying the open innovation concept at all levels of value creation in the biotech sector.

From the perspective of open innovation as an innovation concept and phenomenon, this study aims to contribute to the following themes and subthemes:

2.6.2.1 Open Innovation Behaviour and Cognition

This research study will add new insights into the individual-level attributes of a serial entrepreneur and his commitment and motivation for starting a new business based on his invention of a radical technology. The longitudinal case study design enables the researcher to observe and monitor the founders decision making in the field of research, business development, IP creation and collaboration partner identification and network building. All these activities are defining the open innovation phenomenon (De Jong et al., 2008). With the entrepreneur and founder of the spin-off biotech company at the individual level of analysis, new insights in regard to open innovation behavior will contribute to this specific gap in the literature.

The human side of open innovation (Bogers et al., 2018b) will be visible in shedding light on the process of adopting and adapting open innovation by the team members of the newly founded organization. Essential parts of the data collection are semi-structured interviews with the team. These personal statements and attitudes towards the different perspectives of innovation management will add new knowledge to the human side of open innovation.

2.6.2.2 Open Innovation Strategy and Design

The biotech spin-off is developing a radical innovation, the Multi-Organ-Chip (MOC). This project is embedded in a governmental funded project GO-Bio (Strey, 2015). The comprehensive data collection with 210 events is covering a major part of the project activities in the timeframe of five years. Since the development of this highly complex project is under investigation in this research study, the outcome will provide new insides about open innovation in practice on the project-level.

The single case study will further provide an understanding of the entrepreneurial opportunity and open innovation as an enabler to succeed. The nature of this opportunity is a radical biotech innovation in a German ecosystem. The outcome is the foundation of a successful new venture with international COL partners, presenting a platform technology to the global healthcare industry. This type of new products will define a milestone in personalized medicine. Understanding the causality of open innovation and this entrepreneurial opportunity from the biotech sector will add new knowledge to the question how organizations develop an open innovation strategy (Chesbrough and Appleyard, 2007).

By finally answering RQ3, how the evolving business model for the spin-off biotech company can be defined, this study contributes to the demand for understanding business model innovation in three dimensions: at the industrial sector level (biotechnology), at the organizational level (spin-off) and at the individual level (the entrepreneur). Understanding the internal and external requirements for successful inside-out and outside-in knowledge sharing will also contribute to Bagherzadeh's et al. (2019) request for future research about the causality between these processes and innovation performance.

2.6.2.3 Open Innovation Ecosystems

From the macro-level perspective, this study aims to provide more understanding about the innovation ecosystems, which are created by the spin-off, and which are already established in case of the SMEs. Interestingly, the information provided due to the semi-structured interviews, allowing conclusions about the existing ecosystems of the involved SMEs on one hand, and on the other hand, the creation of an innovation ecosystem by the spin-off company. For the SMEs the picture is static, based on the type of data, but for the spin-off a longitudinal perspective provides a fine-grained picture of the evolving ecosystem (Yaghmaie and Vanhaverbeke, 2019). By understanding the new network forms, this study will contribute new insights about the processes which are necessary to combine value creation and value capture.

To provide a profound contribution to the gaps in the literature in the areas of: open innovation behavior and cognition; open innovation strategy and design and, open innovation ecosystems, the quality of the study design is essential. According to Cottrell (2005), there are critical questions regarding the quality and evidence of arguments for the study design; for this dissertation, the following can be stated:

- Suitability of the research design – the **case study** approach to facilitate deep insight into the organisational, project and individual level.
- Effectiveness of the data collection process – the process was very effective by collecting data over a period of five years, including **two years of intensive contact** with the participants from the single (spin-off) and multiple cases (SMEs).
- Validity of the sample selection process – the validity is based on the fact that **multiple sources of evidence** (observation, interviews, documents, archival records) are approached (Yin, 2009).

This implies that the requirements for a profound study are fulfilled.

The outcome of this research study aims to add new knowledge to the body of literature in innovation management, with the focus on open innovation. For practitioners from the life science industry, particularly the biotechnology industry, conclusions and practical advice for the adaption and adoption of open innovation concepts are envisioned. In regard to policy makers, the outcome of this study should provide a holistic picture of the innovation process of a biotech spin-off with governmental seed funding. The outcome and conclusions for these three meta- dimensions are described in chapter 6.

The important role of open innovation from the economic and societal perspective as an enabler for breakthrough (radical) innovation was recently stated by the European Commission:

> "Open innovation will be further served by including more companies that will use the technologies developed to make breakthrough innovations in products and processes, and through extensive societal engagement." (European Commission, 2019; p.8)

In summary, this literature review suggests that future research needs to link the different levels (individual, project, organization, ecosystem) of analysis with each other to provide a profound picture of innovation management in the biotech sector. This research study is focusing on the open innovation phenomenon by investigating the activities: R&D, IP, COL, NET and EL to answering the broad research question, if radical biotech innovation is possible. The outcome is expected to shed light on a multidimensional perspective, including the individual (the entrepreneur), the project (the MOC project), the organizations (spin-off, SMEs) and the ecosystem (the German ecosystem).

The following chapter will provide the research methodology, describing the study design and underlying research strategy. In addition, ethical considerations, generalization and limitations of the study are discussed.

3 Methodology

"Elegant and innovative thinking can be balanced with reasonable claims, presentation of evidence, and the critical application of methods" Whittemore, et al., 2001, p.527

3.1 Introduction to the Research Methodology

Qualitative research, and case study research in particular is gaining growing importance with regard to studying theoretical phenomena (Eisenhardt, 1989; Eisenhardt, 2007; Ozcan and Eisenhardt, 2009; Yin, 2009). The aim of the research methodology is to provide an appropriate framework to answer the research questions by focusing on the causality, interdependency and correlation of the five open innovation activities. There are three important uses for case research according to Siggelkow (2007), namely motivation, inspiration and illustration. With regard to this dissertation, the motivation for the adoption of the case study research design was driven by the question “how” and “why” radical innovation in the field of biotechnology, embedded in the German ecosystem, is possible. Based on the VCOI theoretical framework of the adoption of the open innovation concept in the setting-up of a spin-off biotech company, backed up with the multiple biotech SME cases, the evaluation of the rich, in-depth data collection will serve as an inspiration for new ideas and possible new theories regarding the creation of radical innovation. The chosen case study design can be used as an illustrative example covering the causal relationship between the open innovation activities evolving from the data collection analysis. This is one of the advantages over large-sample empirical work (Siggelkow, 2007). Another important reason for focusing mainly on the case of a particular organization is the unusual deep insights which are provided by the rich and in-depth, longitudinal data collection. Eisenhardt (1989) emphasises that theory building from case study research is appropriate to provide “freshness” to a topic which has been already researched. The aim of this dissertation is, therefore, to provide new, “fresh” theories regarding the open innovation concept in conjunction with radical innovation. Because it is possible to fit the theory behind the open innovation phenomenon to the many details of the particular case and the multiple cases, the creation of complex new theories becomes possible (Eisenhardt, 2007). There is debate about the right, or appropriate research design to apply grounded theory as a research methodology (Suddaby, 2006; Eisenhardt and Graebner, 2007). Starting point for this dissertation was the researchers motivation to understand how and why radical innovation can be created in biotechnology. The next step was defining a theoretical framework for this study, but with no predefined hypothesis to be tested (Suddaby, 2006). By applying the multilevel perspective of the VCOI framework, the open innovation phenomenon served as a broader framework, not as a predefined theory. In Bogers et al. (2017, p. 9) review, the open innovation scholars argued, that open innovation is not a theory per se, rather than a phenomenon, and important parts of open innovation has not been sufficiently theorised. Therefore, theory development should be at the centre of contributions to the open innovation literature. The outcome of this research will provide fine-grained insights about the successful formation of a spin-off organization developing a radical innovation, backed up with valuable research results about the innovation strategy of established biotech SMEs. The results from both case studies will be consolidated in the findings and conclusions chapter 6. This will enable the researcher to provide a holistic picture of the German biotechnology sector.

3.2 Context of the Research Study

Context can be defined as structural conditions that shape the nature of situations, circumstances or problems to which individuals respond with actions, interactions and emotions (Corbin and Strauss, 2008). The contexts of this dissertation are the socio economic conditions under which radical innovations in the biotech sector becomes products, technologies and services that address the demands of the life science market. These conditions are put under investigation in the framework of a concept based on the open innovation phenomenon. With regard to this dissertation, the motivation for the adoption of the case study research design was driven by the question “how” and “why” radical innovation in the field of biotechnology, embedded in the German ecosystem, is possible. Embedded in the Value Chain for Open Innovation (VCOI) conceptual theoretical framework (see 2.5.3.2), the research study is focusing on the setting-up of a spin-off biotech company, where the rich in-depth data collection expected will serve as an inspiration for new ideas and new theories regarding radical innovation. The data collection from the multiple cases will have, to some extent, a retrospective character, since the executive manager interviews are providing a snapshot, but also including questions where the interviewee looks back. Linking the findings and results from the overall study to the requirements for developing grounded theory (Glaser and Strauss, 1967), it can be concluded that qualitative research and the general method of comparative analysis and theoretical sampling is adopted here. Grounded theory is defined by Glaser and Strauss as:

> “Theory in sociology is a strategy for handling data in research, providing modes of conceptualization for describing and explaining.” (1967, p. 3)

According to Eisenhardt and Graebner (2007), justifying theory building from cases is strongly related to the relevance of the research question. There is actually no theory for radical innovation in the biotech sector, which could be applied to newly founded organizations. In this phenomenon-driven research study, the main research question (RQ2: Can open innovation enable the development of radical biotech innovations in a German ecosystem?) is *broadly* scoped (Eisenhardt and Graebner, 2007; p. 26). Even the research categories, the open innovation activities: R&D, IP, NET, COL and EL are broad by nature and cover not only internal, but also external activities and processes. One could argue that these categories set a predefined framework, but no hypothesis were pre-formulated or tested. Besides the fact that these categories served as a framework for the semi-structured interviews a tremendous number of other data were collected from all the cases. These data were constantly compared and contrasted throughout the data collection and analysis process, following the principle of the grounded theory approach formulated by Glaser and Strauss (1967).

Furthermore, according the Glaser and Strauss (1967, p. 79) there is a strong link between *substantive theory* and *grounded theory*:

> "Substantive theory is a strategic link in the formulation and generation of grounded formal theory. We believe that although formal theory can be generated directly from data, it is more desirable, and usually necessary, to start the formal theory from a substantive one. The latter not only provides a stimulus to a "good idea" but it also gives an initial direction in developing categories and properties and in choosing possible modes of integration. Indeed it is difficult to find a grounded formal theory that was not in some way stimulated by substantive theory."

As argued in this statement, the researchers used the open innovation framework as a stimulus and "good idea" for her research study. The motivation was to link open innovation as an interesting phenomenon with the purpose to "discover theory from data" (Glaser and Strauss, 1967, p.1).

Based on the assumption, to build new theory regarding the business model for newly founded ventures, developing radical innovation, the philisophical stance of the researcher is the interpretivist one, described more in detail in the following paragraph.

3.3 *Research Study Philosophy - Ontological Assumptions and Epistemological Stance*

Choosing a research methodology is making a decision on the "how" of the research (Holden and Lynch, 2004). There are three categories in qualitative research based on the underlying epistemology: positivist, interpretivist and critical (Chua, 1986; Orlikowski and Baroudi, 1991). A wider perspective summarizes four paradigms for qualitative research: positivism, post-positivism, critical theory, and constructivism (Guba and Lincoln, 1991). The researcher is following the interpretive philosophy, which ontologically assumes that the world, i.e. social relations, organizational, division of labour, is not a "given", rather the social world is produced and reinforced by humans through their actions and interactions (Orlikowski and Baroudi, 1991). Since the research design embraces an embedded case study approach to focus on the organization and their individual members, Orlikowski and Baroudi's statement regarding the interpretivists' view is applicable:

> "The research methods appropriate to generate valid interpretive knowledge are field studies, as these examine humans within their social settings" (1991; p.16).

Furthermore, interpretive research is appropriate to study phenomena and the meaning that individuals assign to them. Even if this research study is based on a theoretical framework, in the case of this dissertation, the open innovation phenomenon, dependent and independent variables should not be predefined in order not to restrict emerging, possibly unexpected, new phenomena from the qualitative research (Kaplan and Maxwell, 1994).

In contrast to this, the positivist assumes that the reality is given and can be described independently from the observer by measurable variables. Positivist studies are characterized by the purpose of testing theories and hypotheses by searching for evidence of formal propositions (Orlikowski and Baroudi, 1991). Even if positivist research is applicable to the case study methodology, it was identified as not fitting the overall research design of this dissertation. With the focus on answering the research questions, the interpretive approach will enable the researcher to understand social and organizational phenomena due to the lens of the behaviour of the involved individuals.

Nevertheless, the researcher epistemological stance in regard to the research methodology is interpretivist, the data analysis methodology should not be limited to this philosophy.

3.4 Research Study Approach and Alternatives

The chosen case study approach can be used as an illustrative example regarding the causal relationship between the open innovation activities evolving from the data collection analysis. This is one of the advantages over large-sample empirical work (Siggelkow, 2007). Another important reason for focusing mainly on the case of a particular organization is the unusually deep insight which is provided by the rich and in-depth data collection. Because it is possible to fit the concept behind the open innovation phenomenon to the many details of the particular case, the creation of complex new theories becomes possible (Eisenhardt, 2007). In addition, to back up the longitudinal single case design, multiple case studies from innovative, mature biotech SMEs are investigated. Research by Lichtenthaler (2011) suggested that longitudinal, cross-level research is implicated for the future agenda of open innovation. Therefore, the qualitative research design was identified as the appropriate research methodology. In this context, a quantitative research methodology, i.e. including a large sample or number of companies to be studied, was not considered as appropriate. Even if large empirical studies are characterized by profound, statistically approved data, the deep insight at the organizational, project and individual level from the single case would have been missed. Therefore, the longitudinal, in-depth case study, complemented by multiple cases was chosen in order to investigate the open innovation activities and their interdependence with the final goal of answering the research questions. In addition, this resonates well with Bogers et al. (2017) demand for multilevel analysis of the open innovation phenomenon.

In contrast to the case study methodology chosen, action research was an option to be considered for this dissertation. The following table describes the different characteristics of both approaches and compares them to each other.

Table 8: Characteristics of Case Study and Action Research

Case Study Research	**Action Research**
Researcher is observer	Researcher is active participant
Exploratory, explanatory or descriptive	Prescriptive, intervening
Focus on "How?" and "Why?"	Additional focus on "How to?"
Positivist or interpretivist	Usually interpretivist

Source: Adapted from Vreede, 1995

The term "action research" was coined by Lewin and published for the first time in 1946. The main characteristic of this approach is the involvement of spirals of steps, which are composed of a circle of planning, action and fact-finding. Since the researcher becomes an active participant or consultant and is able to influence the case, this research approach is inappropriate for this study. To observe a phenomenon and the grade of adoption and adaption of it, the researcher should be as objective as possible. Thus, the case study research approach was chosen to overcome the challenge of bias.

3.5 Research Strategy and Study Design

Since the researcher has more than 30 years of working experience, this dissertation aims to combine theory and practice to contribute new insights and knowledge about recent developments from an academic and practitioners' perspective into the biotechnology industry. According to Leonhard-Bartons (1990), a dual methodology for case studies is the baseline for the research model conceptual framework. Since the dual methodology uses the synergies between the "close-up lens" of the in-depth, longitudinal case and the "wide-angle lens" of multiple cases, this design is compatible to theory building (Leonhard-Bartons, 1990). Both types of case studies and their specific designs are described in detail in the following section.

3.5.1 In-depth Single Case Study Design

Qualitative research from case studies and the persuasive power of single case studies (Siggelkow, 2007) are of increasing importance to the research community. In this context, grounded theory building (Suddaby, 2006) and the value of the richness of data (Weick, 2007) are strongly related to the case study methodology. Highly regarded and highly cited papers (Eisenhardt, 1989) based on building theories from cases are additionally considered as "most interesting" (Bartunek et al., 2006). Case studies can be defined as rich, real-world, empirical descriptions of a phenomenon based on a variety of data sources (Yin, 2009). Each case serves as a unique, stand-alone experiment. In contrast, multiple cases serve as replications and extensions of data sources. Eisenhardt (2007) emphasises that the "well-done" theory building from cases is surprisingly objective. The outcome of the method can be compared with formal analytical modelling in mathematics (Eisenhardt, 2007). A research question is better addressed by building a new theory from cases than only testing an existing theory. To overcome the common debate about the non-representativeness of a single case study, the observed phenomenon and the unique characteristics have to be described in depth. Thus, a single case study can be a representative, powerful example (Siggelkow, 2007; Siggelkow, cited in Ramachandran, 1998).

Description of the Single Case

The description of the single case aims to summarize the recent developmental status of the new organization, and can only demonstrate a “snap-shot” because of the accelerated growing tempo of the underlying scientific projects and fast moving commercial progress. In contrast to this, the longitudinal data collection aims to provide a fine-grained picture of the innovation management processes studied over time. The spin-off company’s website was launched on October, 5th 2011 under: *www.tissuse.com*. The aim of the launch was to create awareness, on the one hand, to the scientific community and, on the other hand, to the potential market for the innovative technology, products and services. The website is clearly structured to reach both, customer segments by providing information regarding: “our science; commercial focus; about us; scientific advisory board; news and events, and publications”. At this point of development, the website functions as an information tool to create awareness to potential future customers, external scientific and commercial partners, and potential financial capital providers.

The in-depth case study research focuses on the new organization - the *Entrepreneurial Spin-off* , the CEO - the *Open Innovator*, and the radical innovative project, the *MOC Project* (Multi-Organ-Chip Project). Even though this project combines several scientific sub-projects, from the general view, it was required to stick to the superior MOC Project. To demonstrate the link with the theoretical background of the study, based on Lichtenthaler (2011), the following figure shows the adaption of the case study of Lichtenthaler’s theory about his open innovation conceptual framework in regard to the knowledge management.

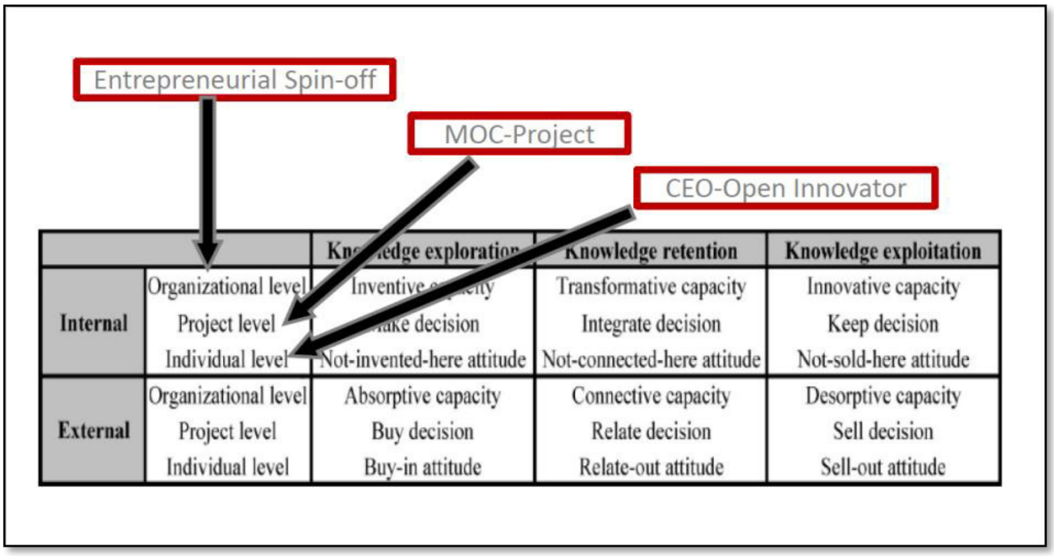

Figure 12: Single Case - Multiple Levels of Analysis

Source: Adapted by the author from Lichtenthaler, 2011, p. 80

In addition, the five key open innovation activities (R&D, IP, NET, COL, and EL), based on De Jong et al. (2008), are investigated at all three levels, namely the organizational (entrepreneurial spin-off), the project (MOC project) and the individual level (CEO - Open Innovator). Therefore, the envisioned results will contribute the demand for multiple levels of analysis (Bogers et al., 2017).

The requirements for an exemplary single case study according to Yin (2009) are summarized in Table 9 in the left hand column, and the characteristics of the selected case, the German biotech spin-off, are summarized in the right hand column.

Table 9: Single Case Study Characteristics

Single Case Study Requirements (Yin ,2009)	Case Study Characteristics German biotech spin-off
"Significant": unusual and of general interest; national, theoretical, political or practical importance.	Radical innovative products and services; unique German spin-off case; adaption of open innovation and beyond: gained governmental funding: case study research findings aim to build new practical impact and theory building.
"Complete": clear boundaries of the case; distinction between the phenomenon and the context; presentation of evidence; collection of evidence: critical pieces are given complete attention; absence of certain artificial conditions; design the case study in the timeframe which can be completed.	One particular high-tech spin-off is observed; clear distinction between the open innovation phenomenon as a theoretical framework and case research of the spin-off; evidence is provided by the rich and complete data collection; complete attention on business and scientific related issues; no artificial conditions because of the real-time observation; realistic timeframe of three years.
"Consider alternative perspectives" : consideration of rival proposition; citing of rival claims or alternative perspectives; challenge the assumptions of the case; different perspectives: alternative cultural view, different theories, variations among stakeholders, decision makers.	Rival proposition and alternative perspectives are given by blending two open innovation theories and perspectives namely: De Jong et al., 2008 and Lichtenthaler, 2011. De Jong et al. emphasise the behaviour of organizations and Lichtenthaler focuses on the different stages of knowledge creation from the organizational, project and individual level in regard to the open innovation phenomenon.
"Display sufficient evidence": database should provide critical pieces of evidence; investigator has to "know" the subject; present evidence neutrally; validity of evidence: maintaining a chain of evidence.	Data collection is rich, in-depth and detailed; investigator is partly participant observer; validity and maintaining a chain of evidence is ensured by the different units of analysis and consistent data collection over time.
"Composed in an engaging manner": written reports in clear writing style; engagement; "earth-shattering" conclusions; inspiration should pervade the entire investigation.	Engagement is assured since the investigator gains new scientific- and business-relevant knowledge; conclusions will be based on radical innovation; inspiration is gained from the entrepreneurial spirit of the case.

Source: Adapted and expanded by the author based on Yin (2009), pp. 185-190

This single in-depth case study is accompanied by multiple case studies of four established German biotech companies and one Dutch biotech company. A Dutch biotech company was chosen to include one other example from within Europe. The Netherlands is known as one of Europe's most entrepreneurial driven economies. The biotech sector especially is of growing importance in the European setting. These companies were selected to become companion cases to augment the data collection from the single case (Yin, 2009). All companies are, by definition, "dedicated biotechnology firms" according to the OECD definition (2005):

> "**A dedicated biotechnology firm** is defined as a biotechnology active firm whose predominant activity involves the application of biotechnology techniques to produce goods or services and/or the performance of biotechnology R&D."

The grade of innovation or innovativeness is not easy to measure. Besides definitions of innovation claimed early by Schumpeter (1934), the *Oslo Manual* was considered as an appropriate definition in regard to the selected companies (OECD and Eurostat, 2005). Innovations must contain the following three types of novelty:

- New to the firm - diffusion of an existing innovation to a firm;
- new to the market - the firm is the first to introduce the innovation to its market; and
- new to the world - the firm is the first to introduce the innovation to all markets and industries.

The selected multiple cases will furthermore serve as valuable sources to gain more insight about the open innovation phenomenon by evaluation the open innovation activities (R&D, IP, NET, COL, and EL) in a retrospective manner. Therefore, the multiple cases must meet at least one or more of the following characteristics:

- Dedicated biotech company founded in Germany/Netherlands and older than five years (OECD, 2005; biotechnologie.de, 2011)
- Former spin-off or start-up, based on the IP of innovative technology, product or service
- Earned governmental funding at the founding stage

- Winner of an national or international “Innovation Award”

The involvement of the companies does not claim to be representative of the German or Dutch biotech sector, but they are representative samples to complement the in-depth single case study. Some of the cases are spin-offs from universities or research organizations and are, therefore, identified as “role models” for the successful NPD based on knowledge generated due to institutional or public scientific research. Since all companies have developed new products, technologies or services and sell them today, they were characterized as examples for successful technology transfer from academia to industry.

The multiple cases were identified to complement the single case with the purpose to broaden the insights from one specific sector, the biotechnology industry. Another advantage expected from the multiple cases, the biotech SMEs is the added value regarding the insights into their innovation management strategies from the perspective of their CEOs and senior managers.

In addition to the five independent multiple cases, a “Pilot Interview” was conducted at the beginning of the multiple cases data collection. It was the intension to involve a senior consultants’ view with an international perspective from outside the spin-off company at a defined point of time. At the end of the data collection, the same interview was conducted with the CEO of the spin-off company, which is connected to the data generation with the view on the spin-off company. The detailed case study design of the multiple cases is described more in detail in the following section and in Figure 16 in Chapter 4.

3.5.2 Multiple Case Study Design

The decision to involve multiple cases in this study was made to design the overall study to be as objective as possible. Conducting multiple case studies is a research methodology which implies studying results from multiple experiences

(Yin, 2009). The advantage, compared to a single case, is the opportunity to get support due to similar results or contrasting results from the multiple cases. Another advantage is the different, wider angle from which the researcher observes the multiple cases. In combination with the single case, this methodology can limit biases to a minimum (Leonhard-Barton, 1990). As stated by Yin (2009), the use of multiple cases should follow a replication, not a sampling, logic. This indicates that the cases have to be chosen very carefully and they should serve as rich sources for the chosen theoretical framework, in this context the open innovation phenomenon, according to De Jong et al. (2008) and Lichtenthaler (2011), illustrated by the VCOI. Since multiple units of analysis are adapted to the overall case study design, an embedded design is used for the multiple cases (Yin, 2009). Additionally, multiple cases create more robust, generalizable and testable theory, since they are grounded on varied empirical evidence (Eisenhardt and Graebner, 2007).

3.5.3 Description of the Multiple Cases

To support the outcome from the single, in-depth case study of the spin-off company, multiple case studies of already established biotech companies will be a complementary source of research data. Notwithstanding, that the multiple cases cannot be compared directly to the single case. An embedded design was chosen for the multiple case studies to gain inside knowledge about the open innovation activities (R&D, IP, NET, COL, and EL). Direct observation and conducting interviews with the Executive Managers regarding their experiences with the open innovation concept are the units of analysis of the embedded design (Yin, 2009).

The multiple case studies focus on the organizational level - the *Biotech Companies*, and on the individual level - the *Executive Manager*, in accordance with Lichtenthaler’s (2011) open innovation theoretical conceptual framework (see Figure 13). The project level is excluded from the multiple case studies, since the companies are mature with a broad product, service and platform portfolio. Another obstacle is the strict confidentiality for NPD projects in the biotech sector. Additionally, the radical innovative nature of the single case project (MOC Project) makes it difficult to find comparable projects; therefore, focusing on one particular project of each of the involved cases was appraised as inappropriate.

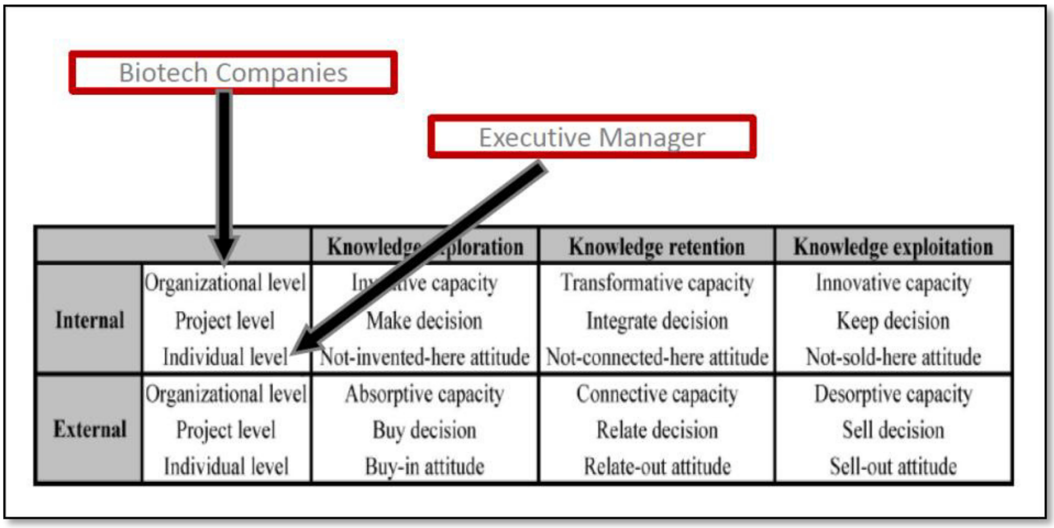

Figure 13: Multiple Cases - Multilevel Analysis

Source: Adapted by the author from Lichtenthaler, 2011, p. 80

The multiple cases are selected biotech companies which are considered as "comparative" SME studies. Each case was carefully selected to either be able to predict similar results, which means a *literal replication*, or predicts contrasting results, which implies a *theoretical replication* (Yin, 2009).

By focusing on the biotech SMEs and their executive managers, the perspective of analysis from the individual and organizational level will not only provide internal insights. Due to the framework of the open innovation activities: R&D, IP, NET, COL and EL, it is expected, that the exchange with external partners at different stages of value creation will become visible. These results are expected to contribute to a better understanding, how innovation ecosystems are managed from the perspective of executive managers and organizations in the biotech sector (Yaghmaie and Vanhaverbeke, 2019).

3.6 *Data Collection & Analysis Methods*

3.6.1 Data Collection Embedded Case Study Research

Since the data collection evolves from a spin-off which is developing radical innovations, the conclusions of this study could be relevant for other high-tech industrial sectors, where radical innovations are the outcome of the NPD process. Innovation management within the company is crucial for all high-tech driven industrial sectors to gain competitive advantage; therefore, cross sector knowledge chairing is one important criterion of the open innovation phenomenon.

The data collection is based on the three principles according to Yin (2009):

- Multiple Sources of Evidence
- Create a Case Study Database
- Maintain a Chain of Evidence

Figure 14: Multiple Sources of Evidence

Source: Adapted by the author based on Yin (2009).

The **multiple sources of evidence** are based on the multiple units of analysis, such as documents, observations, interviews, etc., summarized in Figure 14. They are mandatory for the embedded design of a case study. These units of analysis enhance the insight into the case study and lead to a convergence of evidence. They are the sources of the data collection from the single case study and, to some extent, from the multiple case studies, described in more detail under section 3.7.

The “creation of the case study database” started after closing a Confidentially Agreement (CDA) with the CEO of the spin-off company. The initial step for this collaboration was a written case study research proposal (see Appendix B). The study became a longitudinal study and was possible due to the non-restrictive access to all relevant data regarding events and activities. Based on this fact, the data collection is comprehensive, rich and in-depth. Every scientific and business related event and activity is professionally documented and kept filed. The access and collection of these data created a rich database, which consists of printed documents and a collection of data in the formats of electronic documentation, such as: word, power point, pdf, and excel files. Tables in excel format were created to establish a database for all documented activities depending on the date of occurrence. In addition, a clustering regarding the open innovation activities R&D, IP, NET, COL, and EL was implemented in this excel database. Additionally, all documents collected were organized in a file system and backed up with security copies. Several meetings with the CEO were used to conduct open-ended interviews regarding the recent stage of the company’s development. The meetings were documented by taking notes and summarised in written minutes. Direct and participant observation was practised starting from 2008 until the end of 2012.

Maintaining a chain of evidence is a crucial step to prove the data collection’s reliability (Yin, 2009). Since all the *facts* of the case are collected and analysed with regard to the open innovation activities and their interdependence to each other at different stages of the scientific and business development, the data collection will serve as a chain of evidence. The database claims to be comprehensive and in-depth, which is mandatory to investigate the principles of open innovation according to De Jong et al. (2008) and Lichtenthaler (2011), which provides the theoretical framework for the study. This is another strong link to the chain of evidence gained from the in-depth single case study.

3.6.2 Units of Analysis- Single and Multiple Case Study

The six units of analyses were identified as crucial sources for the in-depth single case study. Since the researcher has full access to all information regarding the scientific and business related activities and events, this data collection is similarly rich and unique, and, therefore, a valuable source for theory building (Eisenhardt, 2007). The following table demonstrates which units of analysis will be included in both types of case studies. In this context it is important to mention, that the units of analyses in the multiple cases are investigated from a broader perspective. In contrast, all units of analyses in the single case are investigated in a very detailed and in-depth mode.

Table 10: Units of Analyses Single and Multiple Cases

Units of analysis	Single Case Study	Multiple Case Study
Documents	√	√
Archival Records	√	√
Open-ended, In-depth Interview	√	-
Focus Interviews	√	-
Semi - Structured Interviews	√	√
Observation direct and participative	√	√

Source: Adapted by the author based on Yin (2009).

3.6.3 Units of Analysis - Single Case

3.6.3.1 Documents

Documents are one of the best available sources for data collection. There are manifold sources of documents, e.g. letters, e-mail correspondence, diaries, calendars, notes, agendas, minutes of meetings, written reports, administrative documents, formal studies, news articles, and so on. These are only extracts from the different types of documents and do not claim to be exhaustive. Documents play an explicit role in case studies and are used to confirm and augment results from other sources (Yin, 2009). Even if documents are reliable resources, they also have limitations. The investigator has to take into account that the documents accessed are created for a special purpose other than in context with the specific case study design (Yin, 2009). Therefore, a critical interpretation is mandatory. The abundance of sources accessible due to the internet could mislead the research to some extent. Documents for the single case study were provided by the CEO and internet search was only necessary to back up some of the information. Thus, only relevant documents are enclosed in the study.

Access to all relevant documents was provided during meetings with the spin-off CEO. The meetings were held every two to three months, dependent on the current activities within the company and resources of time. All meetings were documented by meeting protocols. The provision of documents were physically or virtual. These units of analyses were also collected and documented in the excel sheet "Data Collection Single Case Study" following the date of appearance.

3.6.3.2 Archival Records

Archival records are usually "public use files", such as statistical data, made available by federal, state or local governments (Yin, 2009). Other archival records are, for example, organizational records, maps, charts, and survey data (previously collected). As suggested in regard to the use of documents, the researcher must be aware of the fact that the records are primarily created for a different purpose. Thus, the researcher has to link the scope of the study with the decision of which records are useful. Notwithstanding, that a rich data collection will provide valuable sources of information to be able to develop new theories grounded in the data (Glaser and Strauss, 1967).

The CEO of the spin-off company provided the researcher with all relevant archival organizational records covering 210 events in the time frame of 2008 - 2012. These documents are valuable, rare resources for the researcher to gain inside knowledge about all activities during the pre-founding, founding and early product development phase of the spin-off company. The archival records were collected and documented in the excel sheet described above.

3.6.3.3 Open-ended and In-depth Interviews

The interviews, no matter what type, are one of the most important sources of information in the context of a case study. Open-ended interviews allow a certain degree of flexibility, which is important if new issues arise during the interview process. An interview guide is important to this process to ensure that the correct information is gained from the interviewees. The interviews should be guided conversations in which the interviewer has two important tasks: To satisfy the needs of the actual stream of questions by simultaneously putting forth “friendly” and “nonthreatening” complementary questions (Yin, 2009). In contrast to this open-ended type of interview, in-depth interviews were conducted with the CEO over the whole period of the longitudinal case study . These in-depth interviews varied in length and were conducted during the regular meetings and additionally conducted as telephone interviews with the CEO. The interviews were documented in written notes, and events and activities were documented in the excel sheet. The purpose of this type of interview was to gain information about recent activities of the entrepreneurial spin-off, as well as the next developmental steps planned. Even though the CEO became the key informant in the single case setting, the researcher chose all six sources of evidence to avoid bias and relied on different sources of evidence (Yin, 2009).

3.6.3.4 Focus Interviews

The aim of focused interviews is to corroborate certain facts that were established during the collection of data (Yin, 2009). The focused interviews were part of the meetings with group members, especially the two team members of the spin-off. They both had in common that they were involved in the formation process of the company from the early beginning. This type of interview focuses in particular on one of the sub-projects. The analyses of focus interviews would provide inside information about the grade of adoption of open innovation principles in the context of the five open innovation activities, but from the perspective of the working group leaders. Written notes were taken and transcribed in meeting minutes.

3.6.3.5 Semi-Structured Interviews

In Table 10 the term survey was put in brackets because, in the context of this dissertation and the case study approach, no surveys regarding generating quantitative data were conducted. The focus was to provide qualitative data, rather than quantitative to serve the complexity and theoretical framework of this study. Therefore, surveys and questionnaires with a larger number of companies did not meet the requirements for this study. Semi-structured and in-depth interviews were one of the units of analysis. During the pre-foundation process, interview data, which had already been conducted were provided to the researcher within the archival records. In addition, the researcher had full access to the outcome and analyses of the interview results. Since the CEO of the spin-off was included, the resulting data were valuable to study the early activities in regard to the corporate entrepreneurship and leadership of the CEO. The researcher had access to the written report of these interviews and the evolving written report.

3.6.3.6 Observation (Direct or Participative)

Observation, direct and participative, is a valuable resource when the study involves a new phenomenon and a new technology (Yin , 2009). The observation can be formal or informal. In the context of this in-depth case study, the formal observation predominated the informal, to avoid bias, since the researcher was aware of the fact that all data are collected by the researcher herself, which buries, to some extent, the risk of getting too involved in the case.

Direct observations of the activities of the spin-off were possible due to several meetings with the team members and the CEO. A few informal team meetings, e.g. bowling, barbeque, evening activities, especially during the formation phase, served for the direct observation of the spin-off and the team members.

Participative observation is a mode of observation in which the observer becomes, to some extent, part of the case study. In the case of the spin-off company, the researcher's function as an active participant is limited and acts only as part of the units of analysis. The advantages of gaining access and such deep insight knowledge about a newly founded organization generally outweighs the potential biases which could be produced. The participative observation, from the researcher's perspective and function as the responsible project manager employed at a Technology Transfer Office (TTO), was an important prerequisite to be able to carry out the overall study. One distinctive opportunity gained by participating in the case was the ability to perceive information in a real life setting of an organization (Yin, 2009), which is mandatory for the single, in-depth case study approach (Eisenhardt, 1989). Hence, there are some disadvantages described in the literature (Becker, 1958, cited in Yin, 2009), but the awareness of such threats can minimize the risk of biases. Therfore, to not threaten the case study, the researcher participated, but did not influenced, the members of the organization. The underlying theoretical framework of the open innovation phenomenon was not presented or discussed within the organization. Information about the open innovation activities was collected during meetings with the team held every three to four months to update the recent status of development. The outcomes of these meetings are documented in the written notes. Activities were documented in the data collection excel sheet.

3.6.4 Units of Analysis - Multiple Case Studies

To back up the single in-depth, longitudinal case study, the inductive, multiple case study approach was identified as the best source of extant theory (Eisenhardt, 1989). Since the adaption of the open innovation phenomenon is a process, inductive studies are useful for developing theoretical insights (Ozcan and Eisenhardt, 2009). Multiple case studies are more effective than single cases, since they enable the researcher to collect comparative data, which could lead to more accurate and generalizable theory (Ozcan and Eisenhardt, 2009; Yin, 2009). Since the VCOI framework was created to involve both, the single and multiple case studies, the data collection, analysis and findings also combine the advantages of both research methodologies; theory building from the observed phenomenon is, at least, the intension. Nevertheless, both types of case studies are conducted and evaluated separately, with the purpose to answer all three research questions and provide profound insights into the biotechnology sector.

According to Table 10, four units of analyses were chosen as data sources for the multiple case study. The same types of data sources, namely documents, archival records, structured interviews and observation were chosen to ensure the convergence of evidence (Yin, 2009). This triangulation of the data collection from multiple sources will strengthen the confidence in the accuracy of the findings (Ozcan and Eisenhardt, 2009). The theoretical considerations of each of the units of analysis have already been described above. Therefore, in this section, the context of the documents, archival records, structured interviews, and observation in regard to the multiple cases is the focus.

3.6.4.1 Documents

As described in context with the single case study, documents are valuable resources for data collection (Yin, 2009). The sources of documents for the multiple cases were limited to keep them comparable from case to case, e.g. press releases about alliances, collaborations or licensing agreements were identified as resources. The information gained from the websites was the most relevant in this context, since it is considered as appropriate and up to date.

3.6.4.2 Archival Records

Valuable sources for the multiple cases are corporate and business records, e.g. annual reports and corporate presentations. These records are available from the individual websites, or, if the company is not public, from other resources, e.g. special industrial reports. Although these records are useful sources, the main in-depth information was collected from the structured interviews with the executive managers of the biotech companies.

3.6.4.3 Semi-Structured Interviews

The most important unit of analysis is the semi-structured, in-depth interviews. This type of interview is determined by a high degree of standardisation or uniformity. It was identified as the best method to guarantee the compatibility of the research results, even if this might lead to missing the opportunity of discovering important information owing to the inflexible nature of this type of interviews (Brymann and Bell, 2003). The standardisation and uniformity is a basic requirement to investigate the activities: R&D, IP, NET, COL and EL with regard to the open innovation phenomenon. An interview guide is important to this process to ensure that the correct information is gained from the interviewees. This interview guide was created at the beginning of the multiple cases study. The executive managers from the different biotech companies were identified as reliable, valuable sources to investigate the adoption of the open innovation concept in their organizations. As described above, these managers have strong records and long-term experience in the business development of their companies. Therefore, they are identified as representative resources Even if the number of five companies seems to represent a small sample, the former analyses and chosen criteria overcome this limitation (Leonhard-Barton, 1990).

3.6.4.4 Observation

In the context of the multiple cases, the biotech companies, observation over a period of at least five years and, for some cases longer led to the identification of these companies as being valuable sources for the study. The approach was rather direct observation than participative. The researcher observed the business development of these companies from the professional perspective and experience due to company presentations, panel discussions and meetings at national and international conferences. Even so, the data collection from observation served to provide an overview about the company's recent developmental status. In contrast, the open innovation activities are investigated in-depth in the structured interviews.

3.7 Ethical Considerations

The research undertaken for this dissertation was approved by the Universities Research Ethics Committee (UREC) in June 2011. The interview guide, participant information sheet and consent form were submitted based on the advice of the committee and the document "Code of Practice for Research Involving Human Participants" (LSBU, 2010). The confidentially agreement (CDA) closed with the CEO of the spin-off company was included in the documents.

Later on, after approval, only participants who accepted participation in advance were involved in the study. No personal risk has been identified because the data provided do not interfere with the health and personal rights of the participants. The data collection, especially personal data, is collected in compliance with the Data Protection Act 1998 (see http://www.ico.gov.uk/).

All personal information about the participants is kept confidential and will not be published. All information relevant for the data collection and the analysis has been anonymized. Hence, the CEO and participants from the single case agreed to be mentioned by their names and functions.

In order to communicate the framework of the research to the UREC, a research proposal was submitted. All relevant documents were approved by the director of study to cover the requirements of the university's regulations (Remenyi et al., 2011).

3.8 Reliability, Validity, Generalisation and Limitations

Reliability and validity of a study design and strategy are important indicators for the overall quality of the research. Applying an appropriate methodology to enable the researcher to answer the research questions is the first crucial step for providing validity and reliability. As suggested by qualitative methodology literature (i.e. Yin, 2009) this study aims to fulfil the requirements. The following paragraphs are supporting this statement.

3.8.1 Internal Validity & Reliability

Case studies refer to an evidence-based empirical approach (Bergen and Weil, 2000; Yin, 2009). The embedded case study design of this dissertation is of a descriptive and explorative nature (Vreede, 1995). Furthermore, the research design is embedded in a real-life context – investigations about a spin-off and mature organizations – based on the theoretical framework of the open innovation concept. These are two distinctive features that make this research unique and a reliable source to expand our current knowledge base (Flyvbjerg, 2006). The credibility of the study design is comparable to the traditional concept of internal validity (Riege, 2000). The use of multiple sources of data, i.e. data collections from the single and the multiple cases, strengthens the internal validity. In addition, on the level of the in-depth single case, as well as the multiple cases, different units of analysis are under investigation (see Table 2).

Since the study uses qualitative methods, internal validity is demonstrated by the evaluation of the open innovation activities and their interdependence, to achieve meaningful descriptions of the case and ensure internal coherence of the findings (Riege, 2003).

Another positive impact on the internal validity is triangulation and the ability to cross-check data from different points (Lee et al., 2010). If, by triangulation of multiple data sources, the evolving patterns coincide, the internal validity of the case study is strengthened (Yin ,1984).

3.8.2 External Validity and Reliability

External validity can also be described as transferability (Lee et al., 2010). The transferability and generalizability of this study is given by the VCOI created, which is based on the open innovation concept and can be adapted to other sectors and used by other researchers. Studying a phenomenon in the context of radical innovation can be generalized, since the global economy depends on innovations. There is a strong link between the open innovation activities evolving from the open innovation phenomenon and radical innovations. Leifer et al. (2001) defined radical innovation more than one decade ago as follows:

> "A radical innovation is a product, process, or service with either unprecedented performance features or familiar features that offer significant improvements in performance or cost that transform existing markets or create new ones." (Leifer et al., 2001; p. 102)

This definition is universal and applicable to every economic sector independently, no matter where in the world. Therefore, the outcome of this dissertation will be applicable to innovation management in general, not limited to the biotech sector.

3.8.3 Generalization

For this study three pathways for generalization from the qualitative case studies are chosen (Mayring, 2007). The first is *argumentative generalization*, based on the quality of the compared cases; the second is *theoretical sampling* (Glaser and Strauss, 1967; Strauss, 1987), based on the selection of the cases and the third is *triangulation* (Denzin, 1979). By covering these pathways the researcher aims to draw conclusion for the biotechnology sector, and particularly for new founded biotech organizations. Due to similarities in the high-tech sector, it is expected that further generalizations can be provided based on the outcome of this research study.

3.8.4 Limitations

This dissertation aims to answer the question whether radical innovation in the biotech sector in a German setting is possible, and, if so, under which conditions? The chosen methodology of the case study research design has its advantages, but also some disadvantages - the limitations. Qualitative research methods, such as case studies, play an important role in socio-economic research to contribute to our knowledge of individual, group, organizational, social, and related phenomena (Yin, 2009). Forms of the research questions of this dissertation are "what" and "how". Schramm (1971, cited in Yin, 2009, p.17) emphasis his definition of a case study as the following:

> "The essence of a case study, the central tendency among all types of case study, is that it tries to illuminate a **decision** or set of decisions: why they were taken, how they were implemented, and with what result."

In the context of this definition, other research methods, such as experiments, surveys, archival analysis, and history studies, are inappropriate to the scope of this dissertation (Yin, 2009). Even so, the chosen methodology faces some limitations. The main resource of the data collection is a single in-depth case study, backed up with multiple (5) case studies from established, mature biotech companies. In contrast to results from quantitative research, e.g. surveys, this is a relatively small number of samples.

Flyvbjerk (2006) identified and discussed the common misunderstandings about case study research illustrated in the following Table 11:

Table 11: Five Misunderstandings about Case Study Research

Misunderstanding	Restatement
1. General knowledge is more valuable than context-specific knowledge.	Universals cannot be found in the study of human affairs. Context-dependent knowledge is more valuable.
2. One cannot generalize from a single case, so a single case does not add to scientific development.	Formal generalization is overvalued as a source of scientific development; the force of a single example is underestimated.
3. The case study is most useful in the first phase of a research process; used for generating hypotheses.	The case study is useful for both the generating and testing of hypotheses, but is not limited to these activities.
4. The case study confirms the researcher's preconceived notions.	There is no greater bias in case studies toward confirming preconceived notions than in other forms of research.
5. It is difficult to summarize case studies into general propositions and theories.	Difficulty in summarizing case studies is due to the properties of the reality studied, not the research method.

Source: Adapted from Flyvbjerg (2006), pp. 219-245.

The restatements are important arguments concerning the limitations of the research methodology. However, there are some limitations concerning the researcher's point of view, since the researcher acquires all the data, conducts the interviews and analyses and interprets the data collection. The threat of bias can be limited by taking an open-minded, neutral position towards all information acquired and adhering to the theoretical model framework for the study.

Another limitation of this dissertation is the richness of the data collection from the single case study which is investigated in regard to the open innovation activities (De Jong et al., 2008) and the conceptual framework of open innovation (Lichtenthaler, 2011). This rich data collection could additionally become the resource for other, new and different research questions outside the scope of this dissertation. To overcome this limitation, the researcher plans, in cooperation with the biotech spin-off company, to submit further publications based on the rich data collection.

3.9 Impact of the Research Study Design

The embedded case study research design was considered as the appropriate methodology to answer all three research questions. Since the biotechnology sector, and in particular a spin-off organization and the mature SMEs are at the centre of this study, the qualitative case study approach will address the demand for different levels of analysis according to West et al. (2006). Hence, the case studies are in the focus, additional insights into the individuals (spin-off CEO; executive managers), teams (spin-off team members), the organizations (spin-off; SMEs), and their networks and national innovation systems perspectives are provided. Especially the rare, longitudinal spin-off case study aims to overcome this demand, caused by overemphasis of the firm level (Vanhaverbeke et al., 2014). One could argue that the newly founded spin-off is a new firm per se, but since the comprehensive data collection is covering even the pre-founding phase and sheds lights on the creation of the radical R&D project of the MOC, the outcome of this study will add new knowledge to understand open innovation in theory and practice. Furthermore, to address the following three limitations of understanding open innovation in a broader context (Vanhaverbeke et al., 2014; p.290), the impact of the case study type and scope is demonstrated here:

- *Narrow, managerial top management perspective* - Longitudinal, in-depth case study; framework of the five open innovation activities: R&D, IP, NET, COL and EL.
- *Lack of unbiased view on collaboration with different innovation partners* - Multiple case study; open innovation activities: COL and NET.
- *Lack of understanding the mechanism driving open innovation within an organization* - Longitudinal, in-depth case study; insights about the

interdependence of individuals, projects and innovation ecosystems.

As recently argued by Yaghmaie and Vanhaverbeke (2019), understanding the open innovation phenomenon should not be separated from innovation ecosystems and how value is created and captured. In this context, this dissertation aims to provide profound new knowledge about how radical innovation can be created in the biotechnology sector.

Based on the methodology described in this chapter, the following Chapter 4 will focus on the data collection and data analysis of this research study.

4 Data Collection & Data Analysis

"Modernity is a qualitative, not a chronological, category."
Theodor W. Adorno, 1951

4.1 Introduction to Data Collection

The case study methodology, including the single and multiple cases was identified as the best suitable research approach (Yin, 2009). During the investigation, the researcher was able to verify, that the case study research provides real an in-depth, practical and realistic inside view into the innovation management processes of organizations (Eisenhardt, 1989). The semi-structured, in-depth interviews with five executive managers (multiple cases) and leading four team members (single case); one external consultant and the spin-off CEO are part of the comprehensive data collection. Since the questions are based and focusing on the five open innovation activities, R&D, IP, NET, COL and EL, conclusions how and why companies are adopting and adapting the open innovation concept to their product development processes (De Jong et al., 2008) can be drawn. In addition, a unique, longitudinal, in-depth data collection is covering a huge part of the single case data collection. For the single case the interviews were conducted in response to the iterative data analysis process. Therefore, the interview questions were partly adapted to fit to the longitudinal, in-depth data collection. The concept of grounded theory was applied to the data evaluation process, with the purpose to gain explanations of relationships, events, causes, objects, actions and interactions that emerge directly from the data (Lawrence and Tar, 2013). During the research study process, the researcher was able, to develop a sense for the missing knowledge about the open innovation phenomenon from the ongoing literature review in the field, and the arising questions from her own practitioners, commercial perspective.

The three levels of analysis according to Strauss and Corbin (1990) are applicable to this study process in the following context:

- Present the data without interpretation and abstraction, the participants tell their own story: This was fulfilled by data gathering and building the data base collection based on the interviews for both case study types and the collected longitudinal data for the single case.

- Create a rich and believable narrative using field notes, interview transcripts and researchers interpretations: Here the iterative process of data evaluation, adopting the grounded theory approach was applied.

- Building a theory using high levels of interpretation and abstraction: The final data interpretation resulted in new theories for the open innovation phenomenon and recommendation for future research.

The use of the grounded theory approach was in addition motivated by the urgent need for connecting the phenomenon of open innovation to the theory of a firm (Vanhaverbeke and Cloodt, 2014). Thus far, there is a theoretical deficit observed in the open innovation literature, while the open innovation phenomenon is not grounded systematically in prior management research. Aim of this dissertation is to fill this gap, from an academic and practitioners perspective. As argued by Bogers et al. (2017), the open innovation literature needs more systematic theory development to understand the multi-level nature of the open innovation phenomenon.

Figure 15 is illustrating the case study design, to provide a holistic picture of the case study design and interrelation of all collected data.

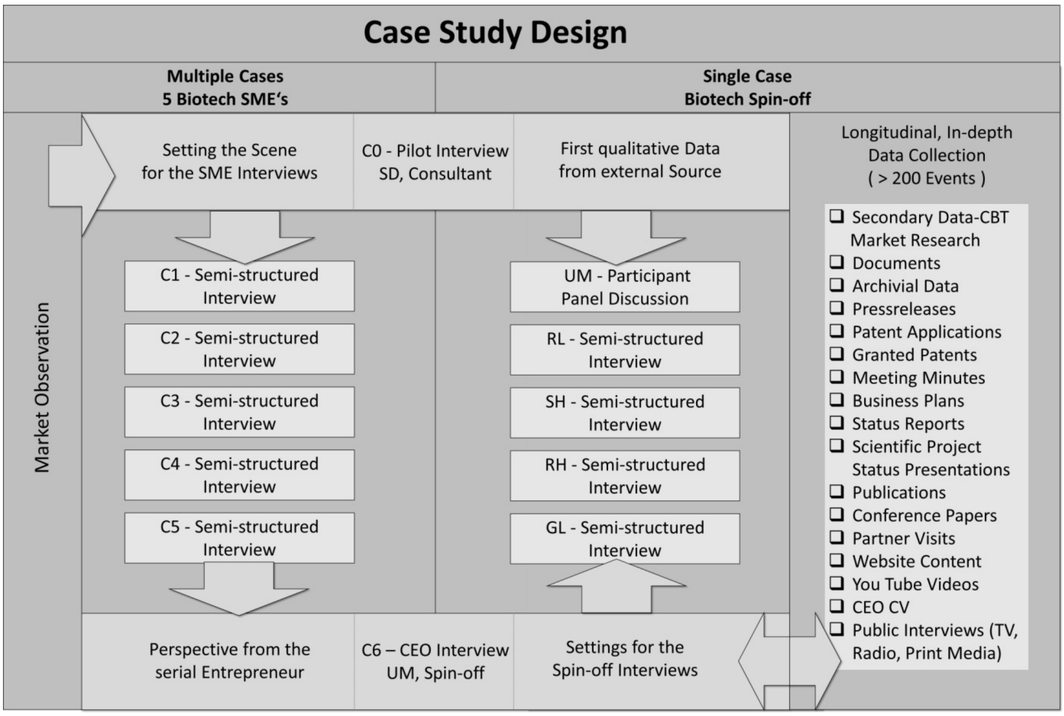

Figure 15: The Case Study Design

Source: Developed by author, based on the case study methodology (Yin, 2009)

As illustrated, the case study design is covering types, the single and the multiple cases. The connection between both was developed over time, by starting with setting the scene for the SME interviews and conducting a pilot interview with an international renowned life science consultant. The analysis of the pilot interview, led to conducting the SME interviews, and then, the spin-off CEO was interviewed, to involve his perspective as a serial entrepreneur. The team member of the spin-off company and the CEO's participation in a public panel discussion was complementing the in-depth longitudinal study of the single case. The setting for the spin-off interviews was influenced by the longitudinal data collection and their first analysis. By doing so, the semi-structured interviews were slightly amended with the purpose to shed more light on the rich data collection on one side and stay comparable to the interviews with the multiple cases on the other. The SME interviews were accompanied with constant market observation of the five selected biotech organizations.

The following section is covering the different levels of analysis by describing the steps of the overall research process. The section is divided into the single case and the multiple cases, following the case study design.

4.2 Single Case Data Collection

4.2.1 The Spin-off longitudinal Data Collection

The data collection started in September 2010, based on several meetings with the spin-off CEO. Data files of documents, presentations, reports and publications were provided for the longitudinal data collection. The documents were updated on a regular basis until the beginning of 2013. Even if the data collection started in 2010, the data itself are covering five years in the timeframe from 2008 to the end of 2012.

The rich data collection consists of all relevant documents concerning every single activity of the spin-off company covering a period of five years. This data collection is unique and in-depth, since usually a researcher did not get such a close view and direct access to such a comprehensive amount of confidential information. It was the intension of the researcher to get as much information as possible, to not miss any important steps in the pre and foundation stage of the spin-off organization. All data were collected in digital and printed format, transferred into an excel spreadsheet and were constantly extended. In order to structure the data, the date of the documented activity was the first category. A short description of each activity followed the chosen methodology of a descriptive, exploratory case study design (Yin, 2012).

The researcher collected and analyzed the longitudinal data collection by applying the following steps:

- Creation of a data collection base in excel format, ordered by date,
- Constant update of data collection base with provided data and data, based on constant own research (i.e. press releases, publications, secondary sources interviews, patent applications, patent status, conference attendances, keynote talks, information provided via company website),
- Iterative qualitative content analysis, applying the deductively, "ex-ante" developed categories of the five key open innovation activities (Schreier, 2012, p. 87).

Since the longitudinal data collection is covering very divers material, (i.e. power point presentations, videos, publications, patent applications, granted patents) the material was approached by investigating the relevance, connection or causal relationship of the five key open innovation activities - R&D, IP, COL, NET and EL.

The researcher developed a certain, unique rating system for the qualitative content analysis by evaluation to what extend the respective activity is present. Since every single document or material provides complex information and cannot be restricted to only one of the five key open innovation activities, this ranking system was identified as a useful evaluation tool.

4.2.2 The Pilot Interview

In preparation of the semi-structured interviews, the researcher conducted a pilot interview with the external consultant SD in November 2010. The interview guide was created to be able to answer the research questions, based on the five key open innovation activities (see Appendix C). This face-to-face interview was aiming to test the logic and clear formulation of the questions and provide profound insights from the perspective of an international renowned life science consultant. Based on the transcribed information and first analysis, the final interview guide was created. This approach is strongly suggested for insuring that the exploration is following an exploratory theory (Yin, 2012).

4.2.3 The Spin-off Interviews

The need for these interviews arisen from the constant data analysis of the rich, in-depth data collection from the single case, the spin-off company. The researcher decided to amend the interview guide, with the purpose to identify highlights and important achievements from the perspective of the members of the spin-off company. Thus, the opportunity of biased could be avoided, and triangulation of the data analysis is secured (Kelle, 2001). Therefore the interviews were conducted at a later stage of the single case data collection. The iterative data analysis process of the comprehensive data collection led to the additional inside view, covered by the interview data. The time period for the interviews was April to May 2012. The participants were contacted via e-mail, after confirmation of time and date; the researcher visited the participants at their workplace. All interviews were conducted in a face-to-face conversation. One of the participants required to conduct the interview in German, but agreed to verify the English transcript. Therefore, a potential incorrect translation and different meaning could be minimized. Nevertheless, the researcher is aware of this limitation, caused by the native language of all of the participants.

The purposeful selection of the interview partner is leading to a fine grained picture, since they have different position and bring in their own different academic and commercial expertise and perspective.

Table 12: Pilot, Single Case Interviews and Panel Discussion

TissUse / GO-Bio / TUB	Position/Function in GO-Bio / TUB	Position/Function at TissUse	Date of Interview
C0/SD - Pilot Interview	External Consultant	External Consultant	November 2010
UM - Dr. Uwe Marx - Panel Discussion	Group Leader	CEO	April 2011
RL - Prof. Dr. Roland Lauster	Head of Med. Biotech	CoFounder; Board	April 2012
SH - Silke Hoffmann	Project Leader	IP Manager	May 2012
GL - Dr. Gerd Lindner	Project Leader	CoFounder	May 2012
RH - Dr. Reyk Horland	Project Leader	Sales & MarketingManager	May 2012

Source: Data Collection by the Author

The interviews were conducted at different times, starting with the pilot interview at the end of 2010. This was the starting point for the overall study and the external consultant was chosen, since he has a strong international record in pharma- and biotech consulting projects. His motivation and external view at the early stage of the GO-Bio project and TissUse - eight month after founding, is a valuable, rare source for studying an early stage venture. The literature review concerning case study research covering newly founded ventures demonstrated that the data are often collected in a retrospective manner. This dissertation aims to overcome this lack by providing a case study based on data collected during the early pre-founding stage until the recent stage of product development. This implies, that the researcher, even after closing the dense, longitudinal data collection, observed recent developments of the company by regularly checking the website for new developments, as well as the media (print, online, radio and television). This was essential to be aware if the company is still commercially successful and reached the milestones for the radical innovative technology. Especially for the conclusions and recommendations (see Chapter 5), the recent status of the spin-off company is essential. Not only the technology of the *Human-on- a Chip* is a high-risk project, but also the financial investment or lack of it, could become a threat. Nevertheless the point of data saturation for the longitudinal data collection was reached at the beginning of 2013.

The first interview with the single case, the spin-off CEO, UM was conducted at the end of the multiple cases interviews.. At this point of time, the GO-Bio project and TissUse GmbH was running for approximately 1,5 years. Finally the interviews with the team members were conducted after two years of development, to get an insight view from the team members and connect their statements with the longitudinal data collection evaluation.

4.2.4 The Spin-off Interview Guide

The interview guide for the participants from the spin-off company was adapted with the purpose to gain additional information, backing up the longitudinal, rich data collection (see Appendix D). While the interviews with the multiple cases are providing a general view on the open innovation activities, the single case, spin-off interviews aiming for a more fine grained view in correlation with the activities collected in the longitudinal study. Nevertheless, the open innovation activities: R&D, IP, COL, NET and EL remained in the focus of the interviews. The following amendments were resulting and based on upcoming questions from the longitudinal data collection evaluation.

The interview guide started with two general questions, covering the five most important success factors and the dependency from the German ecosystem. The R&D questions were changed to gain knowledge about the 3 highlights of the R&D process in correlation with the GO Bio project and the spin-off company.

For the IP section of the interview guide, the question was amended from asking for an "IP strategy" to the "role" of IP. The questions covering "licensing" and "threats to FTO" remained the same. The influence of networking was requested in the context of the GO Bio project and the spin-off company. The next question aimed to evaluate the particular "methods" for networking. Instead of asking for the use of "networking platforms". These amendments enable the researcher to get more inside knowledge from the personal perspectives of the group members in regard to the founding process. The need for these additional interview data demonstrates the iterative process of the overall data evaluation and was identified as an additional source for the saturation of the data (Glaser, 2001 cited in Charmaz, 2006). Since for the single case confidentiality of the participants was not required, the transcribed interviews were assigned to the initials of the particular team member.

4.2.5 The Spin-off CEO Panel Participation

The role and influence of the entrepreneur in founding new ventures is uncontroversial (Teece, 2010). In April 2011, during the international conference "Charité Entrepreneurship Summit 2011", the researcher was attending to the panel discussion: " How to Structure the Financing of Your Start-up - Venture Capital and Other Options for Founders" and identified the contribution by the spin-off CEO (UM) as a reasonable source for the single case data collection. The researcher decided to include only the opening statement of UM in his function as an invited serial entrepreneur for this particular panel discussion. The statement of UM was identified as an additional source, especially to evaluate the research objective EL, but with no limitation to further information about UM’s attitude to the founding process of his company. The whole panel discussion was identified to be to complex and out of the scope of this study. Nevertheless, the researcher is aware that the statement made, has to be seen in context with the panel discussion. The advantage of including this statement in the single case data collection was that the researcher did not interact with the panel participants, but could gain valuable insights in her field of study. To create the transcript, the video was watched and UM's introductory statement was verbatim converted into a word document. The transcript was evaluated in conjunction with the interview data. Because this source is different from the conducted interviews, it was considered as a good authority and data triangulation resource.

4.3 Multiple Cases Data Collection

4.3.1 The SME Interviews

The participants were contacted via e-mail, due to a phone call or in person. The researcher was able to involve executive managers of each chosen biotech company. The participants agreed via e-mail or in person to be involved in the study. After setting up appointments, the interviews were conducted, starting in November 2010, with the pilot interview, until October 2011. The conducted interviews lasted between 15 to 45 minutes; the transcripts reached a length of 3 to 4 pages and were stored in word files for further evaluation. In addition, every interviewee was provided with a "Participant Information Sheet" and signed a "Consent Form", to confirm, that the transcript of the interview is correct, reflects the participants opinions and can be included in the study. Only two of the interviews were tape recorded, since the other participants refused to be recorded. During the interviews, the researcher was able to take notes and went back to the participants with a draft transcript for approval. This approach enabled the researcher, to stay in contact with the participants via e-mail and clarify upcoming questions or getting additional information. The participants reviewed the transcripts and confirmed that the answers are reflecting their opinion. This feedback from every single participant was an important step, to ensure reliability and robustness of this part of the data collection.

The following Table 13 is providing the anonymized information about the participants and their organizations. All of them are dedicated biotechnology companies by definition according to the European Commission (2005).

Table 13: The Biotech SME Participants

Biotech SMEs	Position/Function	Product/Technology Specification	Date of Interview
Company 1 - C1	CEO	Vaccine Development Platform	June 2011
Company 2 - C2	CEO	RNAi Technology	June 2011
Company 3 - C3	CEO	Cancer Drugs	June 2011
Company 4 - C4	Vice President Corporate Communications	AB- Platform Technology	September 2011
Company 5 - C5	Vice President Corporate Business Development	DNA Marker Cancer	August 2011
Company 6 - C6/TissUse	CEO UM	MOC Platform Technology	October 2011

Source: Data Collection by the Author

4.3.2 The SME Interview Guide

The working title: "Open Innovation in Biotech-Startups" was heading the interview guide to awake interest in the participation, but without further explanation of the term open innovation. The final interview guide (Appendix E) was tested in a pilot interview, conducted with the CEO of an international biotech consultancy, based in the US. The guide was slightly corrected, since one of the questions was too complex to answer. To balance the content for each open innovation activity, two regarding questions were ask. In addition two general questions were used as an opener and at the end of the interview, a closing question was ask to test, if the interviewee has his or her own interpretation of an open innovation business model. Since the general opening question aims to identify five success factors, the interviews involving to some extent quantitative content, which gives the researcher the opportunity to quantify, upcoming, comparable success factors. In addition a question was ask, if these factors are national dependent. Background of this question was the intention, to identify national and international differences. The open innovation activities were covered by the following nine questions. For R&D the participant was asking to decide which of the approaches: make; buy and/or make & buy, are relevant to their processes. The IP section was covered with three questions to focus on the specific IP strategy, licensing and internal and external threats to the IP and freedom to operate (FTO). At this stage of the study the open innovation activities networking (NET) and collaboration (COL) were investigated not separately. So, one interview questions is covering networking and collaboration, and the following two are aiming to get information about the specific collaboration approach and best networking platforms for the sector. Entrepreneur-and leadership are covered in the next two questions about the influence of entrepreneurs and the definition of leadership. The closing question was important to get inside information of the participants awareness and knowledge about the open innovation phenomenon and the definition of such a business model.

To ensure the confidentiality of all multiple case participants, the transcribed interviews were assigned to the acronyms C0 for the pilot interview, C1-C5 for the interview in correlation with the date, the interview was conducted, transcribed and confirmed via e-mail by every participant.

4.3.3 The SME Observation, Archival Data Analysis

This part of the data evaluation was used to contextualize the interviews and provide a richer framework to understand the adoption and adaption of the open innovation phenomenon. The researchers role as participant and nonparticipant observer is going back approximately 10 - 15 years for the multiple cases, since she held different positions in the life science sector over this period of time. Therefore all participating companies, CEO's and manager were part of her professional network. In one company, the researcher functioned as participant observer for 4 month, by pursuing a company project for her master thesis in 2004.

For the period of four years, beginning with the SME interviews, the researcher was collecting and constantly analyzing archival data, i.e. annual reports, press releases, website content, patents and patent applications, and company profiles.

These data were analyzed to support the findings from the in-depth- interviews and to follow up with recent developments, to provide a broader picture of each company. The applied methodology was content analysis (Mayring, 2000) in a more holistic approach. The results of this analysis are implemented in the specific story lines, research reports of each participating company. For confidentiality reasons, it is necessary to stick to a broad summary. Hence, the researcher created a dense, rich data collection to gain as much information as needed to evaluate and understand the adoption of the open innovation phenomenon.

In her function as a moderate participant observer, the researcher balanced her position by being an insider of the industrial sector for nearly 3 decades, but on the other side, taken the role of an outsider, studying the innovation processes of organizations, included in the case studies.

4.4 Introduction to Data Analysis

Consistent with the requirements of grounded theory (Charmaz, 2006; Glaser and Strauss, 1967), the researcher started analysing the data as they were collected and went back and forth by applying an iterative evaluation process. This enabled the researcher to identify emerging theoretical arguments, which were used to categorize the raw data into concepts about the adaption and adoption of the open innovation phenomenon. Figure 16 illustrates this iterative process.

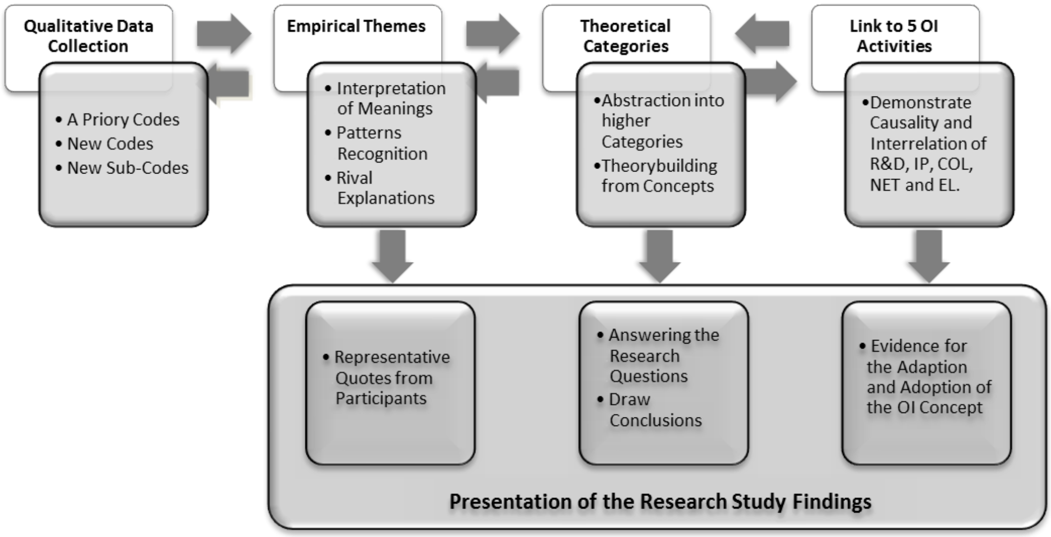

Figure 16: Data Analysis Process Created by the Author

The data analysis process started in line with the onset of the data collection for both, the single and the multiple cases. The data analysis can be distinguished in two main activities, first: the evaluation of the longitudinal data collection of the single case, and second: the analysis of the interviews, panel participation and observation data of both case study types. The following paragraphs focusing on this analysis, which was accompanied by intensive, ongoing literature review.

4.5 Data Analysis - Single Case

4.5.1 Longitudinal Data Analysis and Scoring System

Based on the rich, in-depth data collection and the main resource for the evaluation, the open innovation activities: R&D; IP; NET; COL; EL served as the preliminary frame for the step by step evaluation. The first rough evaluation was started right after receiving the first package of data and during collecting additional material for the in-depth longitudinal case study of the newly founded spin-off company. The comprehensive data collection reached a number of 210 events. The term *events* represents in this context all collected data from the spin-off organization, see Figure 16: Case Study Design.

Based on the comprehensive literature review and the development of the theoretical framework, the VCOI, for this research study, all of these events were rated due to the specific scoring system. This system was created, to evaluate every single event in context with every open innovation activity (R&D, IP, NET, COL, EL). This holistic approach enabled the researcher to analyse all data in-depth in context with the open innovation phenomenon.

Table 14: Scores for the Longitidinal Data Collection

Scoring System	Description
5 - Major Key Activity	clear desicion & distinction between 5 keys
4 - Very Important	second next important key activity, causal to Major Key
3 - Important	plays an influential role in this context
2 - Relevant	plays a minor role
1 - Not Relevant	not applicable here

- *Major Key Activity – 5*

For every single event a decision is made, which of the 5 key open innovation activities (R&D, IP, NET, COL, EL) is applicable here. Five is the highest score and can only be applied once. This gives the event a clear, unambiguous assignment to one open innovation activity.

- *Important – 4*

This is the second next important activity, typical for the event/document. This activity is strongly related to the “major key activity”, by a causal or interrelated relationship.

- *Influential – 3*

This scoring is applied, when there is an influential role, but without a direct causal or interrelated relationship to the "major key activity".

- *Relevant - 2*

When the key open innovation activity plays a minor, indirect role, rating 2 is applied. There is no direct causal or interrelated relationship with the other activities.

- *Not Relevant – 1*

This rating is applied, when the activity is not present here. Due to the decision to apply one and not zero, even if the activity is missing, it is still visible in the diagrams.

This scoring system was developed by the researcher, to analyse and visualize the data for the findings. In the following table, a real example from the data evaluation is used to demonstrate the rationale behind the scoring system.

Table 15: Example Event and applied scoring system

Example Event No. 9	**5 OI Activities**	**Scoring Total 15**	**Rationale**
Patent Application PCT/WO2009118283 "Methods for producing Hair Microfollicles and de novo Papillae..."	IP	5	patent filing is proactive IP management - Major Activity
	R&D	4	IP is based on own R&D activities (Make) - Causal Relationship and interrelated activity
	EL	3	IP was considered for licensing to the spin-off - Influential
	COL	2	patent attorney and TTO as collaboration partner involved - Relevant
	NET	1	no networking partner was involved

Source: Created by the Author

4.5.2 Longitudinal Data Analysis Process

This first step of evaluation has led to the quantitative evaluation of the 210 events collected from the spin-off organization and gained by secondary data collected from additional sources (i.e. company website, internet search, print media etc.). The overall timeframe is 2008 – 2015, a period of nearly seven years. The most dense data collection is covering the time between 2010 – 2012, where the company was founded and produced their first ready to market product. The researchers' role of a direct and participant observer covered the same period of time. This comprehensive data collection, documenting 7 years, from the idea to the first product, fulfils the requirements of an in-depth, longitudinal case study (Eisenhardt, 1989). It represents a very unique source of data, since academic researcher usually do not have access to such type of confidential data, especially, when a new venture is founded.

This study therefore adds value to the body of literature about the adaption and adoption of open innovation in startups and spin-offs , not from a retrospective perspective, but from a real time observational and partly participants perspective. To avoid bias and avoid the potential threat of influencing the data, the researcher stepped back from her participant observer role, after finishing the interviews with the team members in mid-2012.

The next step in the evaluation of the longitudinal data collection was linking the information and data gained from the team member interviews with the events and activities.

The single case interview guide was amended for the purpose to evaluate the longitudinal data collection.

Furthermore, to visualize the clustering, the different five key open innovation activities are coded by colors. Since the data collection embraces 210 single events, this form of visualization was created by the researcher to be able to identify patterns and be able to extract the importance and meaning of the data. This approach is following in addition the constant comparison approach, which is mandatory for theory building (Glaser and Strauss, 2008). The score of 5 was chosen to give each of the 5 open innovation activities only one score and make a clear decision about the allocation to one of the open innovation activity. By scoring “5 - Major Key Activity “, a decision is made to which cluster activity of the 5 open innovation activities the event belongs. The following section is describing the evaluation process for the longitudinal data collection step by step.

First Step - Initial Evaluation

Based on the results of the first step evaluation, it is expected, that every single activity can be assigned to one of the open innovation activities. In addition there is a connection between them by using the others scores. The interdependence of the five key open innovation activities should become feasible in the first evaluation step. Some of the activities might be important in only three or two; some might have no connection, but are of great importance in only one of the activities.

The clustering is enabling the researcher to quantify the five open innovation activities against each other, and identify patterns out of the evaluation. Events, which are reaching a high score by summarizing, can be given more attention in the further evaluation.

Second Step – Deeper Evaluation

The activities with the highest score are in sum meant to be of great importance and demonstrate the causality and interdependence of the open innovation activities to a high degree. These activities are the so called “Highlights” of the single case events.

To approach the data from an internal perspective, the structured interviews within the single case are used, to identifying additional important activities out of the rich data collection. At this stage, internal and external reliability and validity are given, since the researcher got feedback from the case study members, who highlighted some of the activities as "important achievements". Nevertheless, the first stage of scoring was important and the feedback from the team members supported the data evaluation process.

The deeper evaluation of these activities is following Lichtenthalers (2011) approach, by evaluation the different stages of knowledge management from the organizational, the project and the individual level. In addition, the underlying definitions and measurable effects of each of the five open innovation activities, based on De Jong, et al. (2008) are included in the evaluation.

Third Step – Visualisation of the Evaluation

To present the five open innovation activities, their interdependence and causal relation to each other, the researcher created a specific visualisation of the results. This was realised by *easy to understand* and easy to communicate pictures and diagrams. In addition to the description concerning the outcome of this research study, the visualisation is supporting the goal, to draw conclusion for researchers, practitioners and policy maker.

In the next section the data analysis covering the evaluation of the semi-structured interviews, the panel participation and observation data are described in detail.

4.6 Data Analysis - Single and Multiple Cases

4.6.1 Interview Data Base and Coding Process

In preparation to code the interview data, question by question, a data base in excel format was created right after confirmation of the transcripts. The interview data base summarizes all interviews in tables, to do the open coding based on the a priory coding categories, the key open innovation activities: R&D, IP, NET, COL and EL (De Jong et al., 2008, 2010). These first categories are evolving from the definition of the open innovation activities in regard to the open innovation concept. To not restrict the outcome from the interview analysis, open, free coding was adopted. This opens the opportunity to identify new upcoming patterns due to identified sub-codes, new categories and themes, which are coming directly from the data, instead of being restricted by a theoretical framework. Thus, theory building from the cases is grounded in the data (Eisenhardt, 1989; Corbin and Strauss, 2008).

The overall evaluation of the interview data collection allowed the researcher to identify similar and comparable patterns, as well as contrary or opposite opinions and statements. The qualitative case study research approach was chosen to characterize the research findings in a descriptive manner. Some of the answers of the interviewees were identified as strong, representative statements and will be appear as citations in the research findings in Chapter 5.

- *Coding with CAQDAS - MAXQDA 11*

There are advantages and disadvantages regarding the use of Computer - Assisted Qualitative Data Analysis Software (CAQDAS). Even so, the additional features, i.e. memos, reports, visual tools, statistics, word clouds etc. were considered as added value to the data evaluation process (Rodik and Primorac, 2015). All interview- and the panel discussion transcripts were implemented in the MAXQDA 11 software system. The repeated coding process enabled the researcher to compare new categories and evolving themes with the initial first data evaluation, including the results from one external evaluator. Nevertheless, the combination of the excel data base and the use of a CAQDAS added value to the data analysis process (Rodik and Primorac, 2015). There was a balance between the advantages and disadvantages of both approaches. Another criteria was to ensure that all analysis are undertaken in a consistent and well-defined way, this implies a certain degree of standardization in the evaluation process of the qualitative analysis (Gibbs et al., 2002). The early creation of the excel data base prepared the researcher for the effective use of the CAQDAS. All technical questions could be answered by watching the comprehensive online tutorials from MAXQDA.

- *The Coding Process*

According to Glaser (2004; paragraph 47), the conceptualization of data through coding is the foundation of the grounded theory development. He defines codes as the following:

> "A code gives the researcher a condensed, abstract view with scope of the data that includes otherwise seemingly disparate phenomena. Substantive codes conceptualize the empirical substance of the area of research. Theoretical codes conceptualize how substantive codes may relate to each other as hypotheses to be integrated into theory. Theoretical codes give integrative scope, broad pictures and a new perspective. They help the analyst maintain the conceptual level in writing about concepts and their interrelations." (The aim of this research

study is to gain new perspectives of the open innovation phenomenon, by identifying the underlying concepts and interrelations of the five key open innovation activities (R&D, IP, NET, COL, EL). Therefore, again, the grounded theory method was chosen for the data analysis methodology. The researcher adopted the following approach, recommended by Charmaz (2006, p. 49):

"A code for coding:

- Remain open
- Stay close to the data
- Keep your codes simple and precise
- Construct short codes
- Preserve actions
- Compare data with data
- Move quickly through the data."

In the following paragraphs, the different types and stages of the overall coding process are described in detail. However, this process was not linear, but was characterized by constant comparison of the data by going back and forth, until the new concepts and their interrelations have reached a status of saturation. Saturation in this context implies that the newly generated grounded theory has reached a theoretical completeness due to a high conceptual density (Glaser, 2001 cited in Charmaz, 2006).

- *Structuring Data & Initial Coding*

The initial a priori codes are based on the open innovation activities, which have inspired the different questions, ask in the interview guides. The general and closing questions are leading to additional a priori codes, to broaden the information gained from the participants. These first codes are forming categories for answering the research questions. Dependent from the type of transcript, the pilot-, multiple cases and single case interviews, and panel discussion, all information from purposeful selected informants were organized in excel spreadsheets, first analyzed and later transferred to the CAQDAS (MAXQDA) for further evaluation and the iterative process of data analysis (Pratt, 2009).

- *Open Coding*

This analytic process was the starting point for the interview data analysis. All transcripts were collected and saved in two comprehensive excel spreadsheets, one for the multiple cases, one for the single case. Purpose was, to distinguish the databases by case study type. All answers from the transcripts were summarized in one large table, as the basic data spreadsheet. In the next step, the answers were ordered question by question. The content of the questions was delivering the a priory codes, i.e. R&D, IP, NET, etc. This enabled the researcher to start the coding process focusing on each open innovation activity. Due to the open coding process the researcher intended to answer the questions (Lawrence and Tar, 2013, p.32): "What is actually happening in the data?" The close examination of the data is leading to an extract of behaviors, events, objects, actions and interactions, meanings, strategies and consequences the participants experience (Taylor and Gibbs, 2010). These extracts were underlined in the text and collected for each participant and each question. In the next step, these new codes were compared for identifying similarities and differences in the frame of each open innovation activity and participant by participant.

During this stage of the data evaluation, the researcher decided to involve an external source to support the evaluation process. The main reason was to avoid bias and get feedback during the analyzing process. To secure confidentiality, a non-disclosure agreement was signed and the scope of the support was clearly defined. The external source owns an MBA and has a strong consulting background, but not in the life science sector. The researchers aim was to avoid potential bias and to add another type of triangulation to the data evaluation process. The external source evaluated the multiple and single case interviews, by coding the answers of all informants in the excel data base. The researcher compared her own coding with the outside coding. This was an important step, to add external validity to the data analyzing process. The comparison of the researchers own results with the external sources view led to a critical review, where opinions differ and a back up, where opinions matched. In this context the early data analysis triangulation was intended to lead to a more complete picture of the investigated open innovation phenomena (Kelle, 2001).

The coding from the external source was integrated in the data analysis of all interviews, before the researcher did the final coding procedure. Nevertheless, it was an important step during the data evaluation and the comparison of the researchers owns coding with the external coding has strengthened the validity. The additional codes from the external source were added into the MAXQDA data software and marked with her initials, to be able to identify the source. In the final data evaluation these additional codes were implemented in the analysis or discriminated where the researcher decided that there is no logical fit.

- *Axial Coding*

All transcripts were uploaded in the MAXQDA data base for further evaluation. The first set of codes is based on the open innovation activities and the content from the general and closing questions. The transcript from the panel discussion was included, to broaden the perspective on one of the five open innovation activities, Entrepreneur and Leader ship (EL). These data are adding value to the data collection; especially from the entrepreneurs (UM) own perspective on entrepreneurship. His personal view and opinion could be compared and reflected by the spin-off team member's information about this key activity.

- *Memos*

Memos were used to notice the rationale behind the coding process, explanations were used later to review and analyze, "what is going on". Not only written memos from observations, i.e. minutes of meetings, were used. The researcher often used diagrams and self created flow charts for analyzing the rich data collection. At every level of the iterative data analysis process, memos in form of short summaries were written to serve the identification of empirical themes, develop the abstracted theme and the related theoretical categories, and finally develop a theoretical model.

- *Final Data Analysis*

For the final data analysis process the coded segments of all transcripts were implemented in a table, to illustrate the identified empirical themes, the evolving theoretical categories and, the relationship and connection between the five open innovation activities: R&D, IP, COL, NET and EL.

The iterative data analysis process was an important step towards the final data evaluation process. By involving the MAXQDA data base and the researchers own comprehensive data collection spreadsheets, the status of data saturation was reached, one important prerequisite for the validity of the research study.

According to Corbin and Strauss (2008, p.103) "Concepts must be linked and filled to construct theory from data". and concepts that reach the status of a category, are abstractions. The essential element of theory is here, that categories are interrelated into a larger theoretical theme (Corbin and Strauss, 2008).

4.6.2 The Grounded Theory Data Evaluation Process

After creating the empirical themes, grounded in the coded data, the researcher was able to reduce the listed themes into a set of higher interrelated concepts, the theoretical categories. Since grounded theory stands for a conceptual theory generating methodology, the different stages of analyses were adapted to the whole research study data evaluation process (Glaser, 2004). The conceptualization of the data was achieved by an interplay of deductive and inductive analysis (Strauss and Corbin, 1998).

Aim of the final data evaluation was to provide a conceptual theory abstract of time, place and people (Glaser, 2004). In the context of this research study, the following table is demonstrating the link between the conceptual theory abstracts and the different types of case studies.

Table 16: Conceptual Theory Abstract - Case Study Design

	Conceptual Theory Abstract		
Case Study Design	**Time**	**Place**	**People**
Single Case - Spin-off	From Idea to Product 2008 - 2015	Berlin, Germany	CEO, Co-Founder, IP Manager, Sales & Marketing Manager , Consultant
Multiple Case - SMEs	approx. 5-10 years observation, retrospective 5 years	Germany, Netherlands	CEOs, DB Manager, VP Corp. Comm. VP Corp. Dev.

Source: Created by the Author, based on Glaser (2004)

4.6.2.1 Empirical Themes

The identification of empirical themes was pursued to order the raw data into higher first order categories, which are basic to interpret their meanings, search for patterns and identify potential rival explanations. The language used was as close to the data as possible (Strauss and Corbin, 1998). For every of the 5 open innovation key activities (R&D, IP, COL, NET, EL) and for both, the single and the multiple cases, first-order codes, which describing the dominant empirical themes, were developed. After comparing them within and across the interview transcripts, a stable set of themes emerged. This process was characterized by back and forth iteration until a strong set of themes emerged. The researcher returned repeatedly to the literature to strengthen her knowledge about the theoretical meaning and context of the empirical themes (Suddaby, 2006). For this process the MAXQDA data base and self created tables were used. A representative example, covering the coding of the data with MAXQDA is provided in Appendix G.

During this process, in addition exemplary or rivalry quotes were identified for the later presentation in the explanatory, narrative story line in Chapter 5.

4.6.2.2 The Theme and Theoretical Categories

The central theme is funtioning like a roof for the theoretical categories. It has a strong relationship with every single category and fulfils the following requirements (Corbin and Strauss, 2008, p.104):

- Abstract and all others can be related to it,
- Must appear frequently in the data,
- Logical and consistent no forcing,

- Sufficiently abstract, used to do research in other areas,
- Grow in-depth and explanatory power,
- Related to other categories trough statements of relationship.

In the following paragraph, the evolving data structure, based on the comprehensive research study analysis and data evaluations are described in detail by focusing on each type of case studies separately. This enables the researcher to provide a fine-grained perspective on the spin-off, the single case and a broader, sector related perspective on the biotech SMEs, the multiple cases

4.7 Data Structure - Single Case and Multiple Cases

For each of the case studies, the following paragraphs and figures are illustrating the outcome of the iterative data analysis in the respective data structure.

4.7.1 Single Case Data Structure

The iterative process of data analysis, covering the data collection from the spin-off organization TissUse GmbH led to a holistic picture about the innovation processes before, during and after the foundation of the newly founded venture. Evolving from the first order codes, six theoretical categories emerged, to understand the observed open innovation phenomenon. These abstracted higher categories could be aggregated to the central theme of ***People.*** In context with the purpose to answer RQ2, if and how radical innovation like the Human-on- a-Chip technology development is possible, the theme was further defined as: ***The right People for radical Innovation.*** In Figure 17 the data structure is illustrated by representative first order codes, the evolving theoretical categories *Entrepreneur, Idea, Technology, Knowledge, Partner and Finance.*

The aggregated theme *The right People for radical innovation* resonates well with the human side of open innovation (Bogers et al., 2018b). Taken the recent open innovation literature into account, research on the individual level is still an underrepresented area in context with the organizational behavior and cognition and the demand for multi-level analysis (Bogers et al., 2017; Jaafar and Rezaeian, 2019).

The emerging theoretical categories are the result of the methodological procedure of coding and constant comparison across the data. One important step during this process was the identification of passages with co-occurrence of codes, which leads to strong theoretical patterns, which are grounded in the data. One example to mention is the theoretical category *Entrepreneur*. This category emerged from the in-depth data analysis in a strong, repetitive pattern. This pattern evolved from the data analysis, even if the investigated open innovation activity, for instance Networking (NET) is not per se directly related to the entrepreneur or to entrepreneurship.

Representative quotes and the dynamic relationship between codes, theoretical categories and themes (Gioia et al., 2013) are presented in detail in Chapter 5. Furthermore, the abstracted categories are linked with the five key open innovation activities R&D, IP, COL, NET and EL with the purpose to answer all research questions.

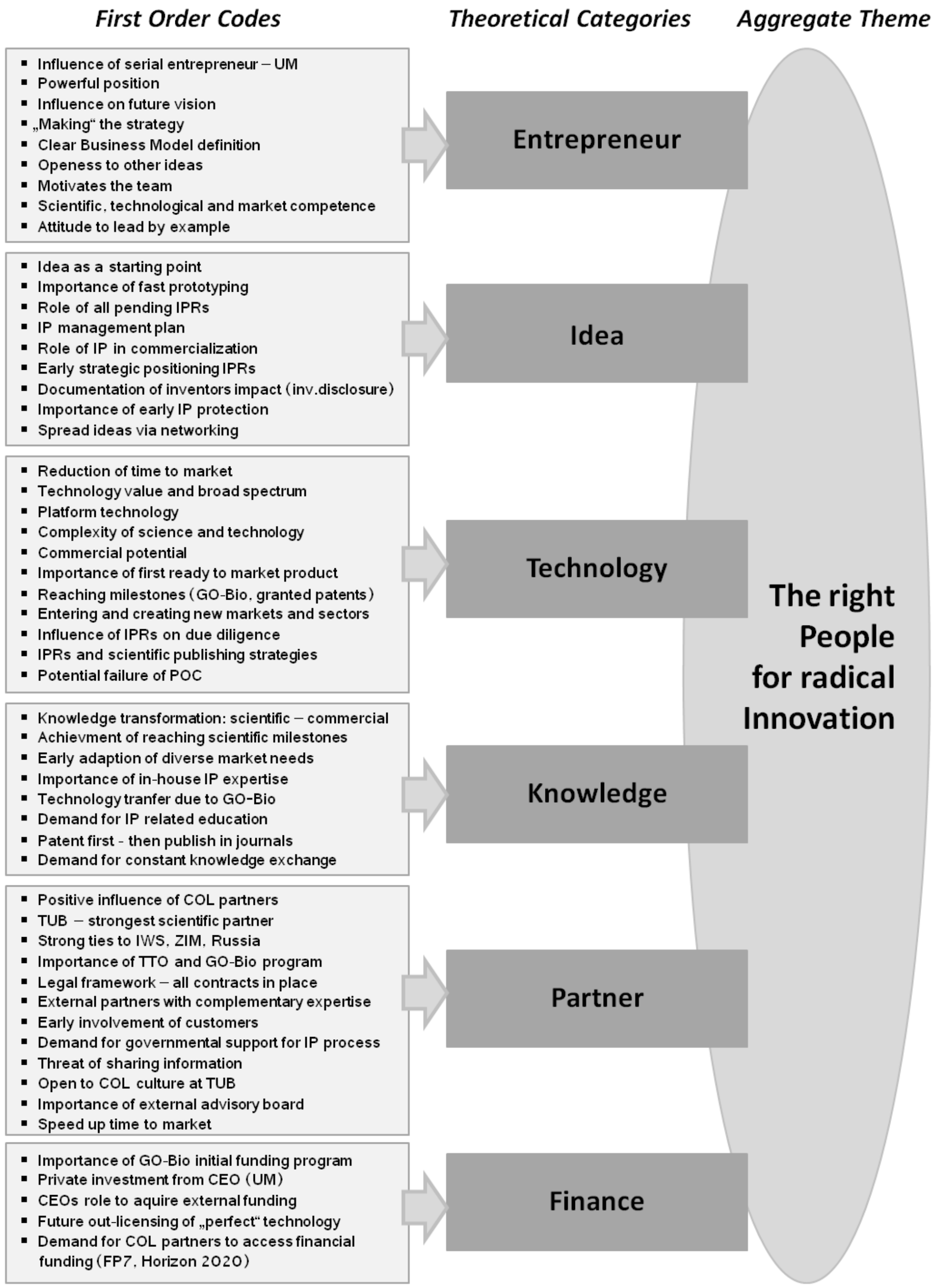

Figure 17: Single Case Data Structure

4.7.2 Multiple Cases Data Structure

By applying the grounded theory methodology, the multiple cases data analysis led to a set of abstracted categories, evolving from the first order codes. The constant comparative method allowed the researcher to develop an understanding about the innovation practices of these five SMEs (Glaser and Strauss, 1967). The coding procedures, synthesizing and organizing of the data, and going back to the literature, convinced the researcher in the final identification of the theme ***Partner***. To support the empirical evidence, this theme can be specified more precisely in ***Innovation Partnerships***. The theoretical categories for the multiple cases are: *Technology, People, Value, Finance, Knowledge and Idea* (see Figure 18). These new categories emerged from the data analysis of all five cases to provide the structure for the findings. These findings are presented in the next chapter, with emphasis on supporting quotes from the participants and further evaluations by linking the new categories to the five open innovation activities. This provides a profound understanding of the innovation strategies of the SMEs and supports the arguments if and how these organizations adopt and adapt the open innovation concept in practice (RQ1).

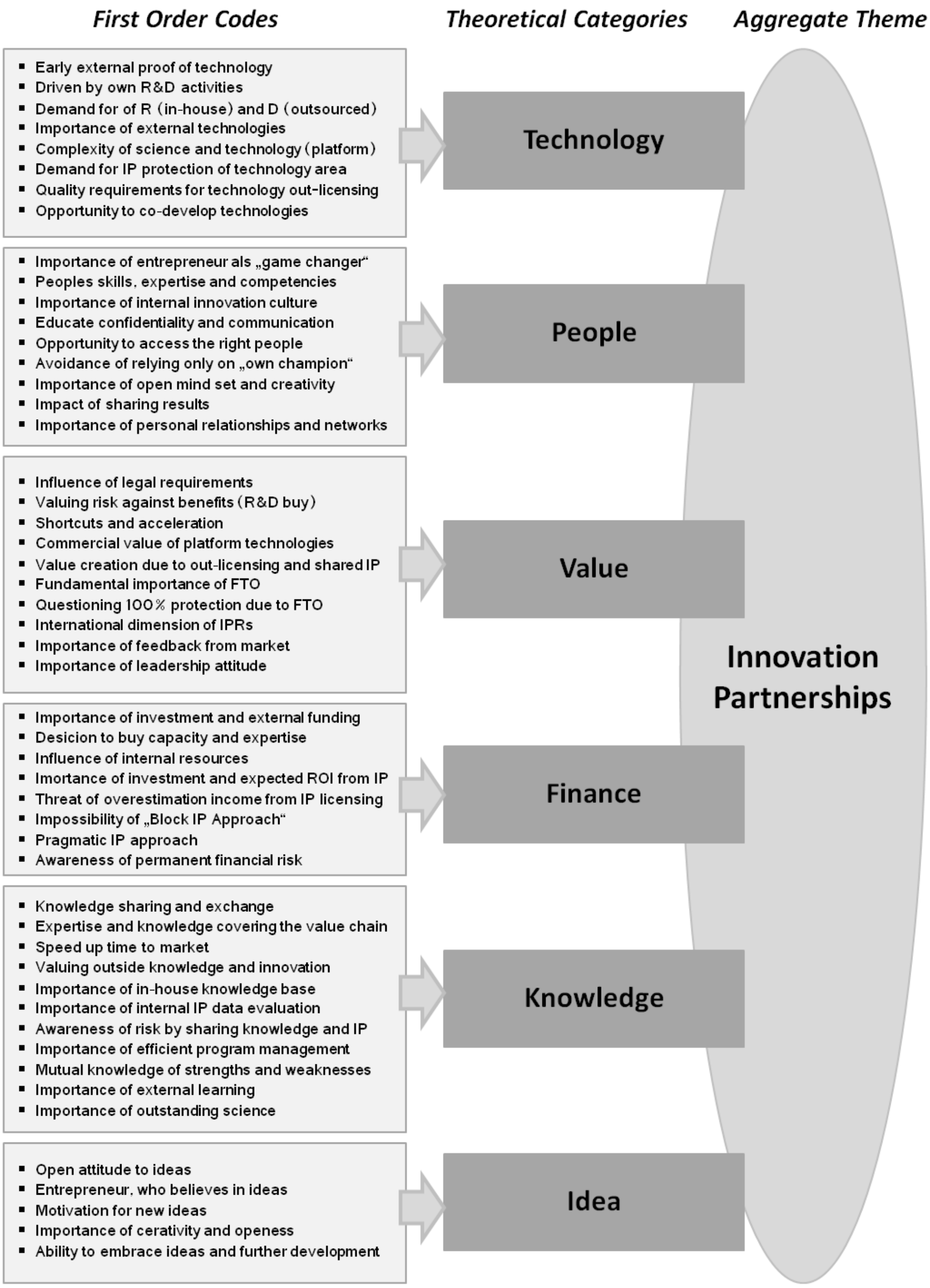

Figure 18: Multiple Cases Data Structure

5 Research Findings & Discussions

"Imagination is more important than knowledge" Albert Einstein

5.1 Introduction

5.1.1 The Research Questions

This chapter aims to answer the three research questions, which guided this comprehensive study. The research questions serving as guidelines for presenting the results. The findings, results and discussions for the single case and the multiple cases are described in storylines, in correlation to the specific research question. The three research questions are the following:

RQ 1: Is the Open Innovation concept adopted by biotech companies?

RQ 2: Can open innovation enable the development of radical biotech innovations in a German ecosystem?

RQ 3: How does the evolving business model look like?

Furthermore, for each case study type, a new business model theory is developed to illustrate the final outcome of the research study. The following paragraph serves as an introduction to the process of theory building and theoretical prescience.

5.1.2 Introduction to Theory Building and Theoretical Prescience

There is a clear demand for new management theories (Suddaby et al., 2011). Byron and Thatcher (2016) ask the questions: *What is theory and where does it come from?* They are suggesting that theory can be build from observing and aiming to solve real-world puzzles. In this thesis the real-world puzzle is the adaption and adoption of the open innovation phenomenon in biotech organizations. The researchers own imagination and engaging in thought experiments, with the goal to create new theory is an important source (Byron and Thatcher, 2016). Nevertheless, these authors concluding, that theory development is not an easy task, as one of their interviewed experts stated:

> "Theory writing is one of the most difficult skills because the rules aren't clear. It is like cooking. You have to try different things, screw up, be creative, and burn a few things before you get it right." (Byron and Thatcher, 2016; p.6)

When a new theory is created from research, the goal of generating new knowledge for the body of existing literature and adding valuable new knowledge to the practitioners perspectives is reached. A simple, general definition of theory is a statement of concepts and their interrelationship that demonstrates, how and why a phenomenon is present or not (Corley and Gioia, 2011). This definition is best applicable to this research study. New management theories, elaborating about a new phenomenon, providing also new knowledge to policy makers and governmental organizations. Besides the fact that we are living in a connected world, were boundaries between academia, industry and society are becoming permeable and diffused, we are facing gaps of knowledge to connect these "different worlds" to each other. To provide theoretical and practical contribution to all of these different stakeholders, researchers should provide theoretical prescience. Prescience can be defined in terms of foreknowledge, foresight, or forecasting of events (Corley and Gioia, 2011). Rather than trying to predict the future, prescience is a matter of anticipating and influencing the definitions of organizational problem domains, like successfully creating value through innovation. Understanding recent phenomena's and creating prescience theory from it, helps to create the future in Abraham Lincolns sense:

> "The best way to predict the future is to create it."
> (cited in Corley and Gioia, 2011, p.23)

Theory building is the final stage and goal of this research study. Driven by the case study methodology, the study design of the single and multiple cases, two different types of business model theories are created. For every case type, a substantive theory is developed. Substantive theory is characterized by being grounded in the study of one area of investigation and one specific population (Griffith, 2012). The area of investigation for the single case is the formation of a biotech spin-off company; the population is the founder and his team. For the multiple cases, the area of investigation are the five mature biotech companies, the population covers the participating CEO's, and managers. Both new theories, one for a spin-off, developing radical innovation, and one for SMEs, creating value through innovation, will contribute to the general theory of value creation through innovation in the biotech sector. Based on the new theory, recommendations for academia, practitioners and policy makers can be made (see Chapter 6). Further conclusions can be drawn to other high-tech sectors. Even if the products, services and technologies are different, technology-based organizations have in common, that it is impossible to go the way to success in the market alone. Since this study is based on a reflective, theory-guided, mixed methodology approach, generalization of the results is envisioned (Mayring, 2007). Furthermore, at different stages of the whole study, triangulation of data sampling, data analysis and evaluation was practiced in order to draw broader conclusions, not only for the biotech sector (Denzin, 1970 cited in Mayring, 2007). Therefore, generalization in a broader context is possible. This does not imply that the new theory will act as a “one fits all” theory, but general conclusions can be drawn for practical, theoretical and societal questions in context with innovation management.

5.1.3 Storylines - based on the Themes and the Theoretical Categories

The aim of this step in the evaluation of the data is to develop a final theory, grounded in the data. The *Theme* was chosen and all *Theoretical Categories* are delineated. Creating the storyline by describing the categories and linking them to each other will lead to a theoretical whole. Only an overall unifying explanatory scheme can raise the findings to the level of theory (Corbin and Strauss, 2008). For the final research evaluation of the single and the multiple cases, two different themes, but similar theoretical categories are identified. Each of them will be described in separate storylines and integrative diagrams, differentiated by the types of case study; the single and the multiple cases.

At this final step, with the goal of developing a grounded theory in context with this research study, the theme and the theoretical categories are related to each other by statements of relationship (Corley and Gioia, 2011). Since for every key open innovation activity these concepts are analyzed, evaluated and illustrated by representative quotes, at the same time the link between R&D, IP, NET, COL and EL can be demonstrated. For illustration purposes whenever a relationship is present, the respective key open innovation activity is in bold letters. In addition, the success factors and participants own open innovation business model definitions are helpful resources to finally answering the three research questions.

5.1.4 The external and internal Perspectives on the Case Studies

The extensive data evaluation, applying the grounded theory methodology, enabled the researcher to draw conclusions based on the evolving new theoretical categories and themes. The comprehensive data collections for both case study types are valuable, partly rare sources for this qualitative research study. Nevertheless, there are some collected data, especially from the semi-structured interviews, which will be presented as the internal perspective, grounded in the direct statements from the participants. This part, the internal view was identified as a meaningful source for understanding the adoption and adaption of the open innovation concept in the biotech sector. The internal perspectives are covering the specific success factors, the influence of geographic areas and the participants own definition of an open innovation business model.

In the following paragraphs, the storylines are provided in order to create a grounded theory. Even if the five key open innovation activities are the theoretical framework for this study, at the stage of evaluation, the new themes and the theoretical categories providing the new structure for the evolving new theories. The fact, that for the different levels of analysis, the individual, the project/product and the organizational level at least one or more theoretical categories are grounded in the data, enables the researcher, to develop a robust theory about the adoption and adaption of the open innovation phenomenon in the biotech sector. A more fine grained substantive theory will be provided for each of the case studies, based on the differences between them (Griffith, 2012). For the spin-off and the biotech SMEs, the researcher linked each aspect of the findings with an in-depth discussion.

5.1.5 Multilevel Analysis for answering the Research Questions

To address the demand for multiple analysis of open innovation (Bogers et al., 2017), the RQs are answered at three dimensions. First, on the organizational level (TissUse and 5 biotech SMEs); second, on the project level (MOC technology platform); and third, on the individual level (Entrepreneur and Team; Executive Managers). This three-dimensional perspective fulfils on one side the requirement of triangulation for a profound research study, and on the other side, the multifaceted open innovation phenomenon is investigated in a holistic manner. The following Figure 19 illustrates the impact of every units of analysis on answering the different three RQs.

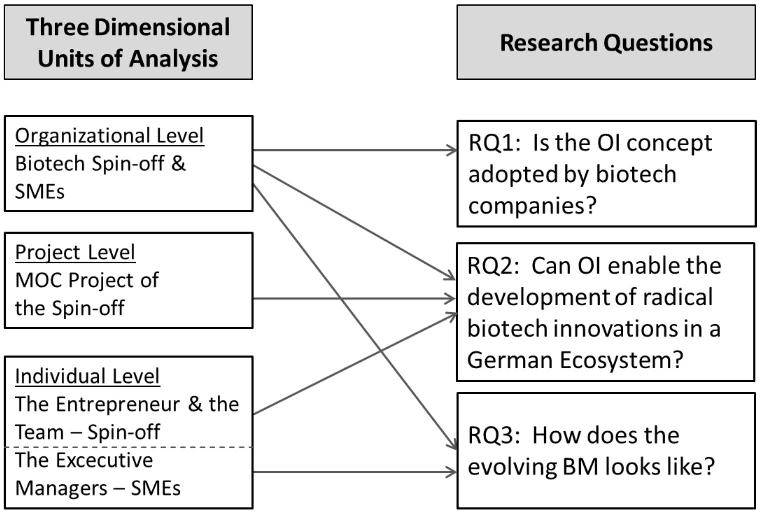

Figure 19: Impact of Three Dimensional Units of Analysis on Research Questions

Even if the cases are summarized under the respective level of analysis, both case study types are evaluated separately, and the complementary insights are connected later in the conclusions (Chapter 6).

5.2 Radical Innovation Made in Germany: The Biotech Spin-off

5.2.1 The Biotech Spin-off - TissUse GmbH - External Perspective

The single case, the spin-off organization TissUse GmbH is at the core of this dissertation. This longitudinal case study is a unique research study because of the in-depth data collection and direct access to the CEO and his team from the very early to the later stage of the foundation. The rich data collection enables the researcher to draw a fine grained picture of the different stages of a spin-off organization, evaluated over time. This German Biotech organization was chosen to answer the research question (RQ2), what makes radical biotech innovation possible and (RQ3), how the evolving business model of this early stage company will look like. In the following paragraphs, the role of the entrepreneur and the findings from the single case, the spin-off TissUse aiming to answer both research questions.

The single case study is a unique source of comprehensive data, which is from the researchers perspective rare, since even in the ongoing literature review, no comparable, in-depth longitudinal case study in the field of biotech spin-off or start-up companies could be identified. The overall coverage of data about the single case study is nine years. It starts with 2008, by mentioning the idea of the Human-on-a-Chip [2] in his book (Marx, 2008), until 2018, having already three products, the 2-Organ-Chip (TissUse 2-OC), 4-Organ-Chip (TissUse 4-OC) and the 10-Organ-Chip on the market. This longitudinal, unique case study adds value to the academic and professional understanding of innovation management in practice. The dense longitudinal data collection with 210 events is covering the timeframe of five years, from 2008 to 2013. Since the spin-off was founded on February, 3rd in 2010, the dense data collection is covering also the pre-foundation phase, which is rare to find data. After the first data evaluation of the different events, based on the framework of the open innovation activities, in mid-2012 the researcher decided to go back to the spin-off core team and conducted interviews, to strengthen the data collection. To finalize the data collection, the researcher observed the spin-off organizations further development due to desk research and observation until 2018.

The following section is summarizing the research results, covering the findings from the interview data, the CEOs participation in a panel discussion and the longitudinal data collection evaluations. The spin-off interviews, panel discussion and longitudinal data collection are providing in-depth inside information about the innovation strategy of the newly founded venture, developing a radical innovation, in a German ecosystem. These findings are embedded in the developed theory and model for the single case, based on the identified theme of **People**.

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[2] The terms *organ-on-a-chip* and/or *Human-on-a-Chip* are describing the spin-offs technology platform, where the *organ-on-a-chip* is regarded to the GO-Bio program title and *the Human-on-a-Chip* is the final goal. Both terms are synonymous for the radical innovation.

5.2.2 The right People for Radical Innovation

The theme *People* evolved from the in-depth data evaluation of the single case. With emphasis on the interviews and the panel discussion statement of the CEO, working with the right people, with the goal to develop radical innovation, becomes the most important requirement for a successful innovation strategy. In context with this part of the study, people is the simplified term for human capital, here embedded in the project, organizational and, individual context. The project is the governmental funded GO-Bio "Organ-on-a-Chip" project, the organization is the spin-off company, TissUse GmbH, and the individuals are the team members and the CEO, the serial entrepreneur, Uwe Marx (UM). Especially in context with a newly founded venture, where the team at the beginning is small, it is not surprising, that "it is all about" the people. Interestingly, at a later stage of development, when companies have grown up to, i.e. SMEs, the observed theme in biotech organizations becomes *Partnership* (see 5.3). In context with the single case, the focus is on peoples knowledge, expertise and experiences and the application of these skills in context with organizational founding and growth. The circle of people is the TissUse team and the CEO, with their different functions, and closely collaboration partners, i.e. the involved consultant (SD, US Consultancy) and Roland Lauster (RL, Prof. at Medbt TUB). The CEO's individual open minded attitude, combined with longstanding experiences and expertise in the field of tissue engineering, but also in founding new companies, are building the foundation for the entrepreneurial spirit of UM (see CV, U. Marx, Appendix F).

The theme *People* can be linked to the literature about human capital. In context with this study, the role of human capital must be narrowed down and connected to the newly founded spin-off organization. According to Grandori (2016) human capital has its traditional components, such as energy, health and personal skills, but the knowledge-based components, such as ideas, projects and know-how are necessary prerequisites to foster innovation. Human capital is no longer a simple source for labor, it generates value due to the afore mentioned additional human assets. Furthermore, in context with the spin-off biotech organization, a multilevel model of human capital becomes an important resource, based on the individuals cognitive and non-cognitive abilities. Research on the complexity of the influence of human capital in the context of organizational competitive advantage is ongoing and in the focus of research programs, i.e. Strategic Organizational Behavior (STROBE) by Ployhart (2015). Based on the outcome of the single case data evaluation, the involved people (here and further on a synonym for human capital), need further in-depth studies in the domain of non-cognitive abilities, like their personalities, interests and values (Polyhart and Moliterno, 2011). To some extent, the general cognitive abilities, knowledge, skills and experiences are visible due to the information gained from the in-depth, longitudinal data collection, but further focused research is recommended (Polyhart and Moliterno, 2011). To understand the influence of the individuals, involved in developing a radical biotech innovation in the German ecosystem, this study adds value to the body of literature by describing the *Entrepreneur's* role more in detail (see 5.2.5.1). By gaining more insights about the role, attitude and behaviors of individuals involved in open innovation, this dissertation aims to fill these gaps in the innovation literature (Bogers et al., 2017; 2018).

The different causalities and inter-relationships between the theme and the theoretical categories are described and evaluated in the following sections. The findings are based on the extensive data evaluation process, adapting the grounded theory methodology (Glaser and Strauss, 1967; Corbin and Strauss, 2008). Each section is headed by the theoretical category, more details are provided in the subsections.

5.2.3 People - The Entrepreneur, Idea, Technology, Knowledge, Partner, Finance and Value

To develop a theory for the radical innovation strategy, the theme *People* must be linked to the theoretical categories, which evolved from the data evaluation of the single case. Not surprisingly, the same theoretical categories, like for the multiple cases are identified, but with different weighting. Nevertheless, the theoretical category *Entrepreneur***,** plays an important role here. This is not surprising in context with this study, but, from the interview data, conducted with the spin-off team, the role, influence and attitude of the entrepreneur gained after *People* in general the highest relevance. Especially as an extract from the interview data, participants have very often stated the importance of the entrepreneurial spirit of the CEO, even if the question was not particularly related to his role and influence. With strong emphasis on the *Entrepreneur*, the subcategories are: *Entrepreneur, Technology, Knowledge, Idea, Partner, Finance* and to a minor extend *Value*. Not surprisingly, the subcategory value plays only a minor role here, since the spin-off was only two years old, when the interviews were conducted. At that stage the value creation of the envisioned technology, products and services was too immature to be discussed in depth at this point of time. Nevertheless, the process of creating value is obvious, even for the spin-off company, but the awareness for it, is at the very early stage. In context with the spin-off, value creation is an ongoing NPD process, with the goal of building the multi-organ-chip (MOC technology platform).

Due to the extensive data evaluation, applying the grounded theory methodology (Glaser and Strauss, 1967; Glaser, 2004), the use of MAXQDA and self created data spreadsheets, this part of the study led to a semi quantitative evaluation of the theoretical categories. In contrast to the SMEs, the theme for the spin-off is *People*. The strongest theoretical category is *Entrepreneur*, followed by *Technology, Knowledge* and *Idea* with the same quantity. *Partner* and *Finance* are positioned at the lower end of the overall ranking. The ranking results are depicted in the following Figure 20:

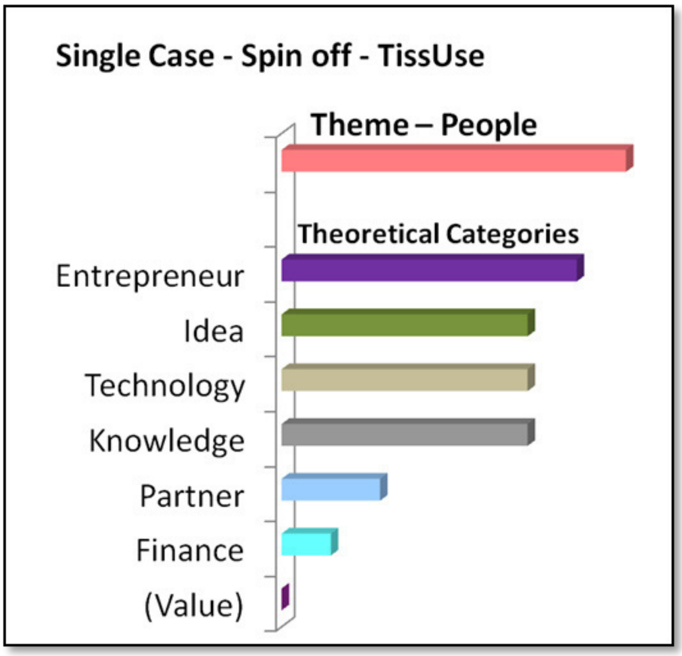

Figure 20: Integrative Diagram illustrating the Spin-off Theme and the Theoretical Categories

5.2.3.1 The Entrepreneur

The entrepreneur and CEO UM was interviewed in line with the SMEs, before the team member interviews were conducted. His view on the spin-off company is therefore evaluated separately, since his perspective is strong related to the theoretical category *Entrepreneur*. By applying in-depth analysis of his statements, it is possible to gain a fine grained insight view of his role as the entrepreneur, forcing the development of a radical innovation. In addition, his statements are linked with the longitudinal, in-depth data collection for supporting these findings.

The Consortium

The competent research consortium was invited by UM in June, 2008. He initiated two workshops with experts from different disciplines (i.e. immunology, tissue-engineering, consulting). This consortium signed a position paper titled "Emulation Human Biology in vitro", which explicitly pointed out the strategy for the radical innovative technology of a Human-on-a-Chip. One of the mentioned success factors was:

> "*Early involvement of really competent researcher consortium, to develop the strategy." (Interview, SME-UM, Q1)*

In concordance with the team members, the entrepreneur claims the importance of the right people as a success factor for his company:

> *"Getting the right people, the right staff for the company."*
> *(Interview, SME-C6, UM, Q1)*

The success factor mentioned second was the researcher consortium, which stands for the sum of partners, with whom UM shared his idea about the Human-on-a-Chip technology. Therefore, the competencies of these academics and practitioners and the early collaboration with them was of great importance. From the market perspective, the involvement of partners from the worldwide markets, for example the US and Asian markets is an important success factor. This implies, to already have partners in these markets, when the idea is at its early stage. For a serial entrepreneur, with more than 20 years in the life science market, this is possible due to his longstanding international network.

To protect the idea, early IP filing is an absolute necessity. UM claimed, that filing the IP early is from his perspective the *most important* success factor:

> "*The most import success factor was early IP filing."*
> *(Interview, SME-C6, UM, Q1)*

This statement is in line with the events collected in the longitudinal data collection. The first patent application, protecting the idea behind the technology for the Human-on-a-Chip was filed one day before (04.06.2008) the consortiums first workshop (05.06.2008). Further evaluations are described in more detail under 5.2.3.3.

Demonstrating the proof of concept for the technology was only possible due to the grant money, in this case, the GO-Bio funding. In this context the financial funding program was the pecuniary enabler for creating and developing the technology successfully.

> *"Acquisition of grant money to make the proof of concept for the main technology." (Interview, SME-C6, UM, Q1)*

The strong scientific and professional knowledge base of the entrepreneur and founder is a unique prerequisite for this spin-off company. Based on his experiences and "lessons learned", he always had a global vision for his company, from the early beginning. He stated this as one of the success factors:

> *"A global view on global markets trying to early understand the base to enter US American and Asian Markets." (Interview, SME-C6, UM, Q1)*

The uniqueness of this attitude and focus on global markets is strengthening by the following statement of SD, the consultant, who is part of the consortium:

> *"UM is the only manager I know, with a company world vision."*
> *(Pilot-Interview, CO, SD, Q12)*

Again, the world vision of the CEO from literally day one is a success factor that is reflected by the entrepreneur himself and acknowledged by the consortium member SD.

Even thought, that the spin-off CEO has a longstanding career in founding companies, he started this company with the support of the consortium, by involving their expert knowledge from the early beginning. Therefore knowledge as a success factor implies, knowing what you don't know and from whom and where to gain this complementary knowledge. The interrelation to the theme here, is finding the right people with the right knowledge. More in-depth information about the consortium is provided under the theoretical category *Idea*.

For starting a venture in the research intensive field of biotechnology, funding, in this case non-diluting grant money from the German government is another important success factor.

> *"Acquisition of grant money to make the proof of concept for the main technology." (Interview, SME-C6, UM, Q1)*

The researcher recalls from a personal conversation, that UM ones stated that he does not want to speak to early to VCs (UM, personal conversation, October, 3rd 2010). This implies that there is an important starting time, when the technology is ready and mature enough for presenting to VCs. Only an experienced founder can make this decision, based on his or her former lesson learned, also from failure in venture founding.

In a discussion with UM, he emphasized, that the incentives for his team are the exchange with COL partners in Moscow, Russia and Shanghai and Peking in China. Other incentives are the opportunity to learn Chinese at the early beginning, right after founding the company. Every year UM organized a special event, to celebrate the milestones of the project. The 4 years celebration took place in a night club in Berlin, starting with a presentation of recent results and looking back to the achievements. All important COL partners (i.e. Board Members, GO-Bio representatives) were invited.

Since 2015, the entrepreneur and CEO of TissUse GmbH, UM is stepping back more and more from keynotes at conferences, radio and print media interviews. He is handling over to RH to present the company in the media. From UM's perspective, this is a logical step, since in his former founded companies, he became CTO or Member of the Board to be still involved, but create room for the younger generation to become C-level managers.

At the end of 2013 until early 2014, there were plans to employ a new CEO from outside the spin-off. During this period of time, the business plan was adapted in collaboration with the potential new CEO. Based on the lack of external financial resources, the CEO could not be hired.

Interesting insights from an external perspective are provided by the consultant SD, who has met UM in 2008 during the annual BIO Convention in San Diego, USA. Both participated in a panel discussion. SD emphasized the following:

> "*He (UM) is an innovative company founder with outstanding competence both in technology and entrepreneurship." (Pilot-Interview, C0, SD, Q1)*

These representatives quotes by UM and SD are taken from the *SME interviews*, nevertheless, the content and context is relevant for the spin-off organization findings. This approach was chosen to connect both case study types, also demonstrated in the research design (see Figure 15 in Chapter 4).

5.2.3.2 Idea

> *"Everyone has ideas. It's the courage, passion and tenacity of the founding team that turns ideas into businesses." Steve Blank (cited in Cardon et al.,2017)*

This quote describes exactly, the important role of the team involved in the development of ideas per se. For the Human-on-a-Chip project, the idea was created by the entrepreneur UM several years before. The idea was based on the need for better and more precise predictions of the effects of medical treatments, by emulating the human biology. A decade ago, in December 2007, this idea was published in *Drug Testing in Vitro, Breakthroughs and Trends in Cell Culture Technology* (Marx and Sandig, 2007). This idea was, in other words the cradle of the radical innovation. Only six month later, in March 2008, the further developed idea was promoted by UM to a handpicked consortium of scientific and commercial experts. The following Figure 21 is demonstrating the collaborative approach, starting with an *Innovation Network*, even at this early idea stage.

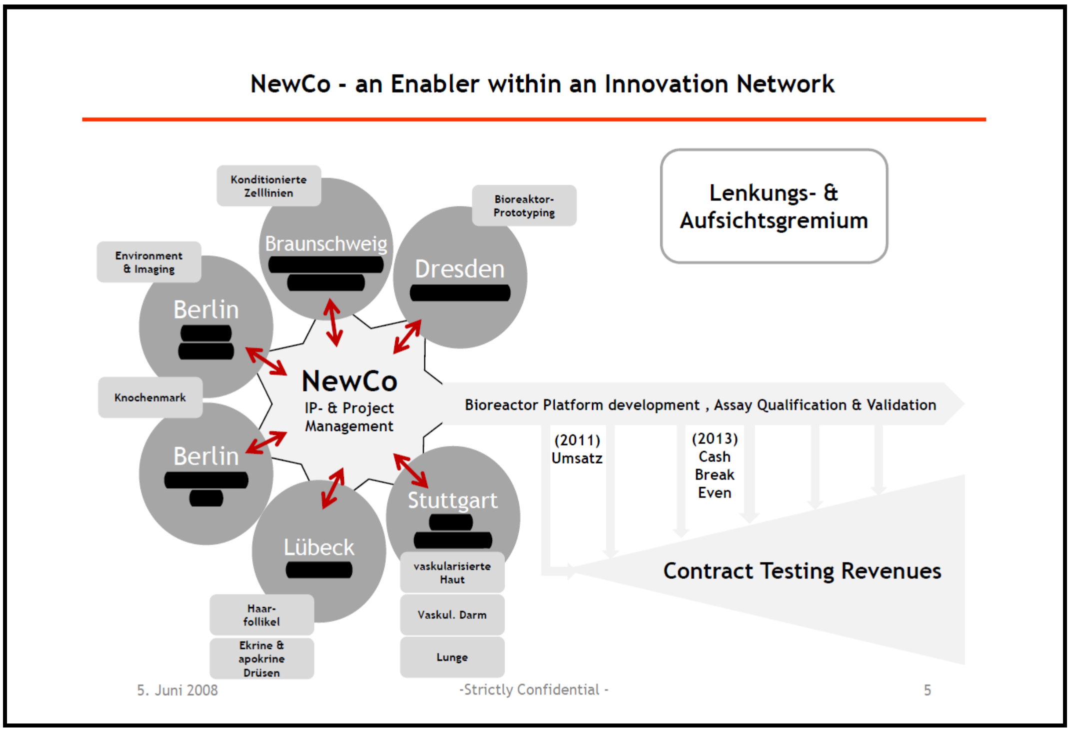

Figure 21: Extract from "First Workshop-Emulation Human Biology in vitro",

Longitudinal Data Collection, Spin-off

This particular slide is also representing the early **COL** partners, who all signed an agreement (Positionspapier des Forschungskonsortiums Prädiktive Substanztestung "In vitro"). Even at this early point of time, the first pre-prototype, the "Organ on Chip" (OOC) was presented. This first prototype envisioned the core technical and biological principles of the idea for the OOC. To protect the invention, UM filed a US provisional patent application 61/058,766 titled "Organ-on-a-chip-Device" on June, 4th, 2008. This patent application was initiated and privately funded by UM. As of the beginning of 2017 it is granted in Europe (EP2335370B1), in Russia (RU2517046C2), Australia (AU2009254177B2), China (CN102257124B), Japan (JP5774477B2), and Denmark (DK2335370T3). In the US, Canada, India, Singapore and Hongkong, the patent applications are at the later stage of the prosecution, the examination phase. With this global **IP** strategy, covering all countries and markets for the MOC platform technology, the entrepreneur and inventor UM aimed to protect the principal design, how the Human-on-a-Chip could work. Even if this was a high risk investment, the early filing and priority date secures the value of the invention against competitors and was the starting point for the IP strategy of the spin-off. Even UM himself argued that this early filing was *the* most important success factor for the spin-off early in 2011:

> *"The most import success factor was early IP filing." (Interview, SME-C6, UM, Q1)*

A second workshop was held after additional six month. During this time period the idea for the technology platform was further developed in a collaborative approach.

The two workshops at the beginning of the project are highlighted as starting points for bringing the idea to life. The important role of the entrepreneur and his early engagement with his **COL** partners implicating, that UM consciously or unconsciously started with the open innovation activity Collaboration (**COL**). He engaged persons from his personal and professional network (**NET**), to support his idea for the radical innovative organ on a chip technology.

5.2.3.3 Technology

As described earlier, the data evaluation for the spin-off case study provides a more fine-grained view into all observed and studied activities, related to the innovation strategy of the new venture. In contrast to the multiple cases, the SMEs, the role of the spin-offs technology is evaluated in more detail. Since the company is developing a radical innovation, deeper evaluation, why and how this is possible, provides the researcher with the answer of RQ2, if open innovation enables this type of biotech innovation in a German ecosystem.

Even from the external view at the early stage of the spin-off company, SD emphasized that the technology is promising and provides a broad spectrum of applications: ...*the platform has the potential to be broadly applied* (Pilot-Interview, C0, SD, Q3). This potential is grounded in various applications of the technology platform in the pharmaceutical, cosmetic- and consumer health industry. Nevertheless, the complexity of science and technical solutions demanding the involvement of external partners from the beginning. As SD stated, this will save time and money to reach the market.

> *"Using outside resources in addition to in-house resources will help reduce the time to market. In vitro assays are competitive so anything that can be outsourced will likely be outsourced. Short cuts and acceleration are important to save time and money." (Pilot-Interview, C0, SD, Q3)*

For the new venture developing a radical innovation, the Human-on-a-Chip platform, the technology itself is at the core of all **R&D** activities. Therefore, for the spin-off company there is a strong link between the **R&D** focus, strategy, outcome and the requirements to develop such a complex technology. The internal **R&D** team was handpicked by the entrepreneur, focusing on young researchers, experienced academics with specific knowledge (RH; GL) and experienced professionals, like SH with high expertise in IP management. Notwithstanding, that the consortium was already committed and the advisory board for the company was engaged. From day one, all deep tie **COL** partners were involved in the communication processes. Geographic distances were bridged by regularly meetings at all sides. UM, the entrepreneur took full responsibility to organize these meetings, to develop a fruitful team spirit from the early beginning of the project.

The Chip-Technology

In mid 2012, at the time, the interviews with the spin-off team members were conducted, TissUse GmbH was two years old and first reached milestones were documented. The growing expertise, skills and abilities of the team internally and the **COL** partners externally led to the positive development of the radical innovation. Technological and scientific highlights mentioned by the interviewees are summarized here (Interviews, Spin-off, RL, SH, RH, GL):

Table 17: Scientific and Technological Milestones

Scientific Milestones	**Technological Milestones**
▪ Vascularisation ▪ Hair follicle into skin ▪ Every organoid ▪ Endothelia cell culture ▪ Blood perfused chip ▪ Testing on disease level	▪ Steady microcirculation (30 days) ▪ Downscaling ▪ Internal pump ▪ Visualization of research results ▪ Customization of the chip
First ready to market chip: DTM-Chip (liver and skin) in 2012	

Source: Single Case Data Collection

Taken into account the complexity and novel approach of the chip technology, this fast product development of a fully functional chip is impressive. The determined milestones of the GO-Bio program are reached. Again, reaching this significant milestone is the result of the strong **COL** within the team, and with external partners, influenced by the entrepreneurial (**EL**) spirit of UM.

From the legal perspective, in regard to the **IP** protection, another milestone is reached. One of the core patents, protecting part of the technology (hair follicle/skin) was issued in Europe on April, 25th, 2012 (EP2274419B1). The overall **IP** protection regarding the components of the chip technology is emphasized as one highlight of the project so far, mentioned by a team member:

> *"All the other patent applications in the field of regenerative medicine, tooth, bone and cartilage." (Interview, Spin-off - GL, Q4)*

Even at this early stage, the team members are not only aware of the need to protect the technology with patents, they are also proud of reaching the **IP** milestones. The following quote is evidence for the awareness for the importance of IP in context with the technology:

> *"IP plays an important role. Without patents there is no commercial protection. The IP management plays also an important role, because the strategic positioning and the markets, where the technology will be commercialized must be defined in advance." (Interview, Spin-off - SH, Q5)*

Figure 23is based on the IP strategy started by the entrepreneur in 2008 with the first IP filing. Interestingly, the first presentation of the prototype looks different from the actual products. This is caused by the early stage of the idea, but the underlying principles of the technology were protected. Reward for the decision to file early, is a granted patent in early 2014. Applying the accumulated new knowledge about the technology of the first working chip (see Table 17), the more realistic scientific and technological solution in form of the 10-Organ-Chip led to a granted patent in 2014.

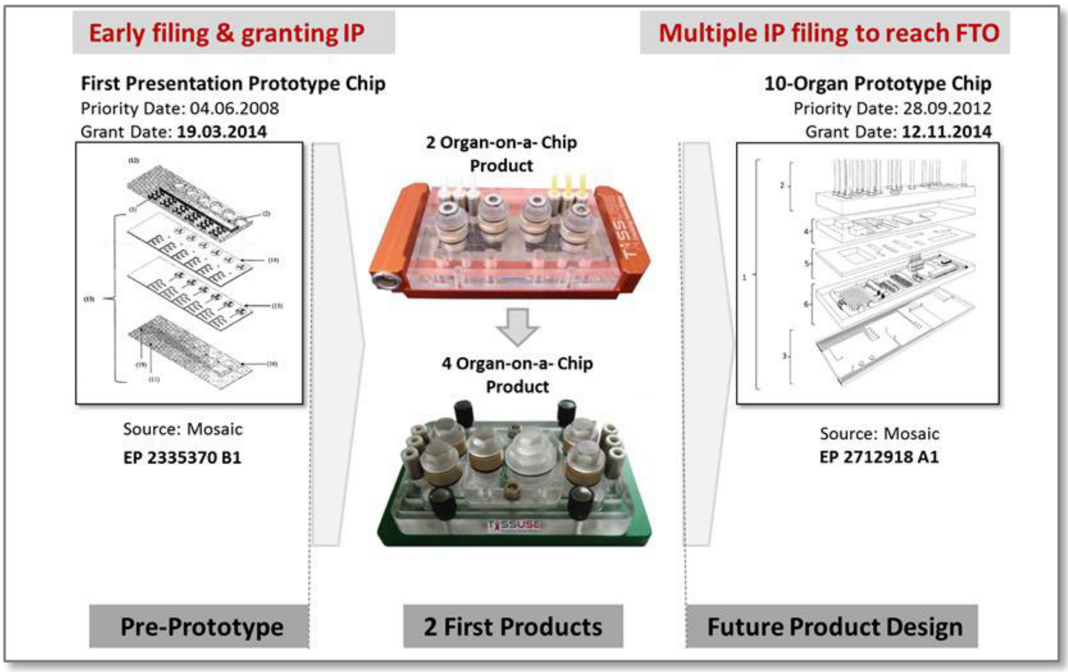

Figure 22: IP filing process and prototype/product development

Source: Longitudinal Spin-off Data Collection

Figure 22 is demonstrating the IP strategy initiated by the entrepreneur in 2008, two years before the spin-off was founded. The process is simplified to envision the importance of the first pre-prototype, which was invented by UM and later built by the COL partner IWS, Dresden. This pre-prototype is an impressive example for rapid prototyping, which is actually often related to 3D printing and formerly on CAD (Computer Aided Design) techniques. The first version of the chip was built to demonstrate the functionality and the underlying basic principles (i.e. cavities for the small organoids, vessels for the circulation). From the perspective as of today, this pre-prototype was a mock-up to present a physical model to the patent office, the consortium and to the potential investors (GO-Bio Project Managers), even if this particular design was not further developed. But the underlying principle, how the Organ-on-a-Chip could work, was adopted. Based on the new knowledge, generated by building the first working chips, the CEO and his team was able to create the future design for the 10-Organ-Chip, filed a patent application in 2012 and got this core patent granted in 2014. More IP was filed and granted during the longitudinal case study, but the core IP is selected to illustrate the importance of the step-by-step strategy for protecting a radical innovation like the Human-on-a Chip technology platform. More information is provided in correlation with the theoretical category *Idea* under 5.8.4.

Latest Developments of the Technology

The researcher had the opportunity to meet the VP Business Development of TissUse GmbH, Reyk Horland (RH) at a biotech conference in Berlin, May 24th, 2016. The following information was gained from the conversation, without explicitly doing an interview. Therefore it will not be included in the data collection and not be coded, like the interviews from 2012. Nevertheless, the information gained is useful resources, to get an update about the recent status of the company.

None of the information is confidential; therefore ethical concerns are not applicable. The researcher acted as an observer and gained useful information to complete the final picture of the single case study, the spin-off company TissUse GmbH.

The company has two products on the market, the two-organ-chip and the four-organ-chip. As RH illustrated, there are different combinations of the organs possible and the chip design can be adapted to the clients requirements. This fits very well to the rapid prototyping approach, since a working product, in this case, the chip, presents the best opportunity to learn from. Especially such a complex, technical and biological system needs also a "trial and error" approach to generate new useful, valuable knowledge. By allowing small failures in experimentation, a mindful learning process is possible. This enables the scientists at TissUse to come up with innovative ideas deductively, which provide the solution for special applications for the Organ-on-a-Chip (Khanna et al., 2016).

The company has several customers from the cosmetics industry, but other sectors, like pet nutrition have shown interest. There are actually much more applications of the Organ-on-a-Chip technology feasible, which RH and the team has never expected. This broader application of the technology was also envisioned by one team member early in 2012. SH had the following vision about the spin-off company:

> *"The company TissUse is much more than only the GO bio project, which is part of it. There are much more new opportunities left and right."*
> *(Interview, Spin-off-SH, Q12)*

This statement summarizes the important role of the technology itself and the visionary view of the team members.

5.2.3.4 Knowledge

Knowledge can be defined as a human asset and one of the key components of human capital (Grandori, 2016). The spin-offs radical innovation is grounded in the combination of existing and new knowledge. Since the development of the Human-on-a-Chip technology is based on a complex knowledge fit, the knowledge requirements and investments are high (Reus et al., 2009).

The idea for the Human-on-a-Chip technology was created by the entrepreneur, based on his in-depth, long-term scientific and market knowledge. As a serial entrepreneur, TissUse was the fifths company he founded over a period of more than 20 years. Therefore, he brings in the experiences to build successful companies (Vita 34 AG, ProBiogen AG) on one side, and he also experienced failures with two other companies (see CV UM, Appendix F). From the teams and partners perspective, he brings in a unique combination of scientific expertise and business acumen. One team member stated the following:

> *"Uwe is a unique person, because he combines the scientific and technical knowledge with the market insights in one person. He has the all-round view." (Interview, Spin-off-SH, Q12)*

All people at the spin-off company, also described as the human capital, constitute the knowledge-capital in the framework of a network of **COL** partners. Knowledge-capital is by definition the set of scientific and technical knowledge and information produced, acquired and used in the value creation process (Laperche and Lui, 2013). This knowledge-capital is embedded in the individuals know-how, technological tools and routines. Therefore knowledge-capital is created due to the continuous process of knowledge combination and accumulation over time. The **R&D** activities are those repeated processes, where the team of the spin-off creates the new knowledge-capital (Quintana-Garcia and Benavides-Velasco, 2011). The influence and importance of the individual team members with specific knowledge are represented in the following quotes.

"We have the experts for all the components of the technology and the biology". (Interview, Spin-off-RL, Q3)

"The structure of the group is great. Uwe runs the whole project, no one is excluded from patenting and there is a constant exchange between the members of the group." (Interview, Spin-off-RH, Q7)

From the internal knowledge base, especially developing a radical, new to the market technology, there is also a potential risk for unwanted knowledge spillover or leakage. Peoples open attitude and wish to share scientific achievements outside of the university and spin-off boundaries can become a serious threat to radical innovation.

"The internal threats are the very open approach of developing new knowledge and IP in teams between the university and the company, so confidentiality often is a measure university people are not used to." (Interview, SME-C6, UM, Q6)

"People at universities should know not to publish before patenting. Usually people don't know this." (Interview, Spin-off-GL, Q6)

Again, there is evidence for a strong awareness about when and how to protect the knowledge via **IPR**s. Here the influence of the entrepreneur UM and the consequent involvement of the whole team in developing an **IP** strategy from the early beginning is mandatory.

Knowledge exchange is one of the motivations for participating in networking events (**NET**) outside of the spin-off company. As one team member emphasized, **NET** events are important platforms to gain exchange and explore new knowledge.

"The not scientific congresses are important networking opportunities. At the more political congresses you meet people from pharma, consultants, regulatory affairs and human societies. One good example was the

congress on "The Future of Toxicity Testing". Attending to these conferences is a very good opportunity to get the idea to a broader audience." (Interview, Spin-off- GL, Q8)

In addition, the **NET** events are platforms to promote the new technology and meet decision makers.

"It is important to talk to decision makers from e.g. regulatory affairs. At one point you get to know the decision makers what you are doing." (Interview, Spin-off- RH, Q9)

Complementary knowledge, provided by **COL** partners combined with in-house knowledge and expertise enables the development of the chip technology. As one team member stated, this exchange is crucial for the **R&D** activities:

"The chip technology could only be developed in collaboration."

"Networking is needed for the project, especially the collaboration with IWS (Dresden) and Fr. Prof. W. (IBG) Stuttgart. We got special equipment and the manuals, so we were able to use their knowledge and know-how." (Interview, Spin-off- SH, Q8)

There is a strong relationship between knowledge and people. The quotes from the team member and the external consultant emphasizing the profound scientific and commercial experiences, the CEO is contributing. Moreover, the different team members themselves are contributing with their specific skills and expertise to develop a radical innovation.

5.2.3.5 Partner

One of the requirements to develop radical innovation is, that regardless how experienced the inventor is, she or he can not pursue the development alone. Complex technologies, in this case the envisioned Human-on-a-Chip platform, demanding the expert knowledge of different partners with different scientific and professional backgrounds. For the early stage spin-off organization, the entrepreneur started developing the idea together with partners from his personal network and with expertise in different application fields (see Figure 21). This consortium was the first group of partners, followed by the handpicked team of young students and professionals. These team members and the consortium became the core group of people who formed the spin-off, directly after acceptance and start of the GO-Bio program in early 2010.

The strong ties for the R&D collaboration are grounded in the long term relationship and friendship between the entrepreneur UM and the head of Medical Biotechnology (Medbt, TUB) Prof. Roland Lauster (RL), also part of the consortium. Another important, trusted person is Silke Hoffmann (SH), group leader of the GO-Bio program and later VP IP and Innovation. All these partnerships are internal and characterized by mutual trust and appreciation for the experiences and expertise. The following quote from RL is emphasizing, that people are an important success factor, by referring to UM and SH.

> *"People - the fact that I know Uwe [UM] for more than 20 years. Silke [SH] worked for Uwe many years and therefore I know that she is the right person for IP." (Interview, Spin-off- RL, Q1)*

Nevertheless, besides the strong internal ties, the partnership with external partners plays an important role too. Some of the consortium members are connected via personal ties; others are direct **COL** partners with collaboration contracts in place (IWS Dresden). This was particularly emphasized as one of the three highlights in the **R&D** process by a spin-off team member:

> *"The contracts with all the other institutions and collaboration partners" (Interview, Spin-off - GL, Q4)*

Driven by the developmental stage of the technology itself, the partners are more involved or less intense engaged over time. In mid 2012, when the first organ on a chip product was sold, which is an impressive milestone, the strong participation and influence of the COL partners was stated as an R&D highlight so far:

"The collaboration programs with external partners:

a. ZIM [German Innovation Funding Program], where the TU and TissUse are involved

b. Russia

c. IWS (Fraunhofer Institute for Material and Beam Technology, Dresden)"

(Interview, Spin-off - SH, Q4)

To draw a more holistic picture, the relationship with and influence of all partners over time, external and internal partners would need more attention, therefore this could become part of future research agenda for studying the interrelation between partnerships and COL in context with the open innovation phenomenon.

For the spin-off company, it is obvious that the interplay of internal and external COL partners enabled the development of the Human-on-a-Chip technology.

In summary, the technology complementarily of the **COL** partners and the trustful long term R&D alliances supporting the development of the radical innovation (Quintana-Garcia and Benavides-Velasco, 2011).

The following figure was extracted from UM's presentation during the first consortium workshop. The researcher identified this specific slide as evidence for the long term and trusted relationships, the entrepreneur had build long before the company was founded. All different **COL** partners names are mentioned and referred to the time, when UM started the relationship and had meetings with them. The slide is marked as "Anbahnungshistorie" which can be translated into *initiation history*.

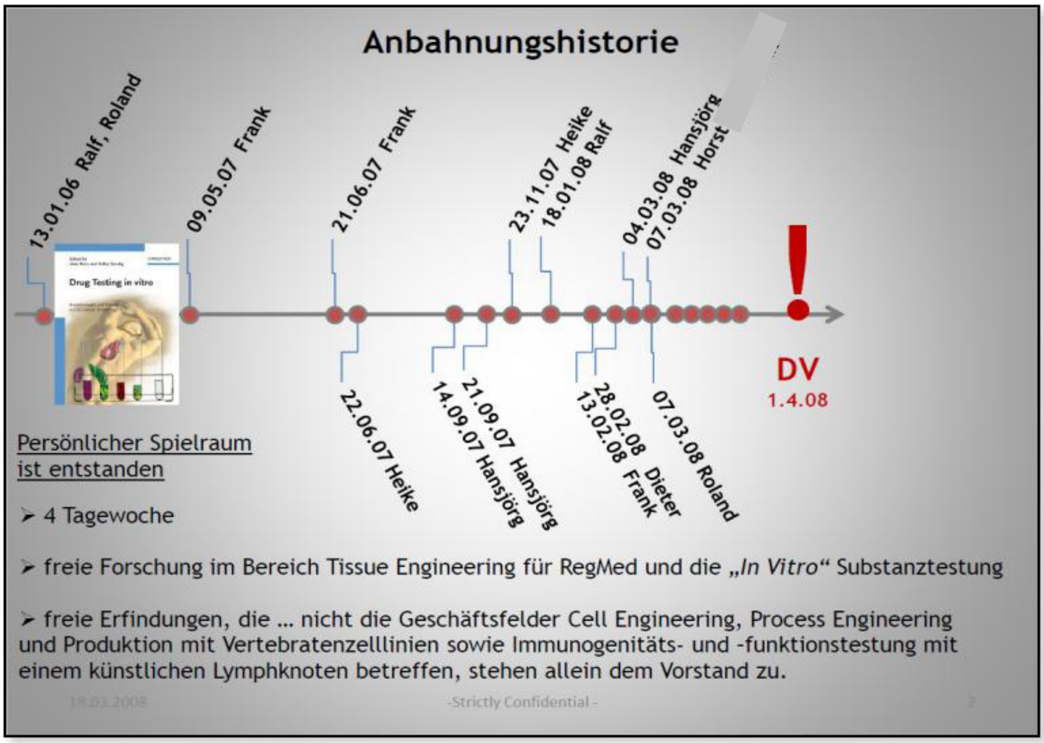

Figure 23: Extract from "First Workshop-Emulation Human Biology in vitro", 2008

Source: Longitudinal Spin-off Data Collection

5.2.3.6 Finance

For every newly founded venture, seed investment or starting capital is essential. In case of the spin-off company, TissUse, the founder himself invested private money during the pre-founding phase. He and his **COL** partners, see Figure 25ensured the seed funding via the GO-Bio program due to investing time and effort to win the governmental grant money (in this case 2,8 Mio €). Here, the role of the entrepreneur as an initiator and enabler becomes crucial (Teece, 2010).

The biotechnology industry is one of the most **R&D** intensive industries, and therefore, with a tremendous demand for initial financing. With his experiences as a serial entrepreneur from this sector, UM brings in his reputation as a founder and scientist. Besides his personal, private investment (i.e. patent costs, consortium workshop), UM initiated the application for the GO-Bio program.

Based on his trusted, long-term scientific and personal relationship with RL (Head of Medbt, TUB), the initial "GO-Bio Skizze" was submitted in the name of the TUB. Evidence for the collaborative (**COL**) approach was the teamwork during the GO-Bio application phase. Notwithstanding, that there was a high risk of not reaching the final round and earning this non diluting, governmental funding. The cooperation of the entrepreneur UM and his partners ensured the probability for the seed funding in a significant manner.

The demand for the consortium and team members complementary expertise is another influencing factor to enable financial success. Two prominent examples in this context are SHs long-term expertise in **IP** management and UMs long term founding history. One participant evaluated these two facts as a highlight of the R&D process.

> *"Expertise of Uwe [UM], who founded 4 other companies, together with Silke and her expertise in patent handling." (Interview, Spin-off - RL, Q4)*

Potential financial income at a later stage of development can also come from out-licensing the technology and respective **IP** rights. But these **IP** assets need permanent investments, as one team member demanded:

> *"There should be more money in place for the IP in general – e.g. side searches, FTO-analysis. The government should give more money for this." (Interview, Spin-off GL, Q5)*

Even if there is a profound internal **IP** management in place, additional external funding is demanded. This implies that the team members are taken full responsibility for the **IP** management process and that they are aware of the importance of early and steady **IP** asset protection.

Another interesting aspect in context with finance is regarded to the technology transfer terms. The IP portfolio comes particularly from the entrepreneur and is also based on inventions from the TUB. Since a technology transfer agency, ipal

GmbH acts as an intermediary, the spin-off company needs all IP rights assigned. Due to different interests it is advisable to involve all partners early on. From the financial perspective the following advantages are stated:

> *"The spin off was already founded, which was very important, otherwise it would have been very difficult to negotiate the licensing contract. In other cases, if you try this 1 to 2 years later, the "Verwertungsagenturen" [intermediary: ipal] want a larger piece of the cake." (Interview, Spin-off - RH, Q5)*

At this early stage of the spin-off company, only two years after funding, this particular team member has already a critical view and commercial driven standpoint regarding financial terms and negotiation timelines.

Besides the awareness for the importance of the initial financing in the GO-Bio framework, the head of Medbt (TUB) described a controversial case from his personal experiences and involvement. From his perspective strong leadership (**EL)** qualities can allow the founding of a biotech company *without* seed money.

> *"As an example for leadership take TIB Molbiol, the founder never got money from investors and the company has today 60 people employed and is in the market for more than 20 years." (Interview, Spin-off - RL, Q12)*

This controversy example would be an interesting case study for further investigation outside the framework of this study. Therefore, the existence and success of biotech companies *without* seed funding needs retrospective evaluation. Focusing on these rare cases could broaden the knowledge and understanding of the adoption of open innovation, even before the phenomenon was described and coined (Chesbrough, 2003).

5.2.3.7 Value

The theoretical category *Value* was in contrast to the SMEs evaluation not significant. Even so, the spin-off team members mentioned the **R&D** highlights from their point of view, and agreed, that the first working chip was a real milestone in the first two years of existence (see 5.2.3.3 Technology). Since the development of the organ-on-a-chip technology is initially financed by the GO-Bio program, reaching all the mutually agreed milestones is a valuable achievement. One team member emphasized the following as a highlight:

> *"Reaching all the milestones of the Gantt Shart of the GO-Bio project plan, especially the microcirculation for 30 days." (Interview, Spin-off - SH, Q3)*

The GO-Bio program milestones were documented in the bi annually "Progress Reports GO-Bio, BMBF", starting with the first report on August 26th, 2010.

Creating future commercial value was pursued by the early and thoughtful **IP** filing strategy. Starting with the first patent filing in 2008, the **IP** portfolio was build up step by step, based on the expert knowledge and expertise of SH and UM. One Team member values the **IP** process as the following:

> *"Due to the special design of the GO-Bio project patenting is exactly planned and is running very well." (Interview, Spin-off - RL, Q5)*

Value creation is the positive effect of the adaption and adoption of the open innovation concept. In case of the spin-off company TissUse's technology, the first organs-on-a-chip is a radical, new to the world innovation.

To answer the research questions, this study aims to provide a holistic picture about the innovation strategy of biotech ventures, even at different stages of their development. For the spin-off company, in Table 18 the interrelation and dependency of the newly identified categories and every open innovation activity (R&D, IP, NET, COL and EL) are illustrated. These findings are grounded in the extensive data analysis, applying the principles of the grounded theory methodology (Glaser and Strauss, 1967; Corbin and Strauss, 2008).

5.2.3.8 The Causal Relationship between the Open Innovation Activities and the Entrepreneur, Idea, Technology, Knowledge, Partner and Finance

In the following Table 18 the significant attributes, describing the relationship between the theoretical category and the five key open innovation activities are presented. The more in-depth, detailed explanatory results of this evaluation are documented in the following paragraph.

Table 18: The causal relationship between the open innovation activities and the theoretical categories.

Theoretical Categories	TissUse - 5 Key Open Innovation Activities				
	R&D	**IP**	**COL**	**NET**	**EL**
Entrepreneur	▪ Importance of Make & Buy in all markets ▪ UMs profound scientific experiences	▪ UM initiated and financed the first IP filing in 2008 ▪ UMs strong IP strategy	▪ UMs open attitude to collaborate and share	▪ Importance of UMs networking competencies	▪ Consortium and Advisory Board ▪ Serial entrepreneur: UM has founded 5 companies
Technology	▪ Development of the MOC technology is the core R&D activity ▪ R&D of complex radical technology	▪ Early filing and granting of core MOC technology ▪ Overall IP protection of regenerative medicine technologies	▪ Strong commitment of all COL partners ▪ Full involvement of all COL partners ▪ Enabler for cross industry COL	▪ NET opportunities at "not scientific" conferences ▪ NET with regulatory authorities and society organizations	▪ In-house leadership role ▪ First prototype developed under leadership of UM
Knowledge	▪ Handpicked R&D team ▪ Specific experiences and expertise of team members	▪ Knowledge about FTO and IP related data	▪ Early COL with academia with complementary, specific competencies ▪ Threat of knowledge sharing	▪ Demand for NET to exchange knowledge	▪ Transformation of scientific project into a business case
Idea	▪ Importance of every inventors impact and share ▪ Demand for first presentation prototype	▪ Start with IP protection at the idea stage ▪ Use of presentation prototype to protect core principles of the invention	▪ Demand for the consortium to develop the idea further ▪ Sharing the future vision with COL partners	▪ Professional and personal network of UM as an important source	▪ Strong leadership qualities of the entrepreneur UM
Partner	▪ The Consortium ▪ Long-term R&D alliances ▪ Access to research infrastructure	▪ Importance of GO-Bio rules for IP management ▪ International IP strategy for future markets and partners ▪ Demand for governmental incentives	▪ Strong ties with COL partners ▪ External partners, i.e IWS Dresden ▪ COL program ZIM ▪ COL with Russia	▪ Positive influence of NET partners	▪ UM initiated long-term relationship with partners early in 2006 ▪ Strong ties with partners
Finance	▪ Importance of non-diluting seed money (GO-Bio) ▪ Fast prototyping and product development	▪ Monetary value is grounded in the idea	▪ Financial expectations of TTO ▪ Importance of German governmental funding program (GO-Bio)	*- not mentioned here -*	▪ Role of Entrepreneur as Initiator and Enabler

5.2.4 Causal Mechanisms between Theoretical Categories - TissUse

To further evaluate the interdependence and causal mechanisms, and to demonstrate evidence for their importance to develop radical innovations, the theoretical categories *Entrepreneur, Technology, Knowledge, Idea, Partner and Finance* are connected to each other. As summarized in Table 18, the different cells providing the extracted facts from the spin-off data findings. Nevertheless, there is a strong cause and effect mechanism behind the new categories, grounded in the data. Learning from these causal relationships will add value to the demand for understanding open innovation mechanisms as factors for success or failures of innovation strategies from a broader perspective. Yaghmaie and Vanhaverbeke (2019; p.2) argue, that analyzing open innovation at the firm level may prevent researchers from properly analyzing open innovation activities. This research study is overcoming this obstacle by setting the research framework exactly in this broader framework. By connecting the theoretical categories with the open innovation activities (De Jong, 2008), the firm perspective is complemented by the individual and the project perspective (Bogers et al., 2017). One could argue, that this might provide only the internal perspective, but since the investigated open innovation activities COL and NET are focusing on the external perspective of the organization, this research study will add new insights to the innovation management literature from a multi-level internal and external perspective. The *Entrepreneur* is functioning for the spin-off organization as the creator of the *Idea* for the MOC, long before the new venture was founded (Marx and Sandig, 2007). Therefore, the value creation process for the *Technology* started early on with the first patent application in 2008 by UM, based on his scientific expert *Knowledge* in tissue engineering. In doing so, he became the actor, who started the early value creation process; nevertheless, he involved the *Partners,* the expert consortium right after the IP filing. At this early pre-founding stage, even providing *Finance* (IP costs; meetings; pre-founding costs) was done by the *Entrepreneur.* These mechanisms and interdependence between the categories are demonstrating the important role of the *Entrepreneur* as the initiator for developing a radical innovation. Due to the longitudinal character of the case study, these relationships are representative for the pre-founding stage. Nevertheless, this stage is exemplary and representative for starting the value creation process.

5.2.5 TissUse' Open Innovation Activities from 2008 - 2013

Ranking the Theoretical Categories based on the interview data and evaluating the longitudinal data collection provided evidence for the importance of the spin-off CEO's role. Interestingly, the rich, in-depth data analysis, described in Chapter 4, led to semi-quantitative results for the weighting and ranking of the five open innovation activities: R&D, IP, NET, COL, EL. By evaluating the importance of the different activities in correlation with every single event, the *Entrepreneur-and Leadership* motivated activities were covering 27% of all events, followed by R&D with 24% and COL activities with 24% . IP activities are presented by 15% and NET activities by 10% (see Figure 24).

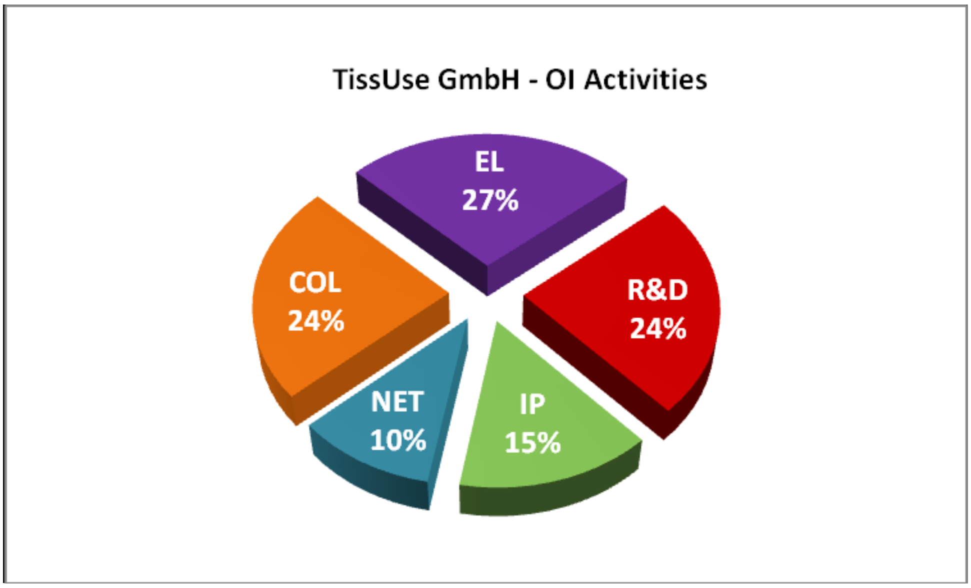

Figure 24: TissUse' open innovation activities in % of the 210 evaluated events

The combination of the qualitative content analysis and the quantitative scoring system added important value to the single case study. The quantitative evaluation by applying a score for the relevance of the open innovation activity in regard to the specific event, is demonstrating the focus of the spin-off company at a given point of time. Not surprising is the fact, that during the early stage of development, the activities are driven by the entrepreneur (EL-27%), R&D activities (24%), but also by COL (24%) activities at a similar percentage.

This implies that the early stage organization has its focus not only on internal technology development, but also on collaborating with external partners. The proportion of IP activities (15%) is slightly higher, than the NET activities with 10%. This overall picture provides an overview about the open innovation activities, but does not claim to allow general recommendations. For a more fine grained analysis, the activities must be correlated with the recent stage of development in dependence from the time. Therefore, the following sections demonstrating the insights about every open innovation activity over time.

To illustrate all open innovation activities, correlated with the 210 events, the following diagram is summarizing the results in a comprehensive way.

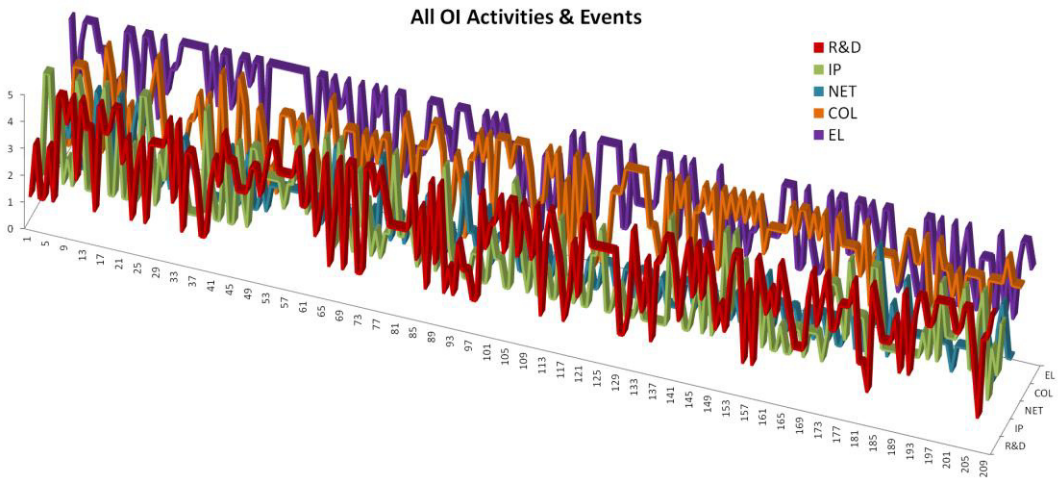

Figure 25:TissUse' open innovation Activities and Events, Longitudinal Data Collection 2008-2013

For every single event, a specific score for the open innovation activity was applied (see Chapter 4: 4.5.1). This scoring system resulted in a fine-grained evaluation of TissUse' open innovation activities. In the following paragraphs for every open innovation activity, a detailed activity diagram is provided. Additionally, all open innovation activities are presented in net-diagrams, see Appendix H.

5.2.4.1 TissUse' Research and Development Activities - R&D

Based on the data evaluation of the longitudinal data collection, the 210 events, R&D activities covered 24% of all measured activities. To gain a more precise picture, to what extend the activities are relevant, the measurement over time is important. In the following diagram, the R&D scores/event is illustrating the findings from the evaluation.

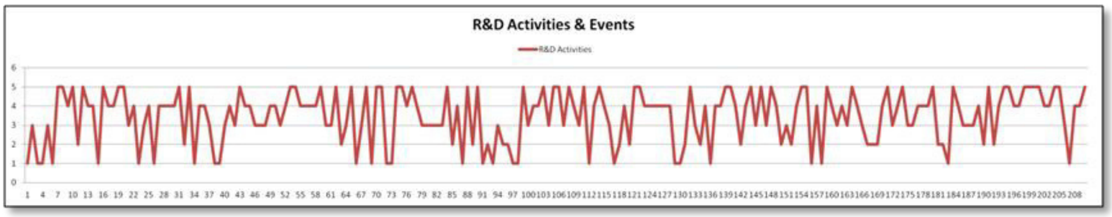

Figure 26: TissUse' R&D Activities, Longitudinal Data Collection

Interestingly, a number of events with the score 5 could be related with the team members statements regarding the technological highlights and reached milestones. One example is the first ready to market chip: DTM-Chip (liver and skin) in 2012.

5.2.4.2 TissUse' Intellectual Property Management - IP

One of the most important activities in developing radical innovation is the creation of IP and the early protection of the R&D achievements. Here, it must be emphasized again, that the very early IP protection in 2008 (WO2009/146911), two years before TissUse was founded, is one of the most crucial success factors. Therefore, the 15% of IP activities over time are not related to the importance of that activity, it is more relevant, when the start.

Figure 27: TissUse' IP Activities, Longitudinal Data Collection

As illustrated in the figure above, the IP activities started early (events 1-3) and over time, peaks with the score 5 are present. Nevertheless, the CEO stated recently, that there are longer periods of times, when in-house know-how is developed without direct IP protection.

5.2.4.3 TissUse' Networking Activities - NET

Networking activities are at the lower end (10%) in regard to all measured activities. This implies, that especially at the early stage of a newly founded venture, the focus is not on networking per se. From the CEO's perspective, he brings in his own valuable scientific and commercial network, which is build up over years. In contrast, the newly founded spin-off started their business activities at the TUB and aimed in the early years to be "under the radar". Therefore, networking was consciously a minor activity. The following figure is demonstrating this.

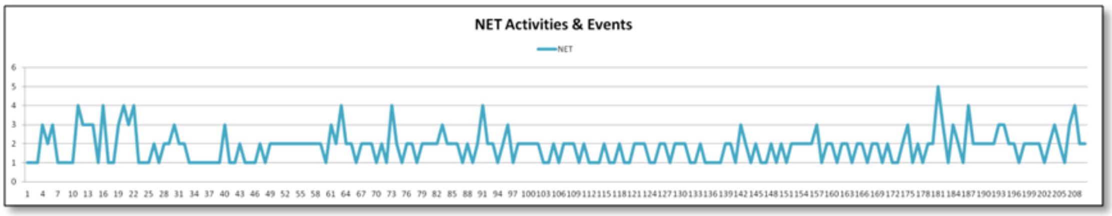

Figure 28: TissUse' NET Activities, Longitudinal Data Collection

5.2.4.4 TissUse' Collaboration Activities - COL

With a percentage of 24%, COL is besides R&D and EL, one of the most frequently identified activities. Notwithstanding, a closer look is requested here. The high frequency of COL is grounded in TissUse' collaborative approach. Even the pre-founding phase is characterized by the CEO's early involvement of the consortium (see Figure 21). Another important factor is the close collaboration with the Medbt at TUB. These deep ties are also mentioned as important success factors (see Figure 33). Due to the complex scientific and technological requirements for the envisioned Human on a Chip platform, collaborating at every stage of the value chain is mandatory. The following diagram is supporting the above mentioned factors.

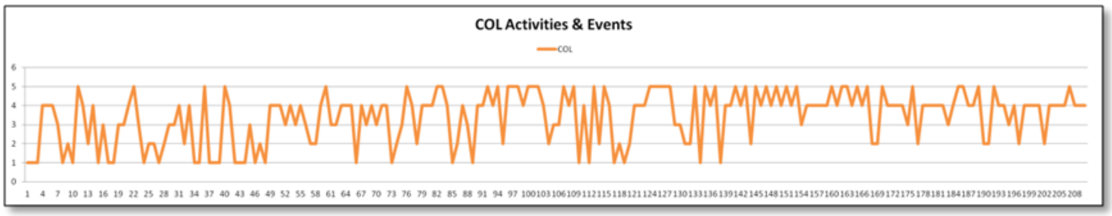

Figure 29: TissUse' COL Activities, Longitudinal Data Collection

5.2.4.5 TissUse' Entrepreneur & Leadership - EL

The open innovation activity entrepreneur and leadership is the most frequent measured activity, with 27%. Not surprisingly, nearly one third of all activities are driven by EL. In accordance with the findings from the interview data analysis, the activities driven by the entrepreneur UM are at the core of the pre-founding, founding and later stage of the spin-off organization. Supported by the team members and COL partners, but also evaluated by the researcher, entrepreneur- and leadership activities are the building blocks for new ventures. In this case, a biotech company, which is developing a radical innovation. The frequency of the EL activities over time is illustrated in the following diagram.

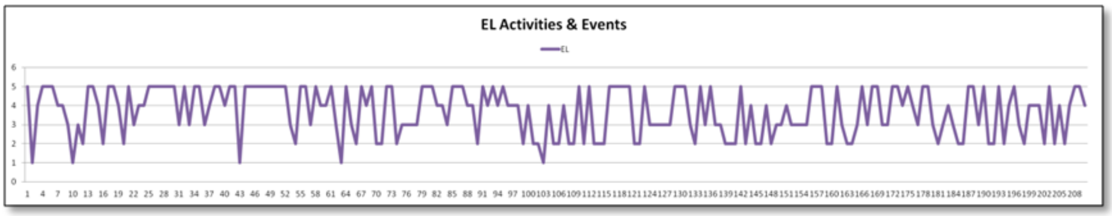

Figure 30: TissUse' COL Activities, Longitudinal Data Collection

These diagramms covering the investigated 210 event are valuable data sources for additional new research studies in the field of entrepreneurship, new venture creation, open innovation and radical innovation in particular. Since this comprehensive, longitudinal data set is a rare, unique source, it could be envisioned, to provide other innovation research scholars with access to the data.

5.2.4.6 TissUse Pathway to Radical Innovation

Based on the evaluation of the longitudinal data collection, the following documents are identified as valuable sources of information. These documents are demonstrating the development of the spin-off, even from the pre-founding perspective. Starting in 2008, the idea for the organ on a chip is summarized in the first "Skizze" as a draft proposal for the governmental founding project GO- Bio (BMBF, 2008). After submitting the "First Stage" proposal in 2009, the research group was selected to submit the "Final Proposal" in May 2009. On 17th of December 2009 the BMBF announced the approval of the funding due to a letter of intent (LOI). The next step was founding the venture in March 2010, followed by the final written approval of the GO Bio funding in April 2010. Even if the company was founded in early 2010, at this time, the formation of the research group at the university was embedded in the scientific framework. Therefore, the transition from the research project into a commercial venture was an iterative, step by step process. Nevertheless, the entrepreneur UM created the first draft of business plan in August 2010. The researcher identified these sources as rare, since companies usually do not give access to their business plans. These documents are confidential and only shared with potential investors and board members. To evaluate the development of the spin-off over time, the latest business plans from 2015 and 2017 are added and included in the data collection. The following Figure 31 demonstrates the timeline for these important documents.

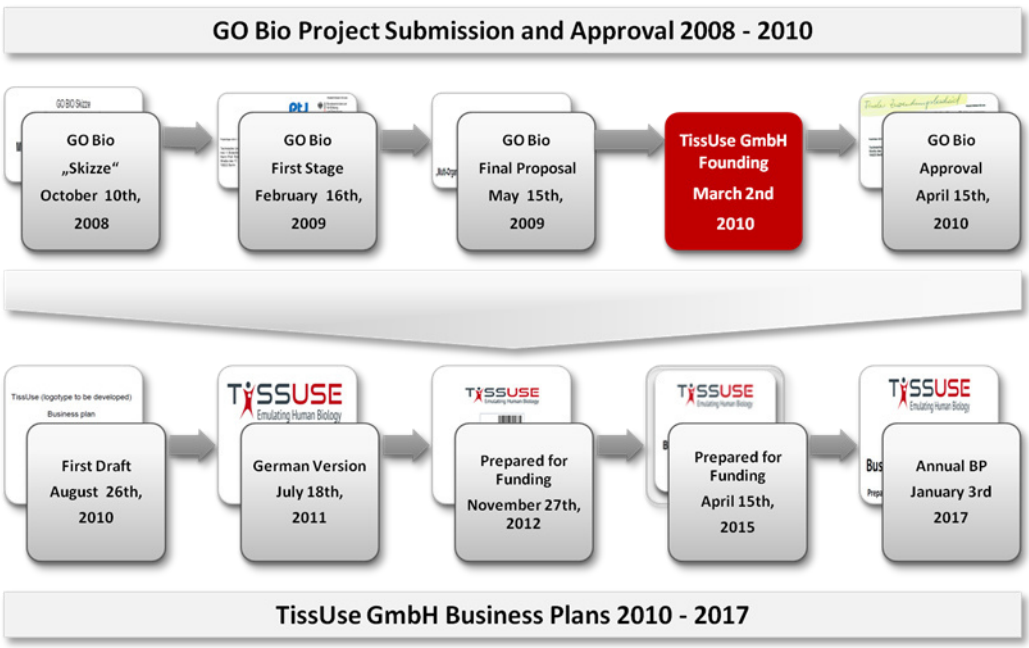

Figure 31: Timeline of Project Proposals and Business Plans

This pathway from the first proposal *"Skizze"* in 2008 to the latest version of TissUse' Business Plan from 2017, is demonstrating, that a radical innovation can be created in a German ecosystem. Strongly supported by the GO-Bio initiative and the experienced entrepreneur, TissUse GmbH is today a successful, growing biotech company. From the open innovation perspective of in-bound and out-bound knowledge transfer, open innovation scholars identified strong tendencies to outside-in technology transfer (Gassmann and Enkel, 2004). The strong ties between TissUse and the TUB enabled the foundation of another spin-off, developing a 3D printing technology for organs from living cells. The company *Cellbricks - Next Generation Bioprinting* was founded in 2015 by one former GO Bio project team member. The head of Medbt RL and UM are dedicated mentors to this technology spin-off. This inside- out approach is evidence for the intensive adoption of the open innovation concept (TUB, 2019).

5.2.6 TissUse' Radical Innovation - The internal Perspective

5.2.5.1 The Role of the Entrepreneur

The following paragraph is focusing on the theoretical category: *Entrepreneur*. The in-depth research about the spin-off organization allows to draws a picture from different perspectives. On one side the longitudinal data collection provides a fine grained internal view on what is going on at the different stages of the organizations innovation processes, and on the other hand, especially the pilot interview with the consultant SD provides an external perspective. The entrepreneur and CEO (UM) himself, illustrated at the *Charité Entrepreneurship Summit Panel* discussion his owns perspective, which adds additional value to the findings. Notwithstanding, that the researchers final evaluation and conclusions broaden the perspective further and summarizes all different perspectives.

Implementing the data from the panel discussion: *"How to Structure the Financing of your Start-up - Venture Capital and Other Options for Founders"* (Charité Entrepreneurship Summit, 2011), where UM emphasized and illustrated his own transformation from being a *creative inventor* into the *inventive practitioner*, added significant value to the research study. The following Figure 32 is illustrating a snap shot of the German biotechnology sector, focusing on the specific capital demand and the requirements for the profile of an entrepreneur at the early stage of founding. The diagram is based on the CEO's personal draft document, which he prepared for the talk.

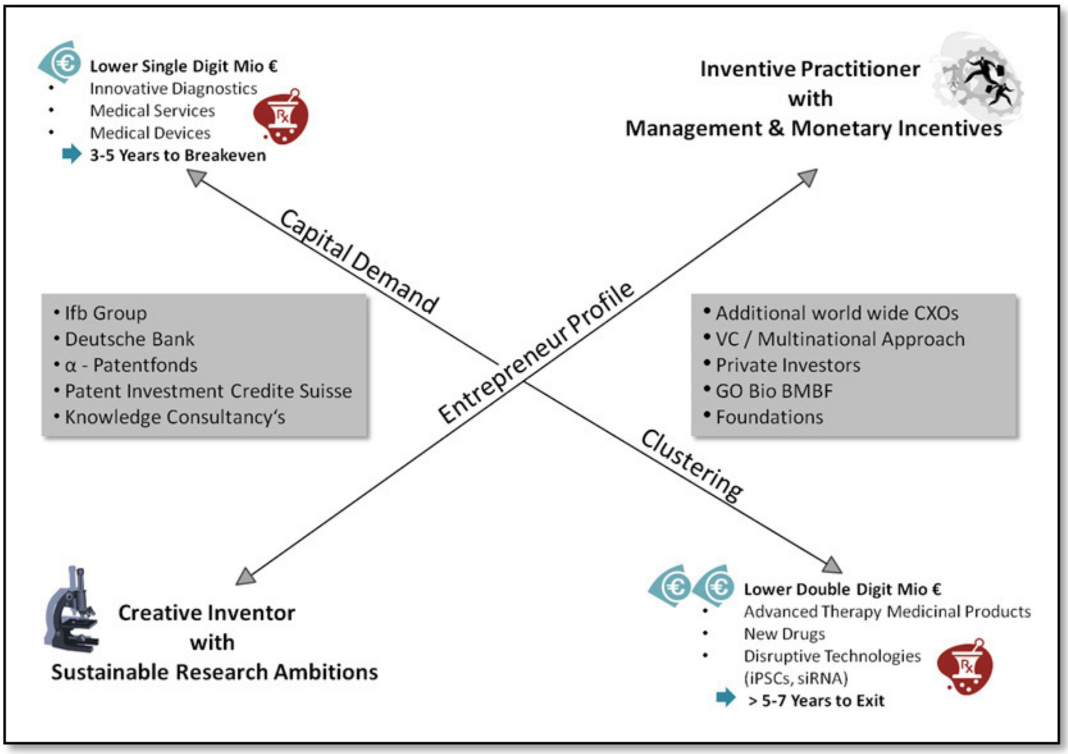

Figure 32: Entrepreneur Profile & Capital Demand,

Created by researcher, based on spin-off CEO's personal draft diagram

As shown in the diagram, radical (here disruptive) technologies are demanding lower double digit Mio € investments, with potential 5-7 years to exit. This cluster consists further of new drugs and Advanced Therapy Medicinal Products (ATMPs) which is demonstrating the high demand for these innovations (EY, 2016).

The following quote from this panel discussion emphasizes, that the German biotechnology sector is not used to radical innovation, which underlines the uniqueness of the single case study. UM stated the following:

> "*But what I have learned during this process [founding 5 biotech companies]; that is high product quality, high process quality, smooth human resource management and later stage, let's call it incremental innovation, here in Germany the favorite innovation, but we are not delighted for radical or cutting edge technologies." (Charité, Panel Discussion, Spin-off, UM)*

Furthermore, recruiting the team and the importance of the team and the people for success was mentioned by UM. The content analysis of his talk and the diagram leads to new perspective towards the qualities of the entrepreneur for pursuing radical innovation, in a German ecosystem.

Entrepreneurship is one of the most influential theoretical categories, arising from the single case study. Based on the data evaluation of the longitudinal data collection, the team member interviews and UMs own statement during the panel discussion, this theoretical category is evaluated comprehensively to provide a deep insight into the single case and the role of entrepreneurship in developing radical innovation. Especially the qualitative evaluation of the longitudinal data collection provided evidence, that entrepreneurship is the most important activity during and before the formation of the spin-off. In context with this overall study, the entrepreneur is the driving force of all other activities; he is also the initiator for many partnerships (i.e. The Consortium early in 2008).

5.2.5.2 Success Factors and Business Location

The success factors from the spin-off perspective are strong related to the GO-Bio project, because at the point of time, when the interviews are conducted, the team was part of the research group at the TUB. The interviewed team members perspective influenced in two ways, firstly by the culture of a research group, but secondly also as team members of a spin-off, a company with a commercial perspective. Nevertheless, the spin-off organization is at its early stage. In contrast to the SMEs, which participants have longstanding carriers, the spin-off team members are sharing their fresh experiences from the newly founded organization. The following figure is illustrating the semi-quantitative analyses of the identified success factors.

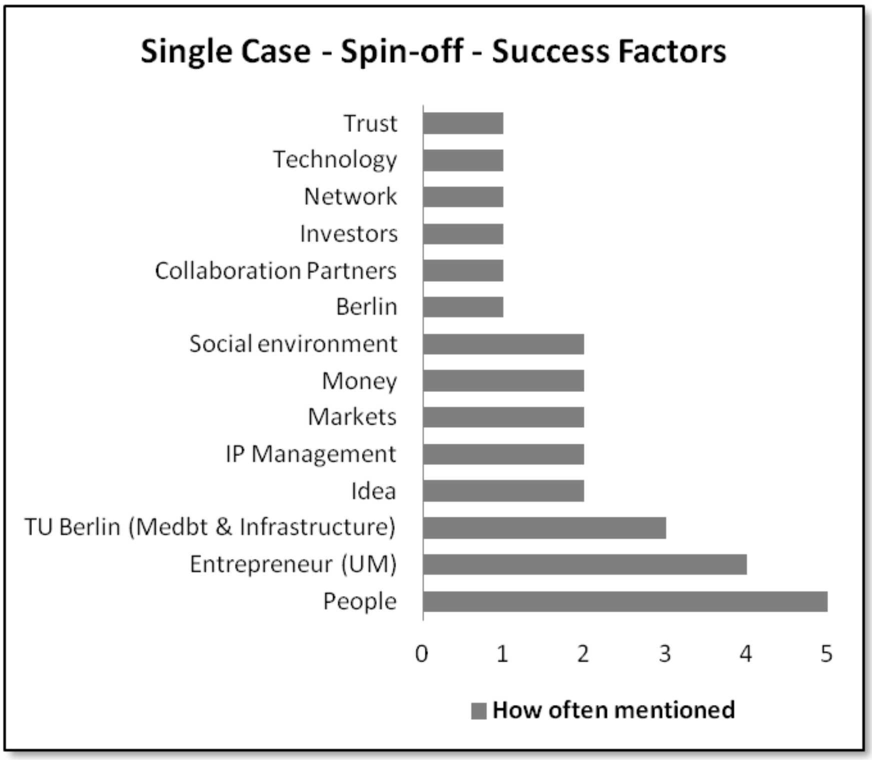

Figure 33: TissUse' Success Factors

Order of magnitude: 5 = high, 4 = moderate/high, 3 = moderate,

2 = moderate/low, 1 = low (Miles et al., 2014)

Source: Author based on Single Case Interview Data Collection.

The semi-quantitative evaluation approach for this part of the interview data was chosen to illustrate the personal perspectives of the spin-off team members. Their statements regarding the success factors are demonstrating their perspective in the second year after founding TissUse GmbH. Here, in compliance with the identified theme, **People** is the most often mentioned success factor, followed by the experiences, expertise and influence of UM, *the Entrepreneur.*

Again, this leads to a more fine-grained analysis of the participants statements. Even if the magnitudes are clustering the importance of the factors, if a factor was only mentioned ones (1=low), these factors are of importance from the particular team members perspective.

To develop the theory of people in context with the outcome of the single case study, the terminology people stand for human capital resources. These resources are the building block for creating radical innovation in context with this study. Therefore people, respective human capital are the most important success factors.

The mentioned success factors are described more in detail in the next sections, but one factor regarding the location, the Technical University Berlin, with its Institute for Biotechnology and the department of "Medizinische Biotechnologie" (Medbt) with its laboratory, technical equipment and infrastructure earns more attention. Especially for a spin-off company, a deep tie relationship with their academic mother organization, in this case the TU Berlin is of great importance. On one side, the research oriented culture is similar to a "breeding station" for the young technology, and on the other side, the entrepreneurial spirit of the serial founder (UM) is inspiring the team to force the technology development to become commercially available. Due to participant observation at several meetings, the researcher was able to experience the commitment and enthusiasm of the team for reaching the different milestones of the GO-Bio project (participant observer at meetings .

By applying the grounded theory methodology (Glaser and Strauss, 1967; Corbin and Strauss, 2008), these described success factors were included in coding the data and identifying the theme and the theoretical categories. In the following section, the theme of people and the related theoretical categories are described more in detail. In addition the findings are strengthened with representative quotes by the spin-off team members and the entrepreneur to evaluate the success factors more in depth.

- *Success Factor - People*

The broader meaning of people in context with the spin-off organization is human capital in its function as employees, respective team member. The more focused definition is narrowed down to the specific function of the team member and their role in regard to the specific GO-Bio project. In a team of 15 people, and with the complexity of the "Human-on- a-chip" project, the specific expertise and experiences of every single team member is of great importance. This is illustrated by the following quote, describing what people bring in:

"People with the certain and the right background and skills."
(Interview, Spin-off - GL, Q1)

Mutual trust due to a personal relationship, competencies and special knowledge, i.e. in IP management are also prerequisites for success.

"People - the fact that I know Uwe [UM] for more than 20 years. Silke [SH] worked for Uwe many years and therefore I know that she is the right person for IP." (Interview, Spin-off - RL, Q1)

From the beginning of the project and foundation of the company, the roles. i.e. for IP management were clear defined. As a consequence SH functioned as the IP and project manager.

Another important human capital related success factor is the attitude of the single team members. Here a highly motivated team is envisioned. The fact, that the majority of the team members is between 25 and 30 years old, is another success factor.

"The environment of the TU Berlin - many students, young people with ideas and power are the perfect environment for success."
(Interview, Spin-off - RL, Q1)

"All the involved people are highly motivated." (Interview, Spin-off - GL, Q1)

Regarding the highly motivation of the team members, the researcher herself experienced this during an IP related meeting in early 2012 at Medbt TUB. The researcher was very impressed by the high confidence, motivation and professionalism in which the inventors/scientists presented their ideas. They took full responsibility for their results and discussed questions very openly and with profound scientific knowledge.

- *Success Factor - Entrepreneur*

There is no doubt about the strong influence of every entrepreneur in a newly founded company. Nevertheless, for the spin-off company, especially the interview participants emphasized this in a repetitive manner. Therefore, without a dissentient vote, the commonly agreed success factor is the CEO UM. His leading role is emphasized by the following quote:

> *"A good CEO [UM] with experiences. Most of the founders do not have enough experiences in science as well as business. It is not enough to be experienced in one of the areas." (Interview, Spin-off - RH, Q1)*

Here the importance of the entrepreneur, as the scientific and business leader at the early stage of the organization is demonstrated from a team members view. This is discussed more in detail by evaluating the role of the entrepreneur, based on UM's participation in the Charité Entrepreneur Summit Panel Discussion (see 5.2.4.1).

As already cited under the theme people, in addition, the long-term personal relationship between RL and UM is one crucial success factor. The influence of mutual trust and believing in the others strength is important to start a high risk program, like the development of the Human-on-a-Chip platform.

- *Success Factor - Technology*

The idea and realization of the radical innovative technology of the Human-on-a-Chip is from the scientific and the economic perspective, the competitive advantage of the spin-off company. Therefore the chip-technology itself, with all its complexity is an important success factor, as stated like the following:

> *"The Technology [of the chip] itself." (Interview, Spin-off - SH, Q1)*

Another enabler is the access to newest technologies due to the research infrastructure at TUB (i.e. 2-Photonenmicroscop). The chip-technology is the building block for the product and market positioning of the company. With this new to the market technology, animal testing can be exchanged by emulating the human body and its functions in the field of substance testing.

Success factors are not limited to specific facts or circumstances. In context with the technology, the process of technology transfer was mentioned as a success factor:

> *"The transaction of the GO-Bio project into TissUse GmbH, that means the market positioning and the product positioning."*
> *(Interview, Spin-off - RH, Q1)*

This statement emphasizes the importance of the transfer of a governmental funded project into a commercial organization. The technology transfer is the underlying process here, the enabler are the entrepreneur and his team. Interestingly, at this early stage, this team member is valuing the transformation of the scientific project into a business as one already existing success factor. This statement demonstrates the strong commitment and identification with a successful journey towards the radical innovative technology in a commercial environment.

- *Success Factor - Knowledge*

Knowledge as a success factor, has to be linked to the team members expertise and skills. Here, the knowledge to handle IP gains special intension. Two interview participants are mentioning SH's experiences and expertise in IP management as a valuable success factor:

> *"Silke [SH] worked for Uwe [UM] many years and therefore I know that she is the right person for IP." (Interview, Spin-off - RL, Q1)*

> *"Good IP management." (Interview, Spin-off - RH, Q1)*

Again, the entrepreneurs/CEO's scientific, as well as his business background, expertise and network of people is mentioned in context with knowledge as a success factor.

- *Success Factor - Idea*

Every great invention is based on an idea. In case of the spin-off company the entrepreneur and CEO UM had this idea for several years and mentioned it in a co-edited book already in 2007 (Marx et al, 2007). But nevertheless, the team members are committed to this idea and the importance for success, as stated by one participant:

> *"The idea behind the project, the idea which is marketable and which gives financial success." (Interview, Spin-off - GL, Q1)* [3]

This quote also implies, that there is commercial value in the idea, when it is mature and ready for the market.

UM's role as the head of ideas and the driver behind the program was mentioned by the team members several times. In regard to the mentioned success factors the following quote is supporting this:

> *"The driver, head of the idea is Uwe [UM], who brings all the important people together." (Interview, Spin-off - GL, Q1)*

Another evidence for the confidence of the team members that the chip-technology will succeed. The source of ideas is in addition linked with the young team of students with *ideas and power.*

- *Success Factor Partner*

The complex and unique chip technology needs a strong network of partners with expert knowledge. Therefore the closest collaboration, the TUB is one *basic* success factor:

> *"The basis is the Institute of Medical Biotechnology with all the infrastructure." (Interview, Spin-off - GL, Q1)*

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3 This started very early, only two years after founding, with the 2-Organ-Ship, with 20 external collaboration partners, one of them was Beiersdorf. First revenues were generated in 2012 (Source: Longitudinal Data Collectin).

The network of external partners and investors (at this point of time the BMBF) are contributing to the envisioned success.

> *"TissUse's investors and collaboration partners."*
> *(Interview, Spin-off - RH, Q1)*
> *"The network, without it, the GO-Bio project would not be possible". (Interview, Spin-off - SH, Q1)*

A successful partnership is based on trust, and needs a stabile social environment. These two success factors are present:

> *"The social environment is also key for success." (Interview, Spin-off - RL, Q1)*
> *"Trusting each other is also one of the basics to succeed."*
> *(Interview, Spin-off - RL, Q1)*

- *Success Factor - Finance*

Without seed funding, especially in the science and technology based biotech sector, there is no commercial success. One of the big advantages of the GO-Bio project is the non-diluting governmental funding of the Human-on-a-Chip project (appox. 3 mio €). This enabled the entrepreneur and his team to start developing the technology as a research group, with no influence of external shareholders. In this case the investors are represented by the BMBF and their respective project managers. The scientific requirements and market opportunities for winning the funding of the GO-Bio project are high. Gaining this funding after a two phase evaluation process, is a privilege in the German Biotechnology community, since less than 10% of all applicants are gaining the funding (Strey, 2015).

- *Success Factors - Business Location Relevance*

Two participants out of the four stated, that their success factors are not German specific, they stated that it could be "everywhere". In summary, their mentioned common success factors are the following:

- *"People*
  - *with experiences*
  - *with skills*
  - *motivated*
- *IP*
- *COL partners*
- *Investors*
- *Idea*
- *Market."*

From the perspective of two team members, these success factors are common factors, not depended on the location , or in a broader sense, not country specific. In other words, the factors are applicable and possible in any other country.

On the contrary, the CEO valued the specific funding program as an important regional competitive advantage. From the CEO's perspective, and with his long term experiences in founding companies, the GO-Bio funding program is specific for Germany.

> *"Specific is the granting, the proof of concept granting, a specific program we haven't seen in other parts of Europe and probably to this extent you won't get this funding in Asia or the US. So the granting system and the specific knowledge of highly educated engineers and biologists and tissue engineers in Germany." (Interview, SME-C6, UM, Q2)*

This was further supported in context with the influence of Berlin and the academic environment the TUB brings in. The specific environmental culture of the university is one basic success factor, especially from the perspective of the Head of the institute (RL). He described the specific environment at his institute in detail. Here, again, the theme *People* is the central theme. This quote is cited completely, since the content describes the culture of the spin-off team and the cultural environment very detailed.

> *"Berlin is very important and of course Germany. We have a very special approach here, no hierarchy between the members of the group and the head and project leaders. You cannot find this everywhere. Every member has the same right to articulate their opinions, suggestions and ideas. People from the team are acting on "Augenhöhe" (at eye level). This is not common*

in other parts of the world. Students are presenting the projects independently. We work in harmony and Uwe (UM) and I, we have the same opinion how to handle the people. Especially our daily lunch (where every member of the group is cooking for the others) is an important social networking event." (Interview, Spin-off - RL, Q2)

From the researchers professional and academic experiences, this in indeed a *unique, special approach,* to lead and motivate people in an academic environment. In contrary to one statement from the SMEs, where a CEO suggested to lead the team with the attitude: " I am the boss, so follow me", the spin-off team is led by the an "at-eye-level" approach.

5.2.5.3 TissUse' own Open Innovation Business Model Definition

The following findings are important insights into the internal perspectives of TissUse' team members, how they understand their own business model. Here, again the role and influence of the entrepreneur, the IP strategy and importance of partners is mentioned and illustrated by supporting quotes.

- *The right People for the Open Radical Innovation Business Model*

Comparable to the SMEs one participant refused to answer the question regarding the open innovation business model definition. The reason was, that he did not hear about the open innovation phenomenon before. All other team members were able to contribute to this question. Interestingly, these team members had a very clear vision about the open innovation business model. There prompt, comprised and content rich answers demonstrated evidence, that they are committed to the business model of the young spin-off organization. This is remarkable, since only one participant had a long standing professional carrier in the biotech sector. In conclusion, these team members have a shared vision and understanding of their own business model.

The participants are describing their understanding of an open innovation business model from their perspective and role at the spin-off organization. For one participant being open minded in regard of the ongoing research leads to positive experiences.

> *"I am very open about my research and I like to share the results with others. So I have good experiences with being open minded in the research community." (Interview, Spin-off, SH, Q13)*

Here, the open attitude and willingness the share is rewarded in and by the community. Another positive effect of an open business model is described by emphasizing the access and exchange of experienced people.

> *"We will get experienced people to help if needed and the other way around." (Interview, Spin-off, RH, Q13)*

From the peoples perspective, the sharing knowledge and experiences is at the core of the open innovation business model.

Not knowing a specific term, like Open Innovation Business Model, does not imply, that the concept is abandoned or avoided. The fact, that one participant refused to answer the question, is evidence for the observation, that theoretical phenomena are existent, even so that involved individuals are not aware of it.

- *The Leading Role of the Entrepreneur*

The leading role of the entrepreneur in context with the business model is indisputable. One participant replied by pointing directly to the entrepreneurs (UM) open mindset.To demonstrate the importance of noticing UM as an entrepreneur and innovator, the following answer regarding SH's definition of the Open Innovation Business Model is exemplary:

> *"From my perspective Uwe is definitely an open minded innovator." (Interview, Spin-off-SH, Q13)*

This quote demonstrates the influence and mindset of the entrepreneur on building up a company and the underlying business model.

- *The IP Strategy*

> "The objective of intellectual property protection is to create incentives that maximize the difference between the value of the intellectual property that is created and used and the social cost of its creation, including the cost of administering the system."(Besen and Raskind, 1991, p.5)

During the overall data evaluation and the final theory development, grounded in the data, in regard to IP management, only UM mentioned *cross-licensing* as *the* IP management approach, embedded in their future IP strategy. The term was not used by any of the other participants, neither from the SMEs, nor the spin-off. Cross-licensing implies that the IP owner is not only willing to share his or her IP, but also seek to get IPR's from the partner. The process is more an exchange, then simply providing IPR's to a third party. Since UM stated this as an advisable approach, even for their "master" patents, the entrepreneur is willing to share the most valuable asset of the spin-off company, for sure, in exchange for useful IP from the outside. In addition, UM underlined the importance of IPR's by his short definition of an open innovation business model like the following:

> "*License-out and license-in on fair conditions all those technologies from my company and the partners." (Interview, C6 - UM, Q13)*

Interestingly, he reduced the definition of an open innovation business model to the process of in-and out-licensing technologies. On one side, this implies the importance of IP and also opens the space for broader concepts of sharing IP. Cross-licensing is defined as the exchange of IPR's between at least two parties, based on a legal contract.

In context with external partners, knowledge sharing and exchange are particularly important in the process of IP sharing, as one participant noticed:

"With our IP we are definitely following an open innovation model. We have international collaboration partners." (Interview, Spin-off - RH, Q13)

This statement implies, that even at this early stage, assets like intellectual property are managed with an open attitude.

- *The Importance of COL Partners*

> *"A contrary example is [disclosed MNC], they seem to have an open innovation Business model, but want to survive by using other people's knowledge. They are in reality the anti-definition of it." (Interview, Spin-off-GL ,Q12).*

This response is an excellent example for how the open innovation concept is experienced in the so called "David versus Goliath" setting. A research team, developing a radical innovative technology, which aims to be a paradigm shift in drug development, experiences, that a MNE downgrades the potential of their technology by leaving the impression, that they are in the "real world" demonstrating the opposite of an open innovation business model. Even thought, that this is the impression of one participant, it is an interesting point of view. As an unexpected fact, this rivalry position needs further evaluation. Questions, i.e. why the larger company seems not to be interested or if their intension was only to get information about what is going on, outside their organizations boundaries, arises.

There is still an ongoing debate about the "David vs. Goliath" issue, independent from any industrial sector. It is still present in many business areas. There is a correlation to the SMEs, which also experienced and mentioned this phenomenon. This opens a future agenda for further investigation in context with the open innovation concept. Does company size matter, and when yes, does it hinder or support the adoption of open innovation? Many studies are focusing on whether SMEs or MNE's, but rarely on the facts, what is hindering collaboration

The overall data evaluation of the spin-off organization, including stepping back from the data, and approaching the data collection from different perspectives, led to the conclusion, that the *Right People* and the *Entrepreneur* are the building blocks for developing radical innovation in a German ecosystem. Especially in the interviews, not depended from the content of the questions, the participants mentioned with great emphasis the role of the founder and serial entrepreneur UM. His positive influence was present and described in regard to all five key open innovation activities. Therefore this theoretical category gained more importance comparing to the others. Not surprising, since in newly founder ventures, the initiator and founder of the company plays an important role.

5.2.5.4 TissUse' Success Factors and Open Innovation Business Model Definition

In the following , the success factors and the participants own definitions of an open innovation BM are summarized. To link the internal perspectives of the team members and the CEO, all important facts are assigned to the different categories. To distinguish between the team and the CEO, the CEO's contribution is in italics. The more in-depth, detailed explanatory results of this evaluation are documented in the paragraphs above.

Table 19: TissUse' Success Factors and Open Innovation Business Model Definition

Theme/ Categories	TissUse - Success Factors	TissUse - Open Innovation Business Model
People	*Competent Research Consortium* *Right people/staff* Mutual trust and personal, long-term relationship Competencies and expert knowledge Young motivated people with ideas and power	*Being open minded in the research community* *Access and exchange with experienced people* *Sharing knowledge and experiences*
Entrepreneur	UM only manager with "Company World Vision" Need for experiences in science and business	UM as an open minded innovator UM's strong engagement with China at the early stage of the scientific development has the potential to be the first truly successful Open Innovation business approach"
Technology	*Grant money for POC (GO-Bio funding)* Human-on-a-Chip technology itself Technology transfer process	Collaborative development *License-out and license-in technologies on fair conditions*
Knowledge	*Global view on global markets and early understanding to enter these markets (i.e. USA, Asia)*	Knowlegde sharing with international COL partners IP management with the open innovation model
Idea	*Protection due to early IP filing* Financial and market potential UM as "Head of Idea" Young team as source for ideas	Clear idea and goal definition
Partner	*Local and global COL partners* MedBt with infrastructure and social environment Trust between partners	*License-out and license-in the partners technologies on fair conditions* Partners for knowledge and experience sharing Contrary example of MNE, which claims to have the open innovation BM implemented, but acts not as an open minded partner Typical "David vs. Goliath" situation
Finance	Non diluting grant money for POC (GO-Bio funding)	*-Finance was not mentioned here-*

5.2.7 Summary and Recent Developments at TissUse GmbH

In the framework of the longitudinal, in-depth case study, the researcher conducted a bi-weekly search for news about the company TissUse GmbH, to follow up with recent developments. The company is partner in the consortium of the EU-ToxRisk project, a Horizon 2020 founded program. It is described as "An Integrated European 'Flagship' Programme Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21st century" (EU-ToxRisk, 2016). This program started in January 2016, includes 40 members from federal agencies, academia, SMEs and MNE's from Europe and the US. The involvement of the spin-off company demonstrated their openness and effort for international collaboration. Participate and winning a Horizon 2020 program is another milestone in the development of the young organization. The following internal document is summarizing TissUse pathway from a concept to the radical innovation of the Human-on-a-Chip platform. Figure 34 is also emphasizing the COL partners TUB and the GO-Bio governmental funding initiative. In 2017, TissUse had already 21 pharma partners and 7 commercial technology transfer projects.

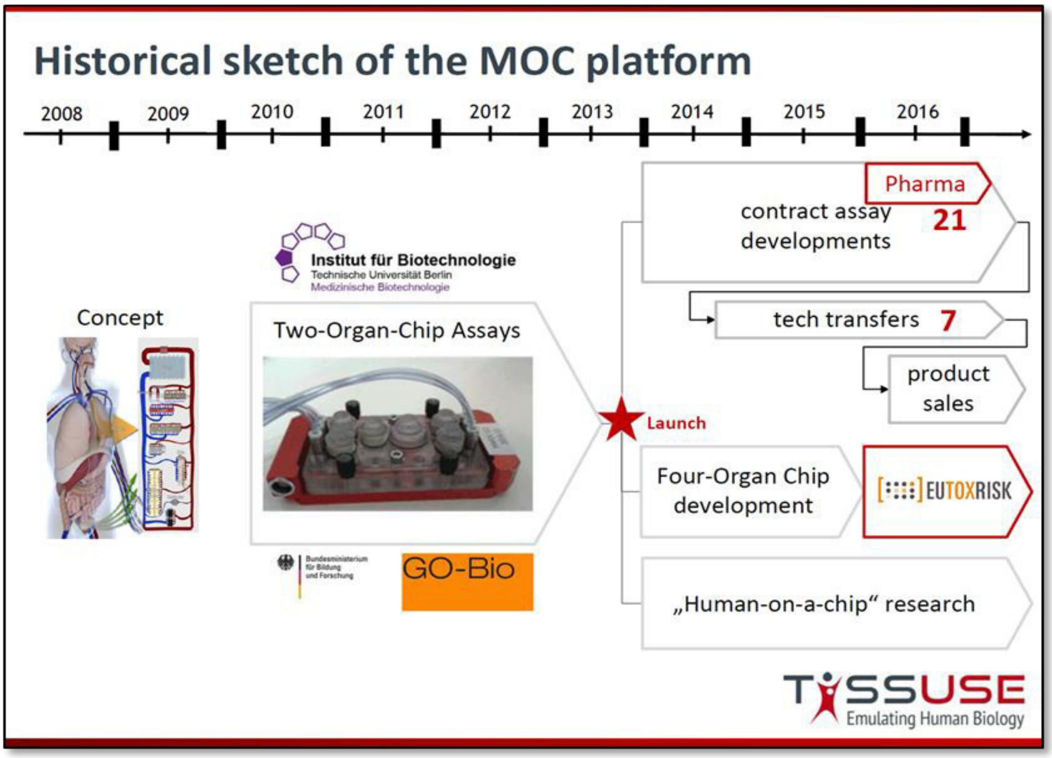

Figure 34: Internal presentation, TissUse GmbH, 2017

5.2.8 Performance Impact of the Right People for Radical Innovation

This research study aims to shed light on the innovation strategy of a biotech spin-off organization developing a radical innovation in a German ecosystem. The in-depth, longitudinal case study of the pre-founding, founding, and product development stage provides a multifaceted, fine-grained picture of *how* and *why* the *Right People* are the most important actors for the success of TissUse. By answering the RQs 1-3, this study will add new insights to the innovation literature and provide a better understanding, how radical biotech innovations are created.

RQ1: Is the open innovation concept adopted by biotech companies

In case of TissUse GmbH, the spin-off company, the outcome of the comprehensive research study suggests, that the open innovation concept is present. The initiator and first value creator is undoubtedly the entrepreneur, UM. However, even before the spin-off was founded, he followed an open model of innovation (Bahemia et al., 2018) by involving external COL partners (US consultant; Consortium; Patent Attorney). This open attitude and approach is the strongest indentified pattern in the data evaluation of the spin-off, not only on the individual level. The entrepreneur influenced and motivated his handpicked team from day one, to follow his "world company vision" (Interview, C0-SD).

RQ2 Can Open Innovation enable the development of radical biotech innovations in a German Ecosystem?

According to Yaghmaie and Vanhaverbeke (2019; p.2) in innovation ecosystems, the focal value proposition is the introduction of new products or services. TissUse GmbH is introducing a radical innovation. On the project level, the internal team of TissUse and all external partners are creating the ecosystem for the radical innovation, the MOC technology platform. Here, the internal R&D capacity is driving the search for complementary scientific expertise in external partners. This leads to strong ties with core partners (TUB; IWS; Russia) supported by legal contracts. The early pre-prototype (see Figure 24) of the MOC was an important milestone, and outcome of the collaborative value creation process at the project level. Over time, there was a clear shift from the entrepreneurs scientific responsibility towards the team members decision making responsibility, based on the growing expert knowledge of all team members. From the broader perspective, ecosystem partners are not only research organizations, but also international partners with the common goal of participating in the development of the radical innovation (i.e. US consultancy; research organizations and institutes in Russia and China). All these relationships with different actors in the innovation ecosystem were initiated by the entrepreneur, UM. Another important partner for the project is the Federal Ministry of Education and Research (BMBF) and the GO-Bio initiative. This program and the non-diluting seed funding provided the financial funds to start the project. All these innovation ecosystem partners are important enablers for the success of the radical innovation project MOC. Nevertheless, this ecosystem was partly existent (i.e. TUB; TTO; GO-Bio), before UM initiated the project, but, the majority of the ecosystem was created by the entrepreneur out of his long standing national and international network. The actors in this ecosystem were selected with the purpose to bring the radical, new Human-on-a-Chip technology to the market. The drivers for success are, again the *Right People* creating and establishing this unique innovation ecosystem. Therefore, to answer RQ2, the findings about the spin-off TissUse suggesting a strong emphasis on the actors (UM; Team; COL Partners) as the enabler for developing the radical innovation. Here, the outcome of this longitudinal study on the organizational, project and individual level overcomes the lack of information on the open innovation mechanisms in more detail (see Table: 18, p.195).

RQ3: How does the evolving Business Model look like?

Spender and scholars argue that the startup phenomenon and open innovation are closely related Spender et al. (2017; p. 4). Since the research study about TissUse is focusing on a startup organization, it is not surprising to learn, that the open innovation concept is adopted and adapted.

The most important outcome from this study is that the evolving *business model* is not a static one. The different developmental stages, especially for a spin-off organization forcing the ongoing business model innovation, with strong emphasizes to a platform design. As a radical innovation driver, the spin-off organization benefits from the adoption, but also adaption of open innovation, by actively forcing the in-and outflow of knowledge, the coupled open innovation mode (Gassmann and Enkel, 2004). This coupled mode is strengthened due to the entrepreneurs willingness to cross-license TissUse's IP, articulated as his understanding of an open innovation business model.

As the CEO articulated his own definition of the business model, he is willing to exchange valuable assets like intellectual property with external partners (Henkel, 2006). All participating team members emphasized the importance of openness to collaboration and networking partners (Downs and Velamuri, 2016). The MOC technology platform, developed by TissUse is a radical innovation and new to the biotechnology sector. The successful exploitation of this type of technology requires different managerial, organizational and strategically prepositions (Bower and Christensen, 2010).

The theory for this specific business model, the causality and interdependence of the evolved theoretical categories: *Technology, Knowledge, Idea, Partner and Finance*, and their role in context with the 5 key Open Innovation activities are implying that TissUse' business model can be defined as a business model ***beyond*** Open Innovation (Kunz and Lloyd, 2017). In the ongoing literature review, focusing on comparable case studies about radical innovation, the researcher could not identify any new sources. Bahemia et al. (2018) argue, that in case of a radical innovation project, the early stages are following a closed model of innovation, to protect the idea and generate more time for preparing the IP application. For TissUse, the entrepreneur filed the most important IP before he shared the *Idea* with the expert consortium in 2008. He created an open business model even before the spin-off was founded, with the purpose to protect the value creation from *day zero*. Important to notice is, that he took the full risk, since the project had no external funding yet. This is one argument for claiming, that TissUse business model is ***beyond open innovation.*** Compared to existing open innovation approaches in the biopharmaceutical industry, outlined in the literature review (Chapter 2), it can be concluded that SMEs, in this case the spin-off company act much more flexible and technology driven, then large companies. Brunswicker and Vanhaverbake (2011; p.32) argue in the title of their publication: *Beyond open innovation in large enterprises: How do small and medium-sized enterprises (SMEs) open up to external innovation sources?* that 42 % of biotech companies (137) are "full scope" searcher for external innovation sources. This is supporting the outcome of this qualitative study by results from a quantitative survey across different sectors.

TissUse' Business model can be defined as *beyond* open innovation, since the open innovation concept was not only present from the pre-founding stage on, also the team members, board members and close collaboration partners are literally "living" the open innovation concept.

Furthermore, *beyond* open innovation is applicable to the business model of TissUse GmbH, since the value creation and value capturing process at this organization is successfully driven by its open minded entrepreneur and TissUse's team and international COL partners, embedded in a self-created innovation ecosystem *beyond* the borders of Germany.

Summarizing the adaption and adoption of open innovation concept at the organizational level leads to a broader perspective, but provides in addition new insights in to the biotechnology sector. Since TissUse was created as a spin-off organization, this longitudinal study provides a rare case with in-depth insights.

In conclusion, the findings, how radical innovations are transformed into novel technologies, products and services are valuable contributions to the body of knowledge in innovation management. Since the researcher conducted the study from the practitioners' point of view and the demand for connecting theory with practice, both areas will benefit from the outcome of this research study.

5.3 The Adoption und Adaption of the open innovation Concept

5.3.1 The Biotech SMEs - External Perspective

The five cases from Germany and the Netherlands, covered by the multiple cases are chosen as a representative sample for this study framework. Since the researcher has longstanding experiences in the life science sector, in addition to the collected primary data, the interviews, observations and in some cases, participant observations are broaden the picture. The researcher applied analytical thinking, but also creative thinking, by stepping back from the data and approaching the findings from a practitioners perspective (Glaser and Strauss, 2008). This was done by asking the question: What can the participating companies gain from this study; what helps them, do become more innovative, what can they learn from each other? The identified aggregate theme for the SMEs is grounded in the aggregate theoretical dimension of **Partnerships**. Besides the findings from this study, the biotechnology industry is an excellent example when it comes to partnerships. Often the foundation of a company starts with a university - industry partnership, by technology transfer of scientific inventions. Interestingly, by going back to the management and innovation literature, there are only a few articles covering partnership and innovation, most of them are related to human relationships in a human resource and organizational context.

In context with this research study, **Partnership** is the abstracted theme, grounded in the data evaluation about the SME`s. All other categories are related to it, the term partner and its meaning in correlation within and outside their organizations was frequently mentioned by all participants. Not only the frequency of appearance, but also the constant data evaluation of the empirical themes, based on the coded data, led the researcher to the conclusion, that the logic and consistent, theme of the multiple case study is partnership.

Partnership in business has a longstanding history and is the foundation of many international success stories. One prominent example from the past is Thomas Edison, J.P. Morgan and the Vanderbilts, who collaboratively founded Edison

Electric Light Co. in 1880, the cradle of the electric light bulb. More recent examples are Larry Page and Sergey Brin, who founded Google in 1998 (Bloomberg, 2015). Even more representative for the scope of this study is the founding of Genentech Inc. by venture capitalist Robert A. Swanson and biochemist Herbert Boyer, in 1976. Genentech is considered as the first biotechnology corporation in the life science sector.

A blog article by Joel West cited Perkins (2015) by emphasizing that in an IO ecosystem: Having "know-who" is far more effective than just having "know-how".

The know-who is implicating that there is a strong demand for the right people and organizations in an open innovation ecosystem. Therefore partnership is an adequate abstracted concept for the open innovation phenomenon in biotech SMEs.

5.3.2 Innovation Partnerships

The dimension of partnership has to be related to the context of this research study. The overall data collection and resulting data base is the foundation to define partnership and its relationship to all other theoretical categories. Especially the identified empirical themes are providing profound insight to define, describe and link the theme partnership with all other evolving categories.

Partnership in context with this part of the research study can be defined as the driving force for value creation trough innovation. Partnerships can be established at different levels, i.e. between individuals, between individuals and organizations and between organizations itself. More precisely, the individuals can be managers, employees, team members or private persons. The organizations can be companies, public or private research organizations, finance companies and institutions, universities, national or international regulatory institutions, national or international governmental and society organizations. This complex dimension demonstrates the abstracted level of partnership in an open innovation ecosystem, characterized by requiring the perfect orchestration of all capabilities (Torkkeli and Mention, 2015).

One of the most demanding conditions for companies is to innovate and gain competitive advantage in their markets. In the biotech sector, products and services are based on intensive and expensive R&D efforts, with a high risk of uncertainty. These preconditions are applicable to all of the dedicated biotechnology firms, involved in this research study. To elaborate further on the conditions for partnership, the OECD definition of biotechnology serves as a reminder for the scope of research:

> "Biotechnology is defined as the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services (OECD, 2005)."

Even if the five SME biotechnology companies, are producing different types of products and services, they all would and could not survive without collaboration with external partners. The data evaluation results demonstrating this in the frequently appearance of the empirical themes, i.e. *importance of external competencies*, *importance of external expertise, influence of external funding, support from external partners and attract potential external partners.* An often mentioned attribute is, finding the *right partner with complementary expertise (Interviews, all SMEs)*. This implies the importance of external competences and experience fitting to the needs of the respective company.

5.3.3 Partner - Technology, People, Value, Finance, Knowledge and Idea

In the following paragraph the relationship between the theme **Partnership** and the theoretical categories: **Technology, People, Value, Finance, Knowledge**, and **Idea** will be explained in detail. The theoretical category **Entrepreneur**, which is very prominent in the single case data evaluation, did not become a theoretical category here, since the interview question was explicitly narrowed to the role of the entrepreneur at the start-up phase. Therefore all information will be related to the single case, the spin-off company. This does not imply that entrepreneurship plays no role for the SMEs, even for mature companies, but in this research context, the researcher aimed to connect both case studies and gain important insights from the SME c-level managers concerning the role of an entrepreneur at an early stage biotech company.

To come as close as possible to the state of answering the research questions, the success factors and the participants own definitions of an open innovation business model were evaluated to strengthen the new theoretical model. Hence, the focus here is also the theme partnership and the relationship to and between the theoretical categories. The extensive evaluation of the coded data using MAXQDA and self created tables led to a semi-quantitative evaluation of the different categories. This enables the researcher to apply a ranking and compare the ranked categories of the multiple and the single case. The variation of the data analysis added value to the results and is consistent with triangulation of the data analysis methodology (Kelle, 2001). Figure 35 is demonstrating the themes and the ranking of the theoretical categories for the SMEs.

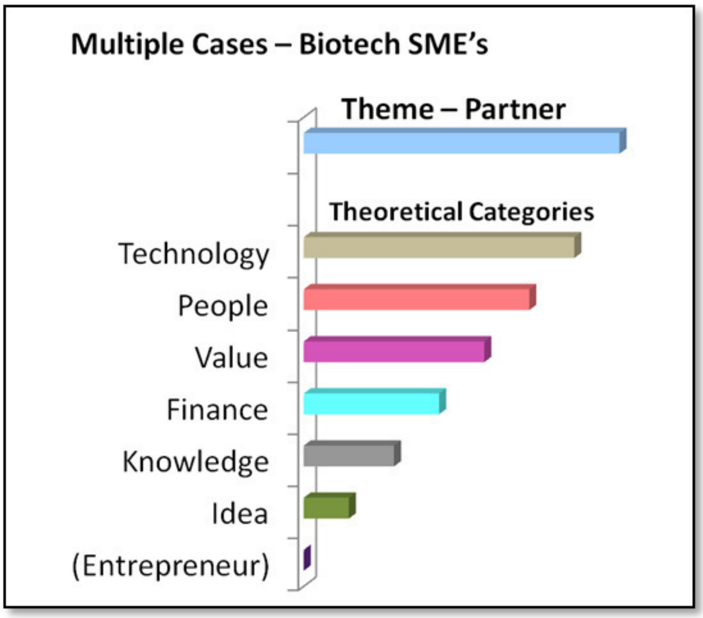

Figure 35: Integrative Diagram illustrating the SMEs Theme and the Theoretical Categories.

In the following section, the resulting theoretical categories for the multiple case are evaluated in depth, by illustrating the interrelation and correlation of the five open innovation activities and the categories by representative quotes and own narratives.

5.3.3.1 Technology

Technology is for the mature biotech companies of great importance, arisen from the data as the most often identified theoretical category. Hence, the biotech sector is science, engineering and knowledge driven, in context with this research study, the attributes and dimensions of the participating companies own technology and the technology of their partners are covered. All biotech products and services are grounded in specific companies own proprietary technology. Therefore the type of technology is driving the demand or no demand for complementary, external technologies from partners outside the company. Their in-house **R&D** activities, based on internal expertise are the starting point to decide what competencies are needed from the outside. If the internal technological expertise is unique and comprehensive, there are tendencies to not seek for external technologies. This implies a closed innovation process at the early stage of **R&D.** This **"**Make" approach was interestingly regretted by one SME participant:

> *"Make: R&D in house; with own resources: This is what we did in the early years. We were focusing on one product in house. It was costly. The market needs are not assumed. The whole product development process was done inside the company. There were no analyses to proof the technology outside the company. Innovation comes also from outside the company. One needs the life cycle approval from the outside. If you develop your technology only research based, you miss the (outside) view." (Interview, SME-C5, Q3)*

Concluding from this statement, it can be a costly, not approved process, if one is focusing on the "Make" approach only. In case of this company, for their second product, they applied the "Make & Buy" approach early on, at the scientific research level.

"Make & Buy: Today the better approach, collaborate with academics and involve them early, get in return the scientific approval early, the setting of the technology/product in the market, Make & Buy has to be well adjusted." (Interview, SME-C5, Q3)

Technology based partnerships, were the external expertise is bought in only, the "Buy" approach are characterized by seeking for supportive technologies, i.e. services like cloning. Again the specific type of their own technology is driving, what is needed from the outside. For the "Make & Buy" **R&D** approach high quality external, complementary technologies, at reasonable costs are crucial.

Rival explanations are important indicators for the in-depth evaluation process of all data. Identified substantive rival explanations, grounded in the data representing alternative explanations about the observed phenomenon, in this case open innovation (Yin, 2012). For two of the participants the "Make & Buy" **R&D** approach seems to be to idealistic and could not work in practice. In contrast, another participant stated clearly, that only "Make & Buy" can work. These contrary positions are important for the theory building. One can find evidence here, that the phenomenon under research provides new insides from the practitioners perspective. None of the different approaches are excluding the others, and it would not be a logical conclusion, to link only "Make & Buy" with the adoption of the open innovation phenomenon. Instead, the developmental status of the technology is driving the decision for the different approaches and the type of partners.

Nevertheless, one SME participant insisted to differentiate between in-house research (**R**) and the potential for outsourced development (**D**):

"Research and Development activities have to be distinguished. They are different things and should be separate evaluated and differentiated. Research activities have to take place in house. The development can be outsourced." (Interview, SME-C2, Q3)

This implies that every technology has different stages of development, before it is ready for the market. Therefore, at different stages of development, partners from outside are needed, or not. In context with this study this leads to the opportunity for more detailed future research in the area of R&D and the open innovation phenomenon. Since for this study five different open innovation activities were investigated, it was not possible to do these more fine - grained analysis, without missing other important information about the other activities.

The term technology by definition covers all techniques, skills, methods and processes used for the production of goods and services (Wikipedia, 2016). Technology without proprietary protection, in form of patents, trademarks, copyrights and trade secrets has not much value. Especially in a high tech sector, like the biotech industry, intellectual property (**IP**) protection is crucial.

> *"IP is basic, necessary and product development makes no sense without." (Interview, SME-C1, Q4)*

In line with the complexity of the technology, is the requirement for a multilayer protection of the respective IP, in this study, patents. Two participants stated representatively the following:

> *"Then you have to create around your core IP a kind of an "onion situation": another skin around it and then another one, another one. So your protection strengthens by having to go through multiple layers to get to the core." (Interview, SME-C3, Q4)*

> *"You must understand your IP-space and how you can protect it. There should be a “wall” around your own IP." (Interview, SME-C2, Q4)*

The **IP** protection of the technology can provide value due to three main functions. First, to protect the intangible assets of the company in form of patents against competitors, second, to create value for these assets in general and through potential in-and out-licensing or cross-licensing opportunities. Third, to demonstrate the value of the technology as the company's asset for convincing VC's, banks and governmental funding programs for external financial investments.

High quality **IP** protection is one basic requirement to gain freedom to operate (FTO). Therefore the **IP** strategy of a firm must be clear and profound at the very early beginning. The protection of the company's proprietary technology must be the starting point at the stage of founding:

> *"You can only start your business on a relevant IP position."*
> *(Interview, SME-C3, Q4)*

Technology in-and out-licensing requires a trustful relationship to external partners. One of the participating companies was facing a long lasting litigation process, which led to reputation and financial losses, besides the costs for the law suit. Even if one cannot reach a 100% FTO status, "proper" **IP** protection is needed. The participant stated the following:

> *"One needs therefore “proper” IP. In case of the lawsuit with company X we were facing a big damage of our reputation during this litigation process. Possible collaboration partners were withholding to work with us at this time."(Interview, SME-C4, Q4)*

Even if the proprietary technology of a company is well protected, in case of a legal infringement process, the reputation, market value and potential for collaboration (**COL**) are jeopardized. Potential partners won't take the risk, to be infected with an assumed negative reputation in the market.

From the perspective of a company the external collaboration partner should value the companies technology as much as possible. Partners should *make your product, their "babies*" (Interview, SME-C5, Q7). In a collaborative partnership, the partners should have mutual respect to their technologies.

The search for the right partners is a starting point for a successful collaboration (**COL)**. The type and developmental status of the technology is driving the decision, which networking (**NET**) platforms to consider. For example, at the very early stage, scientific conferences are (see single case) more appropriate. By reaching a product status, participating in partnering conferences (i.e. BIO Europe, BIO Convention) are time effective and cost/benefit sensitive methods.

Successful companies are often technology leaders, their competitive advantage is grounded in a specific technology. This goes in line with the importance of the leaders comprehensive knowledge about this particular technology.

5.3.3.2 People

People in this context are employees and managers of the companies itself and external scientists, managers, employees and consultants. An important prerequisite for a "Make & Buy" partnership is highly qualified people and scientific **R&D** teams with expertise. The partnerships inside the companies are characterized by an internal innovation culture. Finding the right people with a specific expertise is therefore not always easy. As one participant illustrated by the following statement:

> *"[We] identified two senior former research managers, 76 and 82 years old, from company Y who had own hands-on experience with the production of a [specific] vaccine. Together with them, it was possible to identify the best suited CMO for the process development of a new vaccine with better clinical results compared to the existing (but insufficient) vaccine." (Interview, SME-C1, Q7)*

As described above, it is of great importance to find experienced people to partner with, no matter where and, in this case how old they are. The expert knowledge in a specific field of technology, here concerning a specific vaccine, is basic to the envisioned partnership.

But there are also threats evolving from people interaction with each other in partnerships. The handling of confidential information, especially **IP** related information, in external communication legal frameworks, i.e. Confidentiality Disclosure Agreements (CDAs); Non Disclosure Agreements (NDAs) are requested.

Networking (**NET**) and collaboration (**COL**) activities are important drivers for creating valuable partnerships. There are no doubts, that without both, a company could lose its competitive advantage. The importance is underlined by one participants statement:

> *"The networking and collaboration is key! No network, no ability to be open to collaboration can stuck you in a somewhat lonely situation. The faster you do it, the faster you are on the market and build your track record for your customer base." (Interview, SME-C3, Q7)*

NET is an enabler to find right partners and gain access to the right people. One participant advised to not rely only on your own in-house "champion" (Interview, SME-C5, Q7).

At the level of **COL,** people with a specific mindset are needed. They should be: open minded, creative thinkers, with the willingness to share. A cornerstone is the personal relationship between individuals in the partnership, in-side , between and outside the organizations. The right people for the demanding alliance management are needed.

Personal relationships are basic for effective partnerships. A potential new partnership is often created from an existing network (**NET**) of people. A personal open minded attitude is also important to profit from **NET** partnerships. In regard to this study, repeated personal meetings, i.e. face-to-face meetings at conferences are mandatory.

> *"Nonetheless, by far the most important business development contacts are cultivated via in-person meetings." (Pilot-Interview, C0, Q9)*

> *"Direct approaching people is important. Some conferences, partnering and scientific are good platforms." (Interview, SME-C5, Q9)*

One important function of managers and team members in an organization is the ability to lead. Despite the common understanding, that leader in small business often holding a c-level position, i.e. CEO, CTO, CFO, in biotech SMEs this limitation is rare. Even so, one SME CEO identified himself as the leader. The requirements for successful leadership are described as the following:

> *"Leadership is key to getting your team to where you want to go. Make sure that they are motivated, that they are committed, part of the team of the company. Easy, some sort of a family effort, I would say. Make sure when you are not there that they actually deliver what you set out to achieve and is required from them. Without leadership this not going to happen. Leadership in that sense also means: I am the boss, so follow me." (Interview, SME-C3, Q11)*

In the context of partnership, this implies that there should be a leader, the "boss", but his or her task is it to motivate the team members and make sure that they are committed. Hence, this leaves the impression of an autocratic management style, but the "easy, some sort of a family effort" approach implies to do this in a "nice" way.

In more detail, leadership has different functions and must be linked to the different stages of the value chain. There is a need for leadership at every stage of the NPD process, especially at the project level:

> *"The leadership in projects is important because the people identify themselves with it and become internal champions. They are also responsible for the budget and bring in new own ideas." (Interview, SME-C4, Q11)*

From the partnership perspective internal leadership is an enabler to find the right external partner.

> *"But leadership also means to hire external people which have to offer special knowledge to the company." (Interview, SME-C4, Q11)*

The following attributes of leaders are listed to provide holistic pictures about leadership from the *peoples* perspective:

- Leader identifies and assigns the best capable team member.
- Leader has great respect for his team members.

- Leader develops internal capabilities.
- Leader motivates people, ensures peoples commitment.
- Leader is part of the team.
- Leader has the ability to embrace ideas and foster NPD.
- Leader has comprehensive knowledge about the technology.

Leadership is characterized by trustful delegation of important tasks. In summary, not only one leader defines leadership in a biotech SME, but different types of leaders, with specific expertise are mandatory. This was covered in more detail by one participant:

> *"There is an issue about leadership. A company needs different types of leaders over the product life cycle. [...] Since you cannot find the two or three different leadership types in one person it is extremely rare, that one leader fulfill all required characteristics of the described leadership types." (Interview, SME-C5, Q11)*

5.3.3.4 Value

The theoretical model for value creation trough innovation is the foundation to answer the research questions. Value in the framework of this research study, is linked to the respective open innovation strategy and covers the following types of values, i.e. products, services, technologies, but also value gained from partnerships, i.e. patent in-, out-, cross- licensing, knowledge exchange, technology/service sell- and buy-in.

Value creation starts with **R&D** activities. But for one participating company value creation through own, in-house **R&D**, the "Make" approach is no option. Here we see a rival explanation, grounded in the different business model, a platform organization with no own **R&D** departments. Hence, this company is a very representative example for an open innovation business model, the CEO did not hear about the phenomenon at the time the interview was conducted (2011).

Nevertheless, there is evidence that the "Make & Buy" approach is most valuable. Even so, a risk versus benefits profile has to be established to decide, with whom to collaborate. Again, the specific technology is driver for this decision.

For the value creation trough partnerships, based on the "Buy" approach, it is important that the expected added value is well evaluated. A faster time to market and enhancement of the technology/product/service quality are important indicators here.

Intellectual property (**IP**) in form of patents, are important intangible assets for every biotech company. The **IP** strategy and management with the goal to establish FTO, are internal value creation processes. These processes are supported by managers, team members, financial investments and external partners. These partnerships can be distinguished in supportive partnerships, i.e. patent attorneys, lawyers, tech-transfer organizations, and strategic partnerships, i.e. commercial licensing partners, scientific **COL** partners, and governmental partners.

On one side, the **IP** supportive partners adding value to the quality of **IP**, on the other side, the strategic partners can become in-, out-, or cross-licensing partners, they can add, in return commercial value to the SMEs. This commercial value can be financial, in form of up-front, milestone- and royalty payments, but also value from new strategic alliances through new **COL** partners can be gained.

Freedom to operate is in context with **IP**, value creation and partnerships an important, influential factor. FTO stands for the ability of a company to develop, produce and market products and services without legal liabilities to third parties (Morgan et al., 2008). The value of biotech SMEs IP assets is determined by the ability to practice the technology, claimed under the respective granted patents.

The high quality of **IP** is fundamental and of competitive value, to be protected against competitors and followers, who could copy or "stealing" the technology. Therefore reaching FTO with a robust IP portfolio is the main goal for the chosen **IP** strategy of the biotech SMEs. Even when there is no 100% FTO, all efforts are aiming to come as close as possible. One practical example from a participant is illustrating this fact, also emphasizing, that different supporting patent attorneys provide different FTO analysis results:

> *"FTO grounded your space and the analysis are sources for the informed risk. You will never have a 100% insurance via FTO analysis. But you have to be careful since you can get different analysis from different attorneys. If you mandate 3 different attorneys you got only 1/4 overlapping areas." (Interview, SME-C5, Q6)*

It is therefore advisable, to be aware of the demand for FTO, very early, at the founding stage of a company. A very early, focused FTO strategy for the **IP** positioning of a biotech organization can create later commercial value. The process of filing patents, going through the prosecution process and getting the patents granted, is time consuming and expensive. According to the World Intellectual Property Organization (WIPO) it takes generally over 12 and in many cases more than 18 month (WIPO, 2016) to get a patent granted. From the researchers own perspective and long-term experiences in strategic **IP** management, a granted patent in the life sciences after 24 month is a great achievement. From the international perspective, a more fine - grained view is requested, since the different national and regional patent offices have different timeframes to get a patent granted.

In summary, because of all the facts mentioned above, a strategy for the protection of IP must be clear at the pre-, or at least at the founding stage of a biotech company. The IP strategy has to cover all legal aspects, practical questions, i.e. responsible managers, departments, team members and market aspects, in which countries protection is demanded. In addition, constant market observation from the **IP** perspective is very important to prevent potential infringement. Even with a strong product portfolio and position in the market, one of the participating companies reported a loss of international reputation, and value due to an infringement case. Therefore the manager suggested:

"We observe the international market constantly for possible market confliction. This is important to avoid the infringement of our own patents." (Interview, SME-C4, Q4)

Besides the function to protect the technology/product/service, based on intellectual assets, high-quality **IP** is the cornerstone for potential out- and cross licensing opportunities. Generating value through licensing is a typical revenue source for biotech companies (Tietze et al., 2006; Spurson and Furguson, 2008). On one side the published granted patents and pending patent applications are signaling the field of expertise to potential partners, on the other, the international dimension of the patents are demonstrating the targeted markets. This is demonstrating technological capabilities in order to attract potential external partners for in- and out- licensing. For the licensing or selling itself, **IP** value measurement is mandatory. One participant gave the following advice:

"*You have to do your homework in advance, identify the right model or scenario for the deal. You should come with the business plan for your out-licensing project to provide the licensee with all relevant information. Again a holistic view and stress testing is mandatory." (Interviews, SME-C5, Q5)*

IP portfolio evaluation is an important tool to estimate the value of the intangible assets. There are numerous methods to calculate a "price" for an **IP** portfolio, hence, from the researchers practical insights gained as a senior licensing manager, many factors are influencing the final value of a licensing deal. Therefore, every final contract is looking different and should cover, as advised from the participant, a business plan for the envisioned, new potential business case. In addition it is important to value a signed licensing contract as a legal framework for a long-term collaboration (**COL**) between business partners. In practice, a licensing contract is often accompanied with a scientific collaboration agreement, covering all project development phases and the envisioned outcome. A focused FTO strategy is basic to attract external partners to be willing to in-license a technology, since high quality of the IP is creating a demand and market for it.

> *"The FTO approach is the best and most important for a company's IP strategy. It enables you to in- and out-license IP. Therefore the FTO must be depending and focusing on the commercial success." (Interview, SME-C5, Q4)*

As discussed earlier in this section, a granted patent is of great value. It stands for a so called *negative right*, the owner is allowed to exclude others from using, practicing or producing the specific process or product claimed in the patent. The regional (i.e. Europe), national and international **IP** rights (IPR) are determined by the grants in the specific regions and countries in the world. A typical biotechnology patent should be valid in at least Europe and the USA, covering the traditional health markets, but also in Japan, China and other countries, dependent from the targeted market for the respective technology/product or service.

The statement of one participant, that "getting IP means FTO" must be discussed controversy. Even if the patents are granted, full ownership is clearly stated, there is always a risk of potential infringement from others and to others. As illustrated by one participating company, this risk can lead to a potential infringement case. Important at every stage of the IP management process is therefore to gain as much as possible knowledge about the IP of others in your field of application. This leads to an informed risk, but must become a routine process. Early investments in an FTO opinion by a competent, legal counsel (usually a patent attorney) are additional external sources for protecting the **IP** value.

Value creation through in-licensing of external complementary technologies is part of the **IP** management process. Here again, the in-house technology is driving the demand for external additional, often supporting technologies. The SMEs are gaining additional value from in-licensed technology, since these technologies are complementary and closing gaps in their own inventions. It is recommended to start the process for internal evaluation, what is needed early, at the **R&D** stage of development. In doing so, the organization avoids "reinventing the wheel" approaches and can save an important valuable amount of time to market. The following quote is supporting this:

"It should be clear early on in research what you want to do with your IP. Whether it protect your product or not? A holistic view, especially on the market is important." (Interview, SME-C5, Q5)

Similar to the requirement for own high-quality **IP,** only profound technical and legally approved IPR are in-licensing targets. The licensing process usually starts with first: the internal evaluation, what is needed, second: identification of potential partners, third: approaching the partner and proposing the potential collaboration (**COL**) terms for a licensing agreement. Processing the new partnership requires financial, management and time resources on both sides, especially when the partners dealing with different cultures, i.e. biotech versus pharmaceutical companies. Therefore especially SMEs are facing a kind of "Davis versus Goliath" situation in partnerships. One participant described this situation as the following:

"...larger companies; because they can attack your IP or go around you with a large budget and resources. Especially companies with huge departments, with many legal IP people."(Interview, SME-C3, Q6)

This statement describes the un-proportional preconditions of potential partners of different organizational size. Another barrier for successful partnerships can arise from divergent IPR acceptance in international dimensions. One participant mentioned China, as an example. These special constraints were feasible in 2011, when the interviews were conducted. Recently, China is with 1,3 million the leading and fastest growing country regarding new patent applications national, with an increase of 21,5% from 2015 to 2016 (WIPO, 2018). China is listed after the US and Japan, number three in the world regarding international (PCT) patent applications (WIPO, 2018), with an outstanding increase of 44,4% from 2015 to 2016.

Nevertheless, countries with a different history and acceptance concerning the value of **IP** could become a threat to the SMEs IP strategy. On the other hand, granted patents and patent applications have a positive signaling effect to potential external partners. Even the pending patent applications are of great value, since they demonstrate potential future value and technological advantage (Hoenen, et al., 2012).

Value is created due to the signaling effect of granted patents and patent applications to the outer world and potential partners. Especially the granted patents are evidence, that a technology or product is proven by an authority (international or national patent offices). A granted patent fulfill the requirements for novelty, including an inventive step and has specific utility. Since granted patents are published and valid for 20 years, in case of no infringement. Even so, a granted patent demonstrates only value, if it is in use and exploited in form of innovative technologies, products or services.

These IP data can be obtained by the patent office databases, which are publicly available (i.e. Espacenet, Patentscope).

Collaboration and networking is a key activity for biotech SMEs. Collaborative partnerships are important sources for value creation. Interestingly, one participating company emphasized, that a high percentage, 80% of their **IP** comes from partnering with external partners. They have a very strong own IP portfolio, but also are used to handling all challenges, which shared **IP** is bringing in. So, this company is a good example for value creating partnering. They describe their in-licensing approach as part of the IP management process as the following:

> *"Since today 80% of our IP comes from partnering and is shared IP we have established this process very well. If we discover new drugs we file IP, so there is not so much room for optimizing this." (Interview, SME-C4, Q5)*

This indicates, that, depended from an established **IP** management process, even a large number of shared IPR is manageable. Even if partnerships based on shared IP can generate more value, it can cause asymmetric expectations between the partners. These expectations could lead to issues between the partners, i.e. one party claims an unrealistic proportion of ownership of IPR's. One participant is illustrating this:

"External partners with a policy to demanding shares of the IP in any collaboration project case, regardless of the extent of their input." (Interview, SME-C1, Q6)

To avoid the risk of conflicts between the partners, the early set up of legal contracts is mandatory. Especially in shared IPR's the contribution of every party must be declared in legal documents to demonstrated due diligence in every step of the **IP** management process. In not doing so, there is a high risk for the future, to challenge the value of the intellectual assets, gained from the partnership.

From the perspective of a biotechnology SME, the partnerships with pharmaceutical organizations are, again illustrated as "David versus Goliath". The requirement to meet at eye-level are the following:

"Since a small biotech company is compared to pharma like "David & Goliath" the partner has to respect your technology. Everything should be put on the table. The partner which are used to collaborate should be able to know about each other's strengths and weaknesses."
(Interview, SME-C4, Q8)

Therefore, collaborative partnerships are based on respect and openness to share not only strengths, but also weaknesses. Like in any successful relationship between partners, mutual trust and respect is a prerequisite. Despite the legal framework, every collaborative project includes clear goal definition in a mutually agreed project plan based on the strategic fit. Over the project lifetime all participating parties should bring in critical self-awareness and fairness. All participating members should feel secure and trusted.

In context with the theme partnership, the definition of leadership must be approached from the perspective of value creation inside and between organizations. Leadership from the participating managers perspective is a key activity for value creation. Interestingly, only one CEO identified himself as *the* leader in his organization. For all other participants, leadership is a function of different individuals, at different stages of the value chain. The insights from the

CEO of the virtual platform biotech SME are illustrating the fact, that shared leadership, based on different expertise and knowledge is of great value (Ensley, et al., 2006). He stated the following:

> *"All members of the team benefit from each other. If the CEO from his experience and knowledge is not the right person for a specific task he assigns the best capable team member. The CEO follows their decisions based on facts regarding the specific project. In a small company all the knowledge comes from every single member." (Interview, SME-C1, Q11)*

At different stages of the value chain, different types of leaders are requested. Especially in larger, mature organizations, every business unit has the demand for intergroup leadership (Hogg, et al., 2012). These different types of leadership, i.e. with focus on **R&D**, sales, CRM, have the achievement of joint outcomes in common. One participant described the role of leadership in their organization as the following:

> *"Leadership is important through all structures of the company. Large R&D department's needs internal leadership and responsibility for the programs. [...] One has to split of the value chain and involve leadership at every stage. Little teams own their products and are standing behind their programs." (Interview, SME-C4, Q11)*

In a retrospective view, the leadership types are changing of time. At the start-up phase, newly founded ventures are often led by the scientific expert, who invented the technology. At the next stage, when the product is ready for the market, especially in the biotech sector, the leader should bring in expert knowledge about all legal requirements for the product approval process. The third leadership type is needed for the successful positioning in the market; therefore a sales driven leader could become the CEO. For the participating companies, this was only implemented in practice in one case, as stated for the different stages of the product life cycle:

The start-up stage:

> *"At the beginning, the founder is often the inventor/innovator. Her or she is characterized by being creative and open, embracing the ideas und foster them to be further developed."*

The ready to market stage:

> *"When the product is ready for the market you need a leader who is playing all the rules, e.g. from the regulatory perspective knowing and following the FDA requirements. The leader has to be able to be aware of any risk all the time. A type of "Executer" who is more disciplined."*

The product sales stage:

> *"When the product is on the market a sales driven leader is needed. At this stage a commercial driven leader is preferred over the e.g. founder, which are often lacking the conviction of a market driven person." (all quotes: Interview, SME - C5, Q11)*

The following diagram (Figure 36) is demonstrating the different types of leaderships, dependent from the stage of product life cycle.

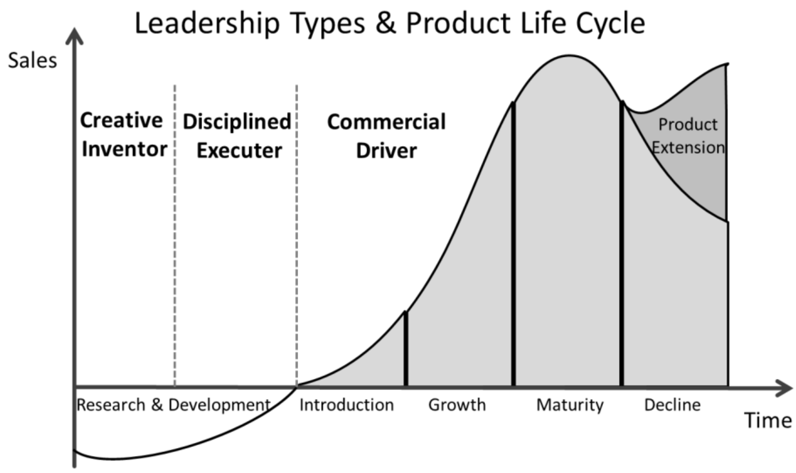

Figure 36: Leadership types and product life cycle.

Nevertheless, which individual acts as a leader, one important attribute is leadership authenticity (Gardner, et al., 2011). Besides his or her influential role, the leader should be fair, know and develop the capabilities of the team members and lead as an example. The leaders knowledgebase is a cornerstone for his or her role. The demand for a constant learning process is illustrated by the next quote:

> *"A good leader should know the subject/technology/product very well. He or she spends much time to learn and never stop learning and is aware of how to learn." (Interview SME- C2, Q11)*

Learning in Action as a leaders attitude and role model function can create a learning organization (Carey, 2000). This is especially in the research intensive biotech industry strongly requested. Other leadership attributes are fairness, trust, and providing security to the team members.

> *The leader has to be fair, he or she has to provide security to the people, develop the capabilities of the people to bring in results."*
> *(Interview, SME-C2, Q11)*

In **COL** with external partners, the assignment of the right leader and team members for a project has different positive effects, i.e. on contract content, negotiation time, and efficiency:

> *"When it comes to interaction with third parties the team defines the goals, the corridor of outcome and the content of the agreement. The team members get the permission to lead the negotiation. That makes the process fast and efficient." (Interview, SME-C1, Q11)*

5.3.3.5 Finance

The financial value of partnerships could be measured by simply counting the income from out-licensing **IP** (gained up-front, milestones and royalty payments). But this does reflect only a part of the overall financial value, based on **COL** with external partners. Since partnerships are grounded on the mutual agreed collaboration and/or licensing contract for a specific project, the financial value has to be projected on future income from new products, technologies and services. Even if financial evaluations, i.e. net present value analyses can predict an expected financial value in figures, the high risk of scientific **R&D** is still present here. Therefore, the exact financial value from partnerships has to take into account on one side the invested money, i.e. in the technology, the **IP**R's, human capital, facilities etc., and on the other side, financial value gained from all types of licensing contracts, new products, technologies and services. Measuring the real financial value is therefore only possible in a retrospective way. As one participant stated, it is wise, to not overestimate potential income from own **IP:**

> *"Never assume that the income from your IP would be huge. [...] The time of high up-front payments is over." (Interview, SME-C5, Q5)*

This statement indicates that there is no guarantee to get the investment made "paid back" from licensees. So the function of invested money in **IP** protection has the following first priority:

> *"The money invested in IP must be used to protect the core assets of the company." (Interview, SME-C5, Q4)*

From the perspective of another participant, the timeframe, when to obtain a licensing partner is influencing the potential financial income from the licensing-out approach:

> *"The rNPV of an "early stage" IP has less value (e.g. € 5.000; 20.000; 40.000) than after reaching clinical Phase I or II. Due to the development process multiples in revenues compared to the value of early stage IP are possible."*
> *(Interview, SME-C1, Q4)*

The further the product is developed, the lower is the risk for the in-licensing or buying partner, and the higher is the price for the offered technology or product. The risk sharing and commitment to incentivize reached milestones is covered in the structure of licensing agreements/contracts (upfront-, milestones- and royalty -payments).

The financial value from innovation partnerships in context with this study is focusing on potential licensing income. A more detailed view on the different stages of the value chain, and different partners, would be an area for future research. For the adoption and adaption of the open innovation concept in innovation management, the SMEs have provided a better understanding of the expected financial income. Their statements are evidence for the fact, that out-licensing is not at the core of their business model.

5.3.3.6 Knowledge

Knowledge, in context with the adaption of the open innovation concept, serves in innovation partnerships as a currency (Bruce, 2012). The partners exchange their complementary knowledge in order to develop their innovative products, or at an earlier stage, to speed up their research project outcomes. The starting point inside an organization is to analyze their own knowledge base in depth to identify gaps and imperfectness. This ongoing process enables the respective individuals of the organization to decide, what type of external knowledge has to be approached outside the boundaries of the organization. Evidence is the following CEO's statement regarding the decision making process:

> *"The knowledge in house is basic to finding the right external partner for the projects." (Interview, SME-C1, Q3)*

On the other hand, it is important too, to constantly screen external knowledge bases for new ideas, fitting to the business model of the SME. Otherwise one could miss opportunities, like one participant suspected:

> *"The whole product development process was done inside the company. There were no analyses to proof the technology outside the company. Innovation comes also from outside the company. One needs the life cycle approval from the outside." (Interview, SME-C5, Q3)*

Especially in knowledge based, research intensive, high-tech organizations, like biotech companies, absorptive capacities playing a crucial role for knowledge exploration from external sources (Lichtenthaler and Lichtenthaler, 2009; Enkel, 2010; Lichtenthaler, 2011). In context with the Make & Buy **R&D** approach one manager emphasized the importance of expertise of their own employees, but also of their partners.

> *"Most important is the expertise of the employees/partners in what they do." (Interview, SME-C2, Q3)*

There is a strong link between expertise and knowledge, since knowledge in a specific domain, field or sector can lead to expertise, when practical experiences are combined with theoretical insights. In context with the role, causality and interaction between partnerships and knowledge, the core activity here is knowledge sharing between the partners. The goal is, to create new valuable knowledge, by learning from and with each other.

IPRs in form of patent applications and granted patents are the legal framework for protecting knowledge. Therefore knowledge in context with **IP** has two different functions: first, knowledge is at the core of **IP**Rs, since the protected technology, product or service is based on that specific knowledge, and second, knowledge about the **IP** process itself is crucial for the envisioned IP strategy of every organization. This implies, for partnerships, that the parties not only share their protected knowledge in form of **IP**Rs, but also share their **IP** strategy, at least in the framework of the respective **COL** project.

As important for their own IP strategy one participant emphasized the knowledge about the value of IP at the different developmental stages:

> "*Therefore IP is important. But basic IP has less value than the further development of the IP, which creates real value for licensing out or selling IP." (Interview, SME-C1, Q4)*

Constant knowledge acquisition is strongly related with constant learning processes. It is therefore important, to reflect on the new knowledge gained to make better qualified decisions for the future. One participant illustrated the different 3 approaches, he and his company identified for protecting their IP:

"There are three IP strategies:

1. Block IP - Blocking anyone's IP around our product/technology never works. It is expansive. It is impossible to manage 600 patents where only 10% are involving the core assets of the company.

2. Protect my product - The "protect my product" IP strategy can help or insure to achieve the market price for your product.

3. FTO - The FTO approach is the best and most important for a company's IP strategy. It enables you to in- and out-license IP. Therefore the FTO must be depending and focusing on the commercial success. The money invested in IP must be used to protect the core assets of the company."
(all quotes: Interview, SME-C5, Q4)

The knowledge gained from their own IP strategy is, that it is impossible to just "block" others IP protecting everything around their own IP. This could be a strategy for big corporations with the respective budget and in-house counsels, but biotech SMEs are not able to afford these expensive, personnel intensive approach.

Therefore the focused "protect my product" and the "FTO" - IP strategies are the most recommended. Another important demand for knowledge about **IP** management in general, is the awareness and constant research about external **IP** in the technology field of the organization. This can be outsourced to the partner patent attorney or counsel, for additional fees. Or, since the national and international patent offices are great resources for such information, patent search can be done in-house on a regular basis. Even if such a constant observation must not be complete, it is advisable to know your direct competitors **IP**. As mentioned earlier in context with **IP** management, it is important to start this process very early, best before the first patent application is filed. All these different types of knowledge and the constant knowledge gaining process are important requirement to approach the right, valuable partners for collaborative new product development (NPD).

In healthcare economics, the ecosystem is characterized by a collaborative approach to gain value from different players with different, often complementary expertise. Networking (**NET**) is often the first step to identify the right potential partner, as one participant stated:

> *"Networking can open doors to the right partners. Via networking you can get access to the right people."(Interview, SME- C2, Q7)*

There is no doubt about the role of **COL** in knowledge sharing with partners, but there are also concerns and experiences from the past, that for a young biotech company it is not easy to handle the **COL** projects with i.e. big pharma:

> *"In the beginning pharma companies had no competencies to handle the collaboration with us. There is also a fear of new pharma companies which are worried about how to handle the results." (Interview, SME-C4, Q7)*

In context with this statement, the "David vs. Goliath" illustration can be applied, as earlier mentioned, in context with **COL**. The SMEs are forced to be taken serious by the bigger corporations. For the participating biotech SME-C4, it worked out over the years, they have recently named over 20 long-term commercial partnerships, besides others, with seven out of the ten world's biggest pharmaceutical companies (Forbes, 2015).

The need for external expertise is one of the driving forces to network (**NET**) and collaborate (**COL**) with external organizations. This process starts early on, before the beginning of new projects, as one participant stated:

> *"No company has everything in house. It is important to identify and analyse timely what is missing to develop the platform. This must happen at the very early beginning of the project." (Interview, SME-C1, Q7)*

Another important requirement, mentioned in concordance with IP management, is the legal framework for every collaborative project. Therefore besides knowing what an organization needs from outside, external contacts, technical and negotiation skills are important for every collaborative approach (SME-C1, Q8).

Every **COL** needs to start with a profound "project plan", covering all partners, their competences and required input. The diverse partners bring in their expert knowledge, i.e. one participant describes their **COL** approach:

> *"Doing research with others means doing proper applied research with an industrial perspective. Otherwise e.g. the filing of an IND cannot be properly prepared. A strategic fit is also of great importance for the collaborative approach." (Interview, SME-C3, Q8)*

From the biotech SMEs perspective, leaders are often the knowledgebase of their organizations. Especially in smaller companies the knowledge of every single member counts:

> *"In a small company all the knowledge comes from every single member. Decisions are made in a very open style." (Interview, SME-C1, Q11)*

The knowledgebase for leadership requires lifelong learning processes and the constant development of internal capabilities. Leadership means also to become the "internal champion" (SME-C4, Q11). Based on their expert knowledge, different types of leadership competencies are needed for the functions in an organization over time, see Figure 36 for Leadership Types.

5.3.3.7 Idea

The idea is the so called cradle for every innovation. In context with this study, the ideas are leading to inventive technologies, partly protected by patents (**IP**). Even so, scientific achievements are based on the scientists ideas how to solve a specific problem by applying scientific knowledge. In case of the SMEs, four have products/services on the market, based on their own propriety technologies. One SMEs business model is based on a project platform, in conjunction with external experts for the respective project. But, there is no question, that they need new ideas to stay competitive in their markets. Important starting point of the **IP** strategy is to protect the ideas behind the invention. For the definition of the term idea, it is important to connect idea with the whole process of value creation. So, idea is strong connected with the inventive technology itself and acts as the source for the invention. This differentiation is necessary, since ideas, in form of thoughts, notions or concepts are not patentable.

For potential new partnerships, it is important to be open to new ideas from outside the boundaries of an organization. This implies an open attitude of managers and employees, to embrace own, internal ideas and external ideas. On the contrary, especially in regard to the FTO, external ideas could become a threat. One participant pointed to the following fact:

> *"External threats to the FTO are the facts that innovation happens every day,..." (Interview, SME-C4, Q6)*

One essential role of leaders is, to motivate team members to create new ideas and share them with the team. If the leader becomes a role-model, his creativity and open attitude can influence others in a positive way. The leaders ability to identify and embrace ideas can foster the NPD process.

> *"Her or she is characterized by being creative and open, embracing the ideas und foster them to be further developed." (Interview, SME-C5, Q11)*

All participants statements have in common, that leadership qualities can be found in every organization, not depended from the specific function or job description. Especially from the CEOs and managers perspective, they value leadership qualities throughout the whole team. Taken into account, that the participating companies are small-and medium sized entities (SMEs), every single member plays an important role for becoming a long-term, successful biotech organization.

In summary, the concept auf partnership is driving the innovation strategies of the multiple cases, the biotech SMEs. To provide a good overview about the causality, interdependence and correlation between the theme **Partnership**, the categories **Technology, People, Value, Finance, Knowledge, Idea** and the **five open innovation activities: R&D, IP,NET, COL and EL**, the most important facts are summarized in the following Table 20. Nevertheless, only the significant attributes, describing the relationship between the theoretical category and the five key open innovation activities are presented. The more in-depth, detailed explanatory results of this evaluation are documented in the paragraphs above.

5.3.3.8 The causal relationship between the open innovation activities and the theoretical categories: Technology, People, Value, Finance, Knowledge and Idea

In the following Table 20, the causal relationship between the theoretical categories and the open innovation activities are supported by first order codes from the data analysis. This table summarizes the statements and discussions provided in the previous paragraphs.

Table 20: The causal relationship between the open innovation activities and the theoretical categories.

Theoretical Categories	SMEs - 5 Key Open Innovation Activities				
	R&D	**IP**	**COL**	**NET**	**(E)L*Leadership**
Technology	▪ Technology type & developmental status counts for external complementary or additional technology ▪ All approaches are possible- make, buy, make & buy ▪ Demand for distinction between **R**esearch and **D**evelopment	▪ Start with profound IP protection ▪ High quality IP protection to gain FTO ▪ Demand for multilayer protection ▪ Out-&Cross Licensing Opportunities	▪ Demand for trustful relationship ▪ Value the partners technology like your own ▪ Threat of negative reputation of COL partners due to litigation	▪ Technology type & developmental status defines best suitable NET platforms	▪ Technology leadership in the market due to technical edge
People	▪ Demand for highly qualified people - experts in their fields ▪ Importance of internal innovation culture	▪ Threat of leakage of confidential information ▪ Demand of legal frameworks for information exchange between partners (i.e. CDA, NDA)	▪ Demand for open minded, creative thinkers, who likes to share ▪ Importance of personal, informal relationship in partnerships	▪ Enabler to find the right people for COL ▪ Existing network - source for new partnerships ▪ Importance of face-to face, in person meetings	▪ Importance of internal leadership - the autocratic leader ▪ Internal champions at different stages of the value chain ▪ Demand for different leadership types dependent from product life cycle
Value	▪ Importance of faster time to market ▪ Enhanced value of R&D outcome due to buy and make & buy approach	▪ Value from shared IP - enhanced quality ▪ Monetary Value from in-, out- and cross licensing ▪ Early focused FTO strategy due to high quality IP supported by expert attorneys ▪ Signaling effect of granted patents	▪ "David versus Goliath" situation ▪ Mutual knowledge of partners strengths and weaknesses ▪ Demand of legal framework & project plan with clear goal definition ▪ Importance of security and trust between partners	▪ Importance of NET as a key activity ▪ Demand to identify potential future partners	▪ Importance of leadership as key activity ▪ Role model function of the leader ▪ Demand for different leadership types (see Figure36) ▪ Leadership role of the whole project team

Table 20 (Continued): The causal relationship between the open innovation activities and the theoretical categories.

Theoretical Categories	SMEs - 5 Key Open Innovation Activities				
	R&D	**IP**	**COL**	**NET**	**(E)L*Leadership**
Finance	▪ Influence of high risk of R&D outcomes	▪ Avoidance of overestimated income perceptions from licensing	▪ Importance of future financial value gained from COL ▪ Importance of financial, management and time resources	-not mentioned here-	▪ Entrepreneur as risk taker ▪ Potential risk at all times
Knowledge	▪ Own expertise drives the type of external demand ▪ Demand for constantly observing the market for external useful knowledge	▪ Knowledge is the core of IPRs ▪ Demand for knowledge about the IP process ▪ Importance of knowledge what FTO means ▪ Demand for constant learning process about own and others IP	▪ Advantage of knowledge sharing between partners of different size and culture ▪ Importance of strategic fit ▪ Demand for profound COL project plan	▪ Demand for NET to identify the right partner ▪ Role of NET to get to know the right partner ▪ Opportunity to share knowledge	▪ Internal leaders provide the knowledgebase ▪ Demand for constant development of internal capabilities
Idea	▪ Demand for legal framework for idea sharing between partners	▪ IPRs protect the idea behind the invention ▪ Awareness of potential threat of external ideas of non-partners	▪ Demand for open attitude towards own and external new ideas	-not mentioned here-	▪ Leadership function to motivate employees and partners to create new ideas and share them ▪ Value of leadership qualities throughout the whole team

5.3.3.9 Causal Mechanisms between Theoretical Categories - SMEs

This section will provide a deeper understanding, how the evolving categories *Technology, People, Value, Finance, Knowledge* and *Idea* affecting each other and influence the performance of the SMEs. *Innovation Partnerships* is the aggregated theme, based on the data evaluation of the five biotech SMEs. It is not surprising, that the SMEs are practicing open innovation with a strong emphasis on their COL partners. Nevertheless, their innovation strategy is driven by the type of *Technology* (product, service, platform), they provide to the market. All SMEs are mature and have products and services on the market. The type of technology is driving their specific R&D approaches, in the range of make, buy, and make and buy. Even so, one SME participant regretted, that they were applying the make approach, a closed innovation model for their first product (C5). Others found the make and buy approach to idealistic (C1; C3). Another important insight was the statement, that Research (R) and Development (D) must be separated and distinguished (C2). This underlines that different experiences of these executive managers (people) lead to different innovation strategies. The protection of their technology is still one of their most important priorities; therefore they all have a profound IP strategy and seeking for freedom to operate (FTO). They have developed trustful relationships with their COL partners, but one SMEs gained negative reputation and experienced withdrawal of important partner due to an IP litigation case. The internal technology development is strongly dependent on highly qualified people (human capital), not only in the field of science. This leads to the category *value*, in this context value creation, but also value capturing. Value creation and value capturing is crucial for every successful business model (Osterwalder and Pigneur, 2010). For the biotech SMEs, specific leadership types have been identified, which are causing the demand for specific qualified managers (see Figure 36). Dependent on the developmental stage, different requirements are necessary for the process of value creation and value capturing. The *creative inventor* is responsible for the *idea* creation in the first instance, the *disciplined executer* will enable the further development, and from the market introduction phase on, a *commercial driver* is needed. To find all these leadership types in one person, is the exception, therefore established partnerships can provide access to people with these specific leadership characteristics. From the *finance* perspective, all biotech SMEs are facing the demand for tremendous investments in high risk R&D. Therefore one advantage of collaboration with external partners, is risk sharing. Nevertheless, the financial value gained trough COL must outweigh the transaction costs, caused by management and time resources. Value creation and capturing is strongly related to internal and external *knowledge* management. Typical open innovation approaches are in-house knowledge creation as a starting point, and complementary, external knowledge sourcing, with the purpose to create value from their own technologies. The big advantages, the biotech SMEs are facing in knowledge sharing with external partners, are the differences in size and culture. They call it the "David vs. Goliath" syndrome, which presents the differences between small biotech and big pharmaceutical companies. From the perspective of the SMEs, these differences can still hinder successful collaborations. The causal mechanisms of the categories *technology, people, value, finance*, *knowledge* and *idea* demonstrating, that the SMEs have adopted the open innovation concept as their innovation strategy, nevertheless, two of the participants did not know the term *Open Innovation.* This implies that there is still a gap between observed business phenomena and the academic perspective. Practitioners do not ask, which innovation concept they should apply, they act from their intrinsic expertise and market knowledge to create successful businesses.

5.3.4 The SMEs Adoption of Open Innovation - Internal Perspective

5.3.4.1 Success Factors and Business Location

For biotech companies, the importance of collaborating with external partners, especially with the pharma industry is one success factor. On the other hand, industry- academic partnerships are also a building block for the SMEs success. But these partnerships are based on the **COL** between people from these organizations.

This interdependence was demonstrated in the responses from the SME participants as summarized in Figure 37.

- *Success Factor - People*

For the SMEs one important success factor are people in general. Hence, this seems to be obvious, people with the right skills, expertise and experiences are envisioned. This plays a role at the individual, team and organizational level. Another influencing determinant in correlation with individuals is attitude. In context with this study, the function of attitudes to process knowledge is of particular importance. Nevertheless, attitudes are more complex and help to maintain and foster self concepts by expressing an individual's central values (Antons and Piller, 2015). The following attitudes are mentioned: perseverance and stubbornness. The role of perseverance can be illustrated by the following quote by Steve Jobs (1995):

> "I'm convinced that about half of what separates the successful entrepreneurs from non-successful ones is pure perseverance."

Supported by this quote, perseverance is an important attitude for success, strongly related with entrepreneurship. Stubbornness, in this context was explained by one participant in emphasizing the attitude: "do your own thing" (Interview, C3, Q1). In this context the meaning is positive and illustrates the way to become successful. Even though, it relates more to one individuals approach and does not imply the relationship to others. People with expertise, experiences, right skills, who are acting perseverant and stubborn. One CEO states his way towards success, as the following:

> *"Stubbornness = don't listen to other people, just do your own thing, otherwise nothing would have happened." (Interview, SME-C3, Q1)*

A to idealistic view on the dimension of partnership is demonstrated by the following, wishful statement of another participant:

"Ideally people from inside and outside the company are connected via friendship" (Interview, SME-C5, Q12)

Even if this seems to be hardly possible, the researcher herself experienced this friendship attitude, especially at this company due to former participant observation. Similar practical experiences were made with people from the spin-off company. So, the friendship attitude in all partnerships might be to idealistic, but evidence from both cases imply, that there is a positive influence on partnerships in general, grounded in this type of personal relationship. More details are provided in context with the single case, spin-off organization.

- *Success Factor - Technology*

The technology itself is an important success factor, explicitly mentioned by all of the participants. At the stage, when their own technologies are robust and propriety, seeking for complementary technologies from outside their organizations is mandatory. External complementary technologies can be acquired via in-licensing, cross-licensing or buying. In case of bigger companies, the technology of interest can be acquired via merger and acquisition (M&A). The following quote is evidence for the added value from the SMEs perspective:

"The in-licensing of technologies from outside the company and the acquisition of companies with complementary technologies and products added value to C4." (Interview, SME-C4, Q1)

- *Success Factor - Knowledge*

Knowledge in form of expertise is required at every stage of the value chain. Here, knowledge based on scientific achievements plays an important role. Biotechnology is very research intensive and requires basic research as well as applied research for further R&D of medicines, diagnostics or medical devices. Therefore access to research activity data, the acceptance in the research community and publications in highly cited journals are important processes in knowledge creation.

Success is grounded in "good science", which implies, that the scientific knowledge is basic to every SME success story.

- *Success Factor - Finance*

Due to the research intensive development in biotechnology, one basic, essential starting point is financial investment in form of seed money and/or public funding. Finance deals with the allocation of assets and liabilities. Important intangible assets are proprietary rights, i.e. patents. These intellectual property rights (IPR) are the cornerstones for success in the biotechnology sector. Own IPR, access to IP related data and the opportunity to in-license external IP were mentioned as success factors by the SMEs. In this regard, Freedom to Operate (FTO) is an important condition to gain value from the IPR.

- *Success Factor - Value*

Regulatory requirements are playing an important role, especially for the development of therapeutics. Therefore compliance with regulatory requirements is another success factor, mentioned by one participant. This implies that the value for technologies, products and services is in addition grounded in reaching the regulatory requirements (i.e. FDA approval for a drug). The participants are valuing the ownership of IP and FTO. From the scientific perspective, the acceptance of their particular science has value and was claimed as a success factor too.
On the organizational level, covering the Theoretical Categories Finance and Value, some success factors are overlapping or were assigned to both. This implies the strong relevance of IPR, FTO and funding investments.

In summary the participants stated the following success factors, demonstrated in Figure 37. The participants answers were not be coded, in contrast to the other interview questions. In doing so, the direct words were presented here, to do not over interpret the statements. Even if the number of participating companies, does not represent quantitative evidence, the repeated references underline the importance of **Money**, **People/Team** and **Expertise**. In this context, the term money can be correlated with finance (see Theoretical Categories in Figure 35).

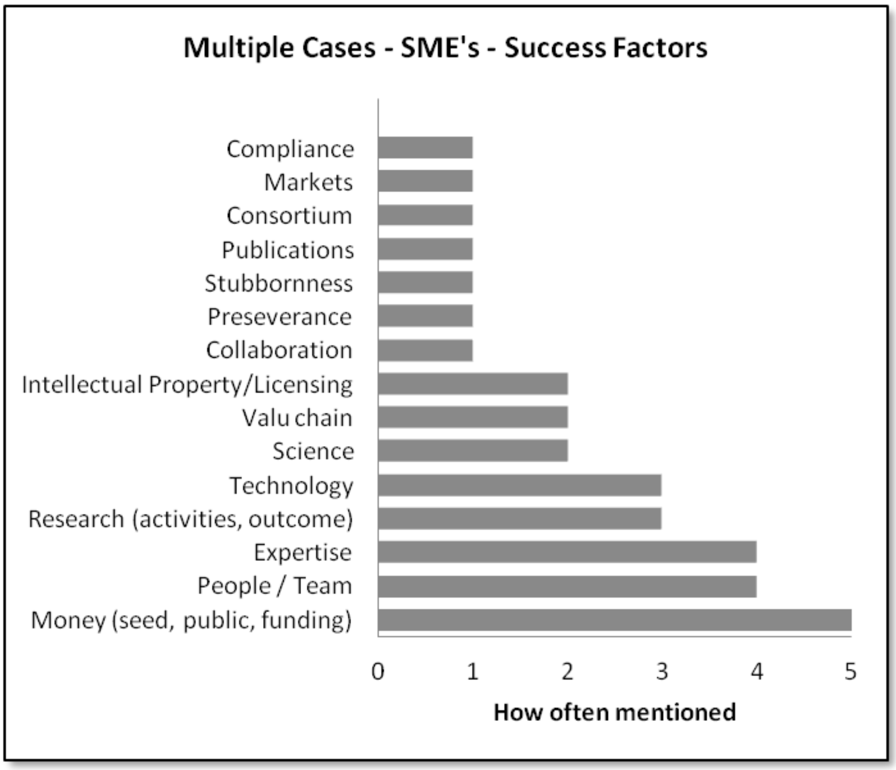

Figure 37: SMEs Success Factors

Order of magnitude: 5 = high, 4 = moderate/high, 3 = moderate,

2 = moderate/low, 1 = low (Miles et al., 2014)

In context with this study it can be concluded, that the fact, that right after the importance of **Money (Finance)** (5 = high), followed by **People / Team** and **Expertise** (4 = moderate/high) strengthen the positive influence of the so called human factor or human capital as one important success factor. This semi quantitative evaluation was applied since all participants were ask to name the most important five success factors. In the framework of this study, these results are representative for the participating biotech SMEs, but the researcher is aware, that this evaluation does not fulfill the requirements for quantitative data evaluation. Nevertheless, where possible in the framework of qualitative data evaluation, these quantitative results had to be included. A mixed methods design according to Miles et al. (2014) was applied here. The mentioned success factors are represented in order of magnitudes. To include all information, the mentioned factors were not aggregated or coded. In doing so, such individual success factors, i.e. the attitudes: *stubbornness* and *perseverance* provide a fined grained view from the practitioners own perspectives.

- *Success Factor - Business Location Relevance*

Three out of five participants claimed that the mentioned success factors are *not* country specific. One participant claimed that from his perspective the factors are the same, but with a different grade of importance in different countries. So, from the participants perspective, these success factors are representative for the German and the Dutch biotech sector.

Two participants emphasized that their companies success is based on factors, which are specific for Germany. Here the identified success factor: *seed money* is mentioned in the unusual business model of one biotech company, which is private, but was founded with public seed money. Another participant emphasized that typical German is still the good quality of engineering, which enables this company to develop their own technology under German conditions.

Regarding differences in Europe, one participant added, that biotech venture capital is stronger in France. This relates to the success factor Money (Finance).

5.3.4.2 SMEs own Open Innovation Business Model Definitions

Interestingly, three of the five participants did not know the term Open Innovation at the time of the interview, one refused to answer at all, one answered, with his spontaneously definition, the other informant gave his definition, after the researcher has explained the term in brief as the following:

> *"Open Innovation is a business phenomenon, described by Henry Chesbrough in 2003 for the first time. The most important requirements are that the company boundaries are not closed. That at every stage of the value chain you are open to others, to collaborate or look for other technologies you can use, and it is not only about in- and out-licensing, also collaboration with scientific partners and get knowledge from outside. That's why it is an open*

approach and an open business model." (Interview, SME-Researchers own explanation to C2, Q12)

This is indeed a very broad definition, formulated by the researcher during the interview, to not influence the opinion of the informant, but nevertheless, here the participant "jumped" on the predefinition, but also added new aspects and stated his opinion from his perspective. Therefore, this response was included in the data evaluation. Only one participant refused to answer this question and was, therefore excluded.

Even in 2016, the researcher learned from market observation and personal contacts the fact, that i.e. in a German Medical Technology company, which is profitable, has a high growth rate and won several innovation contests, the term open innovation is not known at the C-level management. Another successful German biotech company's senior business development manager stated, that they are not practicing open innovation. These examples do no claim to allow general conclusions, but in the framework of this study, the results from the interviews are supported, that open innovation is still an innovation concept, that needs further announcement, especially to practitioners in the biotech sector.

- *Innovation Partnerships*

Every open innovation business model needs external partners. A business model without partners fulfils the definition of a closed innovation business model, which implies the opposite to the open innovation concept. In some cases such a closed model is limited for a defined part of the value chain, i.e. the basic research stage, where the technology or product is created. As one participant stated, this approach was practiced for their first products and for the next product they switched to an open innovation business model:

"At an early stage of development, at basic research a closed model seems to be better. One example for an open business model is the development of the [...] marker." (Interview, SME-C5, Q12)"

Even if some participants from the biotech SMEs were particularly not aware of the open innovation phenomenon, their statements are evidence for the fact, that open innovation business models are characteristic for this sector. In this regard, the long-term involvement of the researcher herself in this sector, provides additional sources of data, i.e. sector participant observations over many years. Even if this type of knowledge collection lies outside of the framework of this research study, it influences the data evaluation and point of view of the researcher herself. Especially for the applied grounded theory methodology, the experiences as a practitioner with close-to-practice insights (Vinten, 1994 cited in Hibbert et al. 2016) supporting the demand to develop a new theory (Corbin and Strauss, 2008).

Partnerships at different levels of the value chain are mandatory for biotech SMEs to gain competitive advantage. All multiple cases have in common, that their core technology has its roots in a research organization. These companies started as a spin-off or start-up, developing a promising technology to enter the market. Therefore, even at the beginning, the founding phase, their business model was based on a collaboration with a research organization (public or private). The following table is exemplary for the partnerships of the SMEs. Sources for this overview are the organizations websites and their annual reports from 2015, where available. Since not all collaboration partners are mentioned and publicly available, and for the sake of confidentiality, this overview does not claim to be complete.

Table 21: SME Partnerships in 2014

Biotech SMEs	Employees as of 31.12.2014	All Partnerships	R&D Organizations	SMEs & MNC's	Countries/Regions
C1	**10**	**26**	**11**	**15**	**Europe, India**
C2	**(-)**	**17**	**(-)**	**(-)**	**Europe, USA**
C3	**72**	**40+**	**3**	**(-)**	**Worldwide**
C4	**329**	**21**	**(-)**	**(-)**	**Europe, USA,**
C5	**37**	**10+**	**(-)**	**(-)**	**Europe, USA, China, Canada**

(-) not disclosed   Source: Author, based on website search and Annual Reports from 2015.

But not only the number of **COL** partners is important here, the quality of the relationship and type of ties are influencing the outcome from partnered projects. All participating SMEs have in common to collaborate with partners from different parts of the world. Emphasis is here, not surprising, on the European and US markets, followed by China, India and Canada. Further research, focusing on the temporal shift of partnerships per region in the world could add valuable information about the diversification of the biotech sector.

Again, the external expertise of partners, fitting complementarily to the SMEs products, services and technologies are important indicators with whom to collaborate, independent from organizational size and origin of the partner. Evidence is the encompassing statement of one participant, who defined the open innovation concept as the following:

> *"Open innovation is a continuous process including internal and external resources, and it is a collaborative approach." (Interview, SME-C4, Q12)*

This collaborative approach adds value to the SMEs business models. Nevertheless, there is a need for continuous internal and external resources, capabilities and capacities. All internal and external activities must be controlled and validated. One important recurring process is measuring inside expertise, gain data from outside, with the goal to identify external complementary expertise. This constant process was described by one participants advice:

> "*Be constantly aware and active in looking for additions to your value chain, with bigger or smaller companies. And being able to find out what your core competence is." (Interview, SME-C3, Q12)*

To really embrace successful innovation partnerships, one still existing syndrome must be abandon at every stage of the value chain: the not - invented - here- (NIH) syndrome. This often mentioned and rarely understood complex phenomenon (Antons and Piller, 2015) is not caused by whole organizations but by individual attitudes and their functions. Even if the term is often mentioned in the open-and innovation literature as a known barrier for the adoption of open innovation, in context with this study the phenomenon was only mentioned by one participant. The manager stated, the NIH syndrome can hinder open innovation and has to be abandoned. He suggested the following:

> *"The NIH syndrome has to be abandoning and the company should embrace it by integrating the people." (Interview, SME-C5, Q12)*

The fact, that the NIH syndrome was only mentioned once, over the whole study, suggests, that this phenomenon plays a minor role, but, nevertheless, the study by Antons and Piller (2015) recommends to investigate further. They see great benefits in understanding NIH better, for applying better approaches to innovation management in general. This could open a future research agenda to answer the question: To what extend can the NIH syndrome hinder innovation in the biotech sector?

- *The Technology driven Business Model*

Every specific biotech business model is strongly influenced by the type of technology; therefore it is not the intention and goal of this research study to develop a theory for a biotech business model per se. Each of the participating companies has a different business model, based on their specific technologies and respective products. Nevertheless, for creating a theory for *Innovation Partnerships*, the business model perspectives of the participants is of great value. A strong focus is combining the scientific and commercial perspectives of the technology.

- *Open minded People*

In context with an open innovation business model, people at the organizations are the driving forces for an open culture. To practice open innovation, all employees must be integrated in the organizations strategy at every stage of the value creation. Trustful partnerships and shared values are prerequisites, when it comes to an authentic collaborative culture, not only on an intra- but also on an inter-organizational level. As complex as human relationships can be, as complex are partnerships in the business context. Therefore not only the professional competence and scientific expertise, the "best" in their field, but also attitudes and personal values of every team member are important indicators. One important indicator is a general open attitude.

An open attitude, shared value and trust of and between people in business partnerships is an important factor for a successful business model. The following personal attitudes are mentioned by one participant as prerequisites for successful **COL:**

- *"open mind;*
- *creativeness;*
- *win-win attitude;*
- *be prepared to share*
- *if you can't divide/share you can't multiply." (Interview, SME-C3, Q8)*

The fact that sharing leads to multiplying is strengthened by a quote from another SME CEO, he stated the following, again in context with a collaborative (COL) approach:

> *"Understanding that collaboration is good for all parties: The whole is more than the sum of its parts." (Interview, SME-C1, Q8)*

Both quotes are implication the importance of the willingness to share and the expected positive outcome for all participating partners.

- *Value Creation based on internal and external Resources*

The purpose of every business model is value creation (Osterwalder and Pigneur's, 2010). There are many different definitions of a business model developed by scholars over the last decades. At this final evaluation stage of the research study, Osterwalders (2004) definition, on which he based the creation of the Business Model Canvas (Osterwalder and Pigneur's, 2010) summarizes the different perspectives and fits to the focus of this dissertation:

> "A business model is a theoretical tool that contains a set of elements and their relationships and allows expressing a company's logic of earning money. It is a description of the value a company offers to one or several segments of customers and the architecture of the firm and its network of partners for creating, marketing and delivering this value and relationship capital, in order to generate profitable and sustainable revenue streams." (Osterwalder, 2004, p. 15)

The fact, that three out of five SME participants did not know the concept of an open innovation business model in 2011 shows evidence, that there is still a gap between the academic and practitioners world. This emphasizes the researchers argument, that open innovation, especially in the biotech sector, is often practiced, without knowing the term and naming it explicitly.

Nevertheless this phenomenon, which is adapted by the SMEs, plays an important role. One participant shared her open innovation definition as the following:

> *"[an] Open innovation [business model] is a continuous process including internal and external resources, and it is a collaborative approach."*
> *(Interview, SME-C4, Q12)*

Another CEO agreed on the importance of this concept for the survival of his firm.

> *"I do agree with that, I think it [open innovation] is key for Biotech and also in Pharma. You need to do that to survive and fill the pipelines." (Interview, SME-C3, Q12)*

An open innovation business model is in addition characterized by openness to change and, of course openness to innovation itself. Value creation due to an open innovation business model becomes possible, when partnerships are transparent within the biotech community. The following quote is underlining this:

> *"You need an open, transparent community for the Open Innovation Business Model." (Interview, SME-C5, Q12)*

The opposite of the open attitude is the NIH syndrome, which can hinder the adaption of an open innovation business model. Nevertheless, on the personal, individual level it can persist, and build up barriers, but on the organizational level, an open innovation business model can work. Further research on the controversy discussed phenomenon of the NIH in context with open innovation is recommended, but was not the scope of this study (see Chapter 6).

Value creation through the adoption and adaption of an open innovation business model, does not mean, that at all stages of the value chain, especially during scientific research (**R&D)**, the organization is "open to the world". As one SME manager described the early years of his company, they did their basic research in a closed model, but learned their lessons, to open up and applied an open approach during the **R&D** stage of their next product (Interview, SME-C5).

Interestingly, in regard to an open innovation business model, the SME participants did not mentioned the term finance in direct context with the business model, but with the similar meaning "money" was mentioned as the most important success factor (see Figure 37).

- *Knowledge Exploration, Retention and Exploitation*

Knowledge management is an important activity at every stage of the innovation process. Every of the five open innovation key activities are characterized by a retreated internal and external knowledge exchange. According to Lichtenthaler (2011), there are three stages of knowledge management: first exploration, second retention and third exploitation. This process must not be linear and can create a constantly growing knowledge base inside and outside the organizations boundaries.

At the **knowledge exploration** stage the internal, inventive capacity (Lichtenthaler, 2011) is based on excellent knowledge and understanding the science behind the product. Therefore the inventive capacity is characterized by best in-house expertise of the managers and the teams. As a consequence, this knowledge leads to the search for complementary knowledge from the outside, but, by finding the right balance. The following quote is emphasizing this:

> *"Following an Open Innovation Business Model means to measure the inside expertise of a company first and use data from the public domain to identify what is needed from outside. But you have to do your homework and find the right balance." (Interview, SME-C5, Q12)*

To complement their own knowledge base, organizations need access to external resources; these resources can be provided by their **COL** partners. Therefore the constant knowledge generation about relevant potential external resources is needed. One CEO advised the following:

> *"Be constantly aware and active in looking for additions to your value chain, with bigger or smaller companies. And being able to find out what your core competence is." (Interview, SME-C3, Q12)*

This implies the importance of constant external, absorptive capacities (Lichtenthaler, 2011) at the knowledge exploration stage. Internally core competences und their potential lacks has to be identified.

For the **knowledge retention** stage, internal transformative and external connective capacities are needed (Lichtenthaler, 2011). For the SME collaborative projects, it must be defined in advance, which competence comes from which partner. Even if this seems to be clear, one participant underlined this:

> *"Be certain about what you have to do and what the party from outside will do. But be aware and know when and where to stop a project." (Interview, SME-C5, Q12)*

Not knowing and not being aware at all stages of a **COL** project, when to stop, could become a threat to the successful outcome of knowledge exchange between partners. So, before proceeding with a project, the critical in-house transformation, which implies bridging internal and external knowledge, is basic to the go- or stop decision for a partnered project.

At the **knowledge exploitation** stage, the internal innovation capacity of an organization was broaden and has benefitted from the partnership. Outcome can be an innovative technology, product or service, which adds value to all participating partners. A great summary about the need of expertise in the healthcare sector is provided here:

> *"The healthcare economics demanding high expertise and this expert cannot be your own champion. A partner from outside is necessary." (Interview, SME-C5, Q7)*

The research study of the SMEs provided fine grained insights into their understanding of an open innovation business model and their innovation management practices. From a more holistic point of view, knowledge is the so called non monetary currency of every partnership. Even if knowledge is hard to measure by specific metrics, in form of the *right partner* and the *right people* with the *right expertise*, the participating biotech SMEs emphasized their importance as success factors and prerequisites for a successful IO business model.

- *Ideas based on "Better Science"*

Business Models are important indicators for the success or failure of a venture. Therefore the business models of the biotech SMEs showing evidence for similarities, but also differences. To successfully innovate in this sector, ideas in form of valuable scientific research results become inventions, which can be patented (**IP**) or become in-house, specific know how. The process from idea generation to developing and positioning a new product, service or technology in the market, demands an open attitude to innovation per se. The importance to innovate and survive is demonstrated by the following quote:

> *"From the business perspective it [open innovation Business Model] has to cover the following requirements:*
>
> - *The science has to be better.*
> - *Open to innovation.*
> - *Open to change.*
> - *Open to criticism.*
> - *Every closed system doesn't work!" (Interview, SME-C2, Q12)*

The statement, that the "science has to be better" can be projected to the quality of the basic idea, which must be ahead of the competition in the specific research/application field. In context with the partnership requirements, being open to change and criticism and being open to the ideas of the external **COL** partners is mandatory. Especially the strong statement that the opposite, a "closed system" cannot work, shows evidence, that the open innovation concept is adapted and adopted by biotech companies.

5.3.4.3 SMEs Success Factors and Open Innovation Business Models - Theme: Innovation Partnerships

The following section serves as a summary for the success factors and the SMEs understanding of an open innovation Business Model . Even if the success factors and the participants open innovation business model definitions are speaking for themselves, the relationship, causality and interaction in regard to the theoretical categories is summarized in Table 22.

Table 22: The SMEs Success Factors and Open Innovation Business Model Definitions

Theme/ Categories	**SMEs Success Factors**	**SMEs Open Innovation Business Model Definitions**
Partner	▪ *The right partner with complementary expertise* ▪ *Support from established companies* ▪ *COL with the Pharma industry*	▪ *Constantly looking for additions to the value chain* ▪ *Partner with bigger or smaller companies* ▪ *Abandon the NIH syndrom*
Technology	▪ The unique technology as a stand-alone success factor ▪ External, complementary technologies via in-and cross licensing ▪ External, complementary technologies via buy in and M&As	▪ Technology is basic for the type of BM ▪ Combining the scientific and commercial perspective of the technology
People	▪ People with right skills, experiences and expertise ▪ People with an open attitude ▪ People, who are willing to share knowledge ▪ People, who know what they want – acting perseverant and stubborn. ▪ Partners are ideally connected via friendship	▪ People are the driving force for open culture ▪ Peoples expertise –plus-open attitudes, personal value ▪ People with win-win attitude ▪ Ideal – people are connected via friendship ▪ Trustful partnerships and shared values
Value	▪ Value of regulatory compliance ▪ Value of IPRs and FTO – intangible assets ▪ Acceptance of good science	▪ Value creation due to internal and external resources, embedded in a collaborative approach ▪ Value creation in an open, transparent community ▪ Value of an IO BM to survive
Finance	▪ Financial investments in form of seed money ▪ Financial investments in form of public/governmental money ▪ Financial investments based on the value of IPRs and FTO	*-Finance was not mentioned here-*
Knowledge	▪ Knowledge in form of expertise in the specific field ▪ Knowledge based on scientific achievements ▪ Knowledge presentation in scientific journals and at conferences	▪ Internal knowledgebase starting point for external knowledge exploration ▪ Knowledge exchange and transformation in partnerships must be planned and defined ▪ Demand for high expertise in healthcare economics
Idea	▪ Not explicitly described but strong link between idea and technology	▪ Valuable ideas must be patented or covert by internal know-how ▪ The science must be better or basic idea must be better ▪ Openness to innovation, change and criticism

5.3.5 Performance Impact of Innovation Partnerships - SMEs

This research study aims to provide insights into the innovation strategies of biotechnology organizations. To complement the single case study and broaden the perspective on this sector, five SMEs (4 German, 1 Dutch) were included. Even if these organizations are not comparable to the newly founded spin-off, their innovation approaches are providing valuable information to better understand the open innovation phenomenon. In this section, RQ1 and RQ3 are answered by discussing the impact of the theme *innovation partnerships*.

RQ1: Is the Open Innovation concept adopted by biotech companies?

The outcome of the data analysis of the multiple case studies, the biotech SMEs inferred that the open innovation phenomenon was not recognized by all participating companies. During the interviews, it was possible that the interviewee did not answer the closing question: "What is your definition of an Open Innovation Business Model?", since he or she was not familiar with this term. Even so, from the multiple units of analysis of the same case, the evaluation of the data inferred that this particular company has adopted the open innovation concept (C1). In summary the open innovation concept is adopted and adapted by all of the biotech SMEs (Brunswicker and van de Vrande, 2014).

Furthermore, a new theory of *Innovation Partnerships* is created by linking the theoretical categories: *Technology, People, Value, Finance, Knowledge and Idea* with the five key open innovation activities R&D, IP, NET, COL and EL (see Chapter 5, Table 20).

The lesson learned from the biotech SMEs, is that they are examples for the successful adaption of open innovation, consciously and unconsciously. Their innovation strategy is on one side driven by their specific technologies, and on the other side, strongly depended from the market need. Therefore the adoption and adaption of open innovation is an ongoing process, which needs more investigation, depended from the stage of the value chain. What one can learn further from the participating SME managers is that phenomena like open innovation are there, but in their practical NPD processes and value creation, the most important driver for innovation is the patient. This resonates with Porters perspective on the importance to focus on the patient (Moran, 2016).

RQ3: How does the evolving business model look like?

Answering this research question is only possible from a broader perspective, since every participating SME has established its own specific business model. Nevertheless, some common characteristics could be identified. The findings from the data evaluation suggesting that all biotech business models are driven by the technology type, the company is offering to the market. One interesting outcome is a very early established platform business model of one SME, were the CEO stated, that he is not familiar with the term open innovation. This SME functioned as a hub organization, with temporary COL partners, dependent from the recent project under development. Insights into the business model of this SME addresses the demand for understanding the creation and evolution of innovation ecosystems (Yaghmaie and Vanhaverbeke, 2019).

What all SMEs are sharing is, not surprising, the common understanding of value creation due to internal and external sources, embedded in a collaborative approach. These partnerships are based on trust and shared values. An ideal prerequisite mentioned here, was that these partners are connected via friendship. This implies, that formal and informal relationship between business partners can be a valuable source for successful, long-term partnerships.

In one strong statement, a CEO emphasized, that an open innovation business model is mandatory for the company to survive. Another requirement to succeed is the early, mindful protection of valuable ideas with patents or as internal know how. The pro-active IP strategies of all SMEs are evidence for the importance of value capturing due to IPRs.

5.4 Generalization from the Biotech SMEs - the Multiple Cases

According to Yin (2012) two types of generalization has to be distinguished: statistical and analytical generalization. Applying the analytical generalization to the case study research design is appropriate, since the logic behind the study's theoretical framework might be applicable to other case studies. Therefore, based on this study, the new theory of innovation partnerships could be applied to other research intensive industries. The analytical claims, describing the relationship, dependence and causality between the theme partnership and the theoretical categories, enable the researcher and other scholars to generalize to other situations, in this case other technology based SMEs.

Further generalizations are provided in Chapter 6.

6 Conclusions and Recommendations

"The true worth in healthcare is value for the patients." Michael E. Porter

As simple as this quotation sounds, Michael E. Porter argued at the International Consortium for Healthcare Outcomes Measurement (ICHOM) conference in London (Moran, 2016), that tools like transparency, and specifically understanding the real outcome for every patient is gathering speed in Europe. This dissertation aims to contribute to transparency and a better understanding, how a newly founded life science organization, developing a radical innovation, become a success story in the German ecosystem. The ambitious goal of the introduction of the Human-on-a-Chip technology will create tremendous value for the patients. Recently developed by TissUse, the 10-Organ-on-a-Chip is a milestone achievement, since emulating the human biology for drug development and drug testing becomes a realistic alternative. From the patients perspective, this will lead to shorter product development, better quality of drugs, and the future opportunity of a *Personalized* Human-on-a- Chip platform (Marx et al., 2016; Beilmann et al., 2018).

6.1 Introduction

This final chapter will provide the conclusions, final answers to the research questions, discussions of findings and recommendations for future research. Additionally, to broaden the knowledge sharing based on the outcome of this dissertation; recommendations for the academic world, for practitioners and policy makers are made.

This study was initiated by the researchers motivation, to understand the specific innovation strategies of biotechnology organizations, and in particular, how radical innovations can be created in a German ecosystem. In her former carrier she was involved in newly founded and established biotech companies for many years and wanted to understand, from an academic perspective, how organizations create and capture value. In addition, the questions how and why these companies succeed in a competitive environment, seems to be unanswered by the innovation literature. Especially longitudinal studies about newly founded ventures are rare. One reason is the fact, that entrepreneurs and new CEOs are busy managers and not easy to approach (Bagherzadeh et al., 2019). By collaborating with the founder of TissUse, similar to the open innovation concept (Chen and Vanhaverbeke, 2019), the researcher got access to the team and valuable data about the prefounding, founding and product development stages. To not limit this thesis to one case study, and to be able to answer the RQs, multiple cases from the biotechnology sector are included. In summary, these research questions are providing new insights into open innovation practices in the biotech industry:

RQ 1: Is the Open Innovation concept adopted by biotech companies?

RQ 2: Can open innovation enable the development of radical biotech innovations in a German ecosystem?

RQ 3: How does the evolving business model look like?

Finally aanswering these questions will provide insights about and recommendations for the successful development of radical innovation in the biotechnology sector, in particular for newly founded ventures. Furthermore, a multidimensional picture of the adoption and adaption of open innovation in the biotechnology sector can be drawn. Due to the conceptual framework of the five open innovation activities: Research & Development (R&D); Intellectual Property (IP), Collaboration (COL); Networking (NET) and Entrepreneur-and Leadership (EL), a multilevel-perspective of open innovation (Bogers, et al., 2017) is presented. The evolving theories for both, the spin-off TissUse and the SMEs providing a profound understanding of their business models.

6.2 Conclusions

There is still a need for open innovation research to address multiple levels of analysis (Bogers et al., 2017). Open innovation scholars from different parts of the academic world recommend focusing on new research categories, for the purpose of comparing, contrasting, and integrating new perspectives beyond the common organizational framework. This empirical study is addressing this demand by providing three dimensional units of analysis. First, the organizational framework: but instead of only established SMEs, this study sheds light on the creation process of a spin-off organization. Second, the project level: here the process of developing a radical innovation from the idea to the market-ready technology platform is investigated. Third, the individual level: the entrepreneur and his team, including close COL partners are involved in the study (TissUse). From a broader perspective, the individual opinions and viewpoints of the participating executive managers are providing individual insights too (SMEs).

6.2.1 The Adoption and Adaption of Open innovation in the Biotechnology Industry

In summary, this empirical research study provides unique insights into the innovation practices of biotech organizations. For the first time, a German biotech spin-off company, led by a serial entrepreneur was investigated in a longitudinal and therefore fine grained manner. Complemented with insights from successful mature companies, this research has made valuable contribution to existing theory about open innovation. This research shows that the open innovation concept is adopted by biotech companies in general (SMEs). In contrast, insights from the single case, the spin-off TissUse suggests that their innovation strategy is *beyond* open innovation.

6.2.2 TissUse' Radical Innovation - A Multilevel Perspective beyond Open Innovation

By answering the research questions, new, comprehensive knowledge is provided, especially from the perspectives of entrepreneurship and value creation and value capturing based on the evolving business model. According to Teece (2010), the entrepreneur has to meet the following criteria:

> "The right business model is rarely apparent early on. Entrepreneurs/ managers who are well positioned and can learn and adjust are more likely to succeed" (Teece, 2010, p.187)

These criteria are fulfilled by TissUse' founder and CEO UM. He is well positioned because of his long-term experiences in the life science sector, and his curiosity and open attitude created the right framework for the radical innovation of the Human-on-a-Chip technology. The positive influential role of the entrepreneur is a key success factor.

The results of this research strongly suggest that value creation in the biotechnology industry is grounded in collaborative R&D activities. Due to the scientific nature of the products, services and technologies, biotech firms needs a level of openness at the different stages of their value chain. What distinguishes them from other sectors is their strong in-house knowledge base, in most cases protected by IP rights. Therefore, even at the early stage, they have established collaborations with universities, public and private research organizations and suppliers, rather than with customers. Networking and knowledge sharing is a common practice, even with some concerns about potential knowledge spillovers.

- *Can Open Innovation enable the development of radical biotech innovation in the specific German ecosystem? (RQ 2)*

The outcome of the single case data evaluation suggests that it is possible to develop radical innovative products and services in a German ecosystem. Results further suggests, that this ecosystem is not restricted to Germany (USA; Russia;

China), since the involved actors are selected based on the competences, they bring in to support the development of the radical innovation. The findings of the research study and the impressions of the unique, open-minded personality of the serial entrepreneur and founder (UM) are evidence for his global vision. Indeed, this is one of the most important success factors (Nambisan and Baron, 2013). Therefore, results point out that besides the theme *People*, the most important theoretical category is *The Entrepreneur*.

This research also shows that radical innovation needs the right people and an experienced entrepreneur. But these requirements are often fulfilled in start-up companies. What distinguishes the success from the failure? One of the most important success factors, extracted from the research study is that the entrepreneur is the person, who is selecting the *Right People* at the right time. Making the radical innovation *their project* from the early beginning is the best approach to succeed in the competitive field of the Human-on-a-Chip project.

Nevertheless, this unique case has its limitations, since only one spin-off organization was under investigation. The results from this case, developing a radical innovation should be compared with others, from the biotech sector, or from other high-tech sectors. Even so, since the "close up" view on this particular case is unique and valuable, the results from the study are adding new theoretical and practical insights to the body of knowledge about the open innovation concept.

- *How does the evolving business model for an early stage company, pursuing the development of radically innovative products and services, look like? (RQ 3)*

Results emphasize that TissUse' business model is rather an evolving business model, than a static on. The longitudinal case design supports this picture very well. For the first time, research provides a holistic picture, how a newly founded venture creates value in a collaborative approach, initiated by the entrepreneur. This evolving business model is embedded in a parallel growing ecosystem with TissUses at the core, functioning as the *hub* organization. Embedded in this network, TissUse business model is characterized by openness to core partners (strong ties) and their external partners, as well as open to the research community. Results further suggest that is possible to develop a radical innovation with a small, highly motivated. This team acts on mutual trust, is build on long-term informal and formal relationships, with emphasis on scientific and business competencies and experiences. Without them, the radical innovation, the MOC technology could not have been created. Furthermore, the TissUse' business model is build on an early clear idea and goal definition by the entrepreneur. This enabled the growth of the team from a university projects group into a successful business. Nevertheless, as argued in the findings in chapter 5, TissUse' business model is *beyond* open innovation. Evidence is the throughout adoption and adaption of open innovation, even at the early idea creation stage. In contrast, Bahemia et al. (2018) argue for a comparable radical innovation, that the closed model is mandatory to gain protection for the idea at the early stage.

To conclude, TissUse evolving business model is as unique as their radical innovative MOC technology. Nevertheless, spin-off organizations can learn from this case study, how to build radical innovation in a collaborative, open to the world manner. Acting just in the framework of a German ecosystem might work for incremental innovation, but not for radical ones.

6.2.3 The Biotech SMEs - An Inter – Organizational Level Perspective

This study suggests, that from the perspectives on innovation ecosystems and innovation platforms, the Biotech SMEs in this study are providing representative insights into the sector. One SME' business model is based on a platform (see Chapter4, Table 13) and all participating companies are part of the biotechnology ecosystem. Results show, that this ecosystem is not restricted to country boundaries, and according to three of the five participants, success factors are not country specific. The international partnership network provides evidence, that the SMEs are in addition embedded in the international ecosystem.

- *Is the Open Innovation concept adopted by biotech companies? (RQ 1)*

The results strongly suggest that open innovation is adopted by the biotech SMEs. *Innovation Partnerships* are the most important enablers for successful value creation. But, it matters with whom the companies collaborate. Established (SME) COL partners supporting the innovation strategy, but "big" pharmaceutical companies seems to differ not only in size, but also in culture. Some of the biotech SMEs is still facing the "David versus Goliath" syndrome, which hinders fruitful collaborations. There is strong evidence that R&D intensive sectors, like the biotechnology industry are leading examples for the adoption of open innovation. Early on in their value creation processes, collaborative inventions are the *cradle* for later economic success. Nevertheless, results also suggesting, that at the later stage of value creation the Not-Invented-Here (NIH) syndrome (Anton and Piller, 2015) can hinder successful collaborations.

In summary results from the multiple cases suggest that the adoption of the open innovation concept is more likely to be a learning process, than a conscious strategic decision of managers. Evidence for this is the fact, that exactly the two SME CEOs, who did not have heard about open innovation (in 2011), are prime examples for the successful adoption of the innovation concept.

6.2.4 Open Innovation at the Industrial, Regional and Societal Level

This thesis allows a closer view on the innovation processes in the biotechnology sector. Since the researcher has long-term practical and academic experiences in this field, the industry dynamics and recent developments are implemented in this study.

The complementary part of this research study, the mature biotech SMEs is of great importance and value to analyze the biotechnology sector from a broader perspective. The findings from these multiple cases allowing drawing conclusions for the German biotech sector. By studying the open innovation phenomenon, also in a retrospectives manner, the adoption and adaption of the open innovation concept has become visible. The analysis and findings from the five SMEs providing an insight view into their innovation strategies and processes. Their success stories are grounded in *Innovation Partnerships.* These *Partnerships* are present at every level of the value chain. The participants stated repetitively the importance of their collaboration partners. The evolving categories from the data analysis are comparable to the analysis and findings from the spin-off, but with a different impact.

The intended knowledge contribution of this thesis will be applicable to the biotech sector, in particular to the German biotech sector, as the outcome of the embedded case study research allows direct comparisons and conclusions. Since the study focuses on the socio-economic conditions and environment to develop radical innovative products, technologies and services, general conclusions and recommendations to other sectors and policy makers are envisioned too (Etzkowitz and Leydesdorff, 2000).

From the public management perspective, this thesis contributes very detailed analysis about the influence of the GO-Bio Governmental Initiative (Strey, 2015) on TissUse' development of the radical innovation, the Human-on-a-Chip technology.

Not only from the *finance* perspective, the GO-Bio funding program is the starting point for TissUse' success story. Without this governmental program, the entrepreneur would have been forced, to acquire the seed money from other resources. This possibly would have delayed the development of the technology. Therefore, the step by step development of the radical innovation shed light on the innovation processes at spin-off organizations, which are funded by the government. Nevertheless, to investigate also the failure cases would add more valuable knowledge about the founding processes of new ventures in the biotechnology sector. From the public management and governmental perspectives, a new study, comparing successful with failure GO-Bio cases would add valuable insights. This research was focusing on the organizational level, but the longitudinal data analysis about TissUse could be a starting point for new research studies in this area.

6.3 Recommendations

This study is motivated by the researchers' ambition for technology transfer in the life science sector. The body of literature about Open Innovation, co-creation and innovation management in general is growing (Chesbrough and Bogers, 2014; West and Bogers, 2014; Spender et al., 2016; Bagherzadeh et al., 2019; Fernandes et al., 2019;). To contribute, not only to the academic open innovation community, recommendations to practitioners and the society are envisioned.

6.3.1 Theoretical Implications for Open Innovation Research

In 2014 open innovation scholars (West et al.) agreed on suggestions for future research. Ten years after creating the term Open Innovation (Chesbrough, 2003) for the first time, the open innovation concept had a tremendous impact on research and practice (West et al., 2014). Nevertheless, there is a demand for novel measurements. These novel measurements are addressing early stage R&D projects, like TissUse' Human-on-a-Chip project. These complex, scientific and commercial projects are rare and their outcome is difficult to measure. Hence, the in-depth, longitudinal data collection from this research could become a great resource for additional innovation management studies. Therefore, the outcome of this thesis could become the starting point for other academics, who are interested in this comprehensive data set. Approaching the data collection from the single and the multiple cases with new questions about the "How" and "Why" could add value to the body of literature about open innovation in particular and innovation management in general. Especially the pro-active IP development and international strategy could become a source for more in-depth evaluation. Again, the data collection from the spin-off TissUse is a rare, unique source for research by providing multi-dimensional units of analysis of a newly founded company (Bogers et al., 2017). The external validity of this longitudinal data collection, could answer in addition the questions "When" and "How often" is the open innovation concept applied (Gibbert et al., 2008). From the perspective of a lecturer, the outcome and critical discussions about the findings from both case studies could become popular resources in learning and education. Additionally, the outcome of this research study implies, that the open innovation research agenda still needs further insight in categories, like open innovation behavior and cognition, open innovation strategy and design and research about open governance (Bogers et al., 2014). Therefore, this research study adds new insights to gaps in the open innovation literature (Bogers et al., 2017) in the following areas:

Open innovation Behavior and Cognition

On the individual level, especially the open minded nature of the entrepreneur and founder, and his influence on the team are interesting insights about the behavior of individuals in context with the open innovation phenomenon. The strong commitment of the team and the constant motivation by the entrepreneur adding value to the understanding of open innovation from the individuals perspective can work. Furthermore, the first order theme *People* has provided interesting facts about the human side of open innovation.

Open innovation strategy and design

This project was highly uncertain and scientifically and technological complex. The longitudinal study about TissUse is providing a fine grained picture about formal and informal organizational structures and the evolving ecosystem around this structures. Interesting insights about the transformation process from the more informal project team to TissUse's professional team addressing gaps in the literature. Even on the project level, the attributes related to the open innovation strategy and design are very valuable, since the research findings are providing a very fine grained picture of TissUse innovation strategy over time.

Open innovation ecosystem

From the ecosystem perspective potential implications and recommendations can be drawn to support newly founded biotech organizations in building their own ecosystems and identify the right partners and actors in this innovation ecosystems (Yaghmaie and Vanhaverbeke, 2019). Here, insights about the creation of the new network and the implementation of existing partners can help other organizations to learn from. For complex, high uncertain radical biotech innovation, the ecosystem must consists always of scientific (Marx et al., 2016; Dehne et al., 2017; Beilmann et al., 2018) and commercial partners.

Linking open innovation to broader theories of management or economics

The extensive literature review and the demand for a theoretical framework have led the researcher to create to VCOI. This visualization can contribute to the better understanding of the five open innovation activities R&D, IP, NET, COL and EL. From the academic perspective, this model addresses the need for linking open innovation to broader theories, in this case, Porters value chain (1985).

6.3.2 Recommendations for Practitioners

From the practitioners perspective this research allows an insight view into the innovation management practices of biotechnology organizations. The perspectives of the participants, who are CEO's, Business Development Managers, Scientists, Entrepreneurs and Academics, are interesting and valuable sources of information. Sharing these information about the success stories of a spin-off and mature biotech organizations, could start a debate about the importance of the open innovation concept and business phenomena's per se. Especially the "lessons learned" in regard to IP management and openness at the R&D stage, could add value to innovation management practices. Presenting the findings from this study at commercial conferences (i.e. BIO Europe), with the focus on start-ups, would connect the academic and the business world.

Great value could be created, by presenting the outcome of this study to GO Bio finalists, which will take the same pathway like TissUse. Presenting the success factors, obstacles and advantages to young biotech founders would promote on one side the program itself, but on the other side, a network of *hands on* advisers could be created. The knowledge transfer from TissUse success case would add great value, and support especially the young and inexperienced founders and team members. From the innovation ecosystem perspective, connecting representatives of TissUse' team with GO-Bio founders and BMBF representatives could create a new ecosystem around this specific governmental funding program.

For Biotech SMEs in general, one could argue, that they already practicing open innovation, without knowing the innovation concept behind it. One prominent example is company C1, their platform was founded long before the term open innovation was coined (Chesbrough, 2003). Therefore, the conclusion can be made, that the product range and technology development is the driving force for opening up the company boundaries. This interesting business model would be in addition a great case to investigate and study further in depth.

Nevertheless, conclusion can be also applied to high-tech SMEs. The comparable high risk R&D phases would allow recommendations for other sectors (i.e. IT, Cleantech). There are similarities in other sectors, which were already compared two decades ago (Swann and Prevezer, 1996) and more recently by Thiel (2014). The latter is focusing on the comparison of Biotech Startups and Software Startups (Thiel, 2014, p.75).

When it comes to collaborations between biotech SEMs and "big" pharma companies, the participants mentioned the "David vs. Goliath" situation during licensing negotiations and other formal business partnerships. Even so, these companies managed this obstacle with their impressive, high quality products and technologies.

One important recommendation for practitioners, practicing open innovation is, not to be impressed or hindered by the potential partners company size. TissUse is also a role model here, the team of actually 20 people is collaboration with pharma organizations, like Bayer, Roche, AstraZeneca and the NIFDC in China (TissUse, 2019).

From the researchers perspective, in her recent function as an open innovation consultant, the lessons learned from these biotech cases can be applied to open innovation workshops and to start-up coachings. Especially the VCOI is a practical, visual tool to support consulting projects with different types of organizations.

Nevertheless, this tool will be most useful for spin-offs, startups and SMEs. Here, it is envisioned to work not only with biotech companies, but with organizations from different sectors. As part of the VCOI, with emphasis on understanding pro-active IP management, the profound IP strategy of TissUse is a great source of information for practitioners in regard to developing radical innovation.

To summarize the outcome of this study for practitioners in the life sciences, the researcher could envision publishing a book, or chapter in a book extracting the practical implications for scientists, entrepreneurs and managers. Here again, the further development of the visual tool VCOI will add a creative solution to visualize the open innovation concept.

Practitioners in the life science sector in general, and in the biotech industry in particular are active members of the life science community. This community is part of an international innovation ecosystem, were the researcher plans to provide workshops and talks. Another practical implication will be the specific knowledge, the researcher can provide to panel discussions and as a moderator. Since the researcher is already engaged as a moderator at technology transfer conferences (BIO Fit 2016; 2018; 2019), sharing the outcome of this study will add value to the understanding of open innovation from a multilevel perspective (Bogers, 2017).

6.3.3 Recommendations for Policy Makers

This study was initiated with the intension to identify the factors for successful technology transfer from universities into the commercial world. The first identified *phenomenon* was open innovation, which is meanwhile a *concept* embraced by many innovation scholars (West, et al., 2014). There is a strong link between the biotechnology sector and the society. Biotech companies are providing a huge amount of new technologies, resulting in new medicines, new diagnostics and medical devices. This R&D intensive sector is also gaining more societal attention, since PET bio-recycling technologies for cleaning the oceans from plastic are available.

All involved biotech companies have in common, that they have successfully developed their innovations for the health care market. They pursued this due to partnerships for innovation, which are not restricted to companies. They collaborate with international public research organizations and universities.

Taken the GO-Bio initiative as a German role model for funding and enabling founding biotechnology organizations, other programs in Europe, i.e. Horizon 2020 addressing the demand for public funding. Actually, the BMBF in Germany is introducing the *"Horizon Europe, the next Framework Programme for Research and Innovation"* (BMBF, 2019). *Open Innovation* is besides *Open Science* and *Global Challenges and Industrial Competitiveness,* one building block of the program for 2021-2027, which is providing impressive 100 Milliard Euro funding. This demonstrates that policy maker on the national and European level does value the advantages of open innovation. Nevertheless, founding a biotech organization is risky and cost intensive. Potential founders from universities often have no access to seed money or other resources (i.e. facilities, offices, human capital), to name only a few. Access to these types of resources are available at universities, like the TUB, but still missing at private or universities of applied sciences. Here more specialized supporting programs could help founders to overcome the so called "valley of death" in technology transfer.

6.4 Limitations and Critical Discussions

This qualitative research study was focusing on radical innovation, developed by a spin-off and on the innovation management practices of mature biotech SMEs. The embedded case study design, complementing both case study types was selected as the best methodology to answer the research questions (see 6.2). The fine-grained, longitudinal data collection from the spin-off TissUse and the broader perspective on the five biotech SMEs, resulted in two interesting perspectives into the biotechnology sector. On one side, the pre-founding, founding and later stage of TissUse allows recommendations for start-up and spin-off organizations, even before they start their businesses, and on the other side, more mature biotech organizations can profit from the innovation strategy of the SMEs. The comprehensive qualitative data collection enabled the researcher to some extend to apply qualitative evaluations (i.e. success factors, appearance of theoretical categories). Nevertheless, there are limitations in this study, which are opening new areas for future research.

First, it could be argued, that the relatively small sample size of 6 organizations does not allow any generalization of the results. This would be applicable for quantitative research but, the case study approach allows in-depth inside information, not only from the informants, but also from other types of data (see chapter 3). To overcome this limitation, further quantitative studies with international biotech organizations could be envisioned.

Second, the data collection investigating in the SMEs innovation strategy was generated at the beginning of the research, at a specific point of time. It would add valuable additional information, if the participant could provide their experiences and opinions about their open innovation concept as of today. One hindering fact would be that not all participants are still working for this particular organization.

Third, even if the rich, longitudinal data collection from the spin-off organization is rare and unique, it would be interesting to find another case from the same sector to compare their innovation approaches. Especially other GO-Bio projects would add value, if they were compared to the TissUse case.

Fourth, all participating companies are successful players in the life science market. This enables on one side, to tell their success stories, but on the other side, failure cases could provide much more new inside, "why and how" the open innovation concept is not helpful or even hindering innovation.

6.5 Future Research Agenda

The recent study does not particularly focus on innovation partnerships per se, but the theme, the outcome of the multiple case study claims *Partnerships*. Therefore, future research should focus on different new perspectives of these partnerships, i.e. type of ties (strong, moderate, weak) and origin of partner countries. By researching the conditions and requirements in more depth, useful information and practical implications can be generated for the biotech sector and other high-tech industries.

The not-invented-here syndrome (NIH) is rarely mentioned in this research study, but further research on the individuals, the team and the organizational level of biotech organizations could contribute to a better understanding of this phenomenon (Antons and Piller, 2015).

The R&D approach is one of the chosen key open innovation activities in this research study. By shedding light on the different approaches: "Make", Buy" and "Make & Buy", the researcher got insight about, "what, why and how" the biotech companies are doing their R&D. Nevertheless, as one participant pointed out, research activities are a different stage from the later development process. So here is room for further investigations especially in the biotech industry. The more fine-grained analyses of the two different open innovation activities could answer the question, when to act open or when a closed approach is more valuable. This could lead to a better understanding of the open innovation phenomenon and focus on different stages in correlation with the value creation and value capturing processes at biotech companies.

Recent research (Yaghmaie and Vanhaverbeke) argue, that there are gaps in the innovation ecosystem literature. They emphasize that these ecosystems are a form of open innovation. This strong link leads to the demand for future research about the different roles of the actors and stakeholders, the innovation ecosystem orchestration strategies and a clear understanding about value creation and capturing processes.

Based on the outcome of this dissertation, shedding more light on innovation ecosystems seems to be the logical next step.

6.6 The Researchers Perspectives on Open Innovation

The open innovation phenomenon was introduced to the academic world more than a decade ago (Chesbrough, 2003). From the practitioners' point of view, the researcher experienced evidence for the implementation of this management practice much earlier in her carrier in the German biotech sector. Even if the term *Open Innovation* was not common, the practical implications were feasible. For example, the researcher was actively involved in the foundation of a diagnostic biotechnology company in 1991, based on in-licensed IP, collaboration via strong ties to a diagnostic laboratory (using the same technical facilities, access to patient material and records), in-house R&D combined with a "Make & Buy" approach, and an open minded founder with entrepreneurial spirit. Typical for the founder was, her scientific background, combined with strong business acumen. Even if the researcher was not aware of open innovation at this time, retrospectively and with her academic and practical experiences as of today, the open innovation phenomenon and the biotechnology industry are practicing open innovation for a much longer time, than the literature suggests.

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Appendicies

The appendices are providing additional and supporting information for this comprehensive research study. Because of confidential reasons, details of the data covering the longitudinal case study about TissUse GmbH are covered.

Appendix A

"How do recent Trends in the Pharmaceutical and Biotech Industry influence Open Innovation Approaches? "

Rafaela Kunz, 2009

Presented and published under The Proceedings of The XX ISPIM Conference 2009 Vienna, Austria - 21-24 June 2009 ISBN 978-952-214-767-7

How do recent Trends in the Pharmaceutical and Biotech Industry influence Open Innovation Approaches?

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Abstract: This research paper derives as a part of the study of innovation management, focusing on Open Innovation approaches and resulting strategies for successful technology transfer.
Aim of the paper is to answer the question, if recent trends in the Pharmaceutical and Biotech industry do influence Open Innovation approaches. It starts with the definition of Open innovation and a comparison of the principles of Closed Innovation versus Open Innovation. Furthermore four internal and external strategies of Open Innovation were identified: First, research and development activities; second, intellectual property management; third, networking and collaboration; fourth, corporate entrepreneurship. These strategies are explained in theory in connection with the innovation model of knowledge transfer. Concerning the aforementioned strategies recent examples from the Pharmaceutical and Biotech Industry were described and analysed. The possible influences on future Open Innovation approaches are discussed and summarized in the conclusions.

Keywords: Open Innovation; Research and Development (R&D); Intellectual Property, Networking and Collaboration, Knowledge Transfer; Pharmaceutical and Biotech Industry

Presented and published under The Proceedings of The XX ISPIM Conference 2009 Vienna, Austria - 21-24 June 2009 ISBN 978-952-214-767-7.

1. Introduction

Chesbrough et.al [5] developed "A framework for classifying Open Innovation research" where the authors emphasised the need for more research in the Industry/Sector of pharmaceuticals and biotech. Their suggestion is to study, analyse and evaluate the outflow and inflow of innovations from biotech and pharmaceutical industry.

Aim of this paper is to identify, analyse and summarize recent trends in the Pharmaceutical and Biotech Industry to answer the question how such trends influence Open innovation approaches, which may lead to more success in the innovation management process.

Trends in the Pharmaceutical and Biotech Industry are useful as important indicators of the innovation management progress. First, both industry sectors are a part of the Health Care Industry and driven by extensive and expensive Research and Development (R&D) activities. Second, the treatment of Global Burden Diseases, e.g. HIV, cancer, cardiovascular diseases, diabetes and mental illness are in the focus of public interest. Third, many companies from both sectors are identified as Innovation Leaders (e.g. Eli Lilly) or as having the potential to become Innovation Leader over the next years (e.g. Genentech and Merck) [19].

Both sectors cannot be analysed without the other because of their complementary core competences. Evidence to the growing role of importance of the Biotech Industry is the fact that one fifth of new medicines launched over the last few years are derived from it. This will rise to over 50% in the next ten years [2].

Collaborations, strategic alliances and partnerships between the Pharmaceutical and Biotech Industry are signs of a new era in the worldwide healthcare product development. A collaborative framework is one of the drivers for cultural change. Knowledge sharing on a global basis will improve the innovation progress and productivity of the Pharmaceutical and Biotech Industry. The common goal of both industry sectors is to provide novel personalised medicine.

2. Methodology

The content of this paper is based on secondary and primary research. The research started with a focused literature review to obtain an overview about the relevant theories and models concerning Open Innovation and the whole innovation management process. In addition to that, the research focused on models, strategies and success factors for technology transfer from academia to industry. First aim of the secondary research was to identify principles of Open Innovation which could be adapted to the Pharmaceutical and Biotech Industry.

The information obtained by the secondary research represents the current state of innovation management described in the literature with strong connection to the Open Innovation Model [4]. Only contemporary and reliable resources were taken into account. Selection criteria for articles were the date of publishing and the link to innovation management and the Pharmaceutical and Biotech Industry. All listed resources are only an extract and do not claim to be complete.
Methods of primary research were mainly job observation. The continuous communication with inventors (researchers; scientists) on one side and business managers (business developers, technology scouts) on the other side allowed a closer look at the implementation of the open innovation approaches in the daily business.

3. Open Innovation – a Paradigm Shift in Innovation Management

3.1 Open Innovation

The term Open Innovation was originated and developed by Henry Chesbrough in 2003 [4]. He published his research findings about innovation practices of multinational companies in a Harvard Business School Press book. This book was targeted primarily to practitioners who are involved in the innovation process. Chesbrough's further research led to a broader picture about the innovation process, its impact on the business strategy of companies, the role of research and development (R&D) at non profit organizations as well as the impact of intellectual property rights (IPR). He defined Open Innovation as:
"…the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively. Open Innovation is a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external path to market, as they look to advance their technology." [5].

3.2 Closed Innovation versus Open Innovation

Despite the fact that Open Innovation approaches have a much longer history than it definition the paradigm shift is still in process. Especially technology driven industries which are facing a strong competitive environment are forced to speed up their innovation process. The following table shows six important principles comparing Closed Innovation with Open Innovation.

Table 1 Principles comparing Closed Innovation with Open Innovation

Closed Innovation principles	Open Innovation principles
The smart people in the field work for us.	Not all the smart people in the field work for us. We need to work with smart people inside and outside the company.
To profit from R&D, we must discover it, develop it, and ship it ourselves.	External R&D can create significant value: internal R&D is needed to claim some portion of that value.
If we discover it ourselves, we will get it to the market first.	We don't have to originate the research to profit from it.
The company that gets an innovation to the market first will win.	Building a better business model is better than getting to the market first.
If we create the most and the best ideas in the industry, we will win.	If we make the best use of internal and external ideas, we will win.
We should control our IP, so that our competitors don't profit from our ideas.	We should profit from others' use of our IP, and we should buy others' IP whenever it advances our business model.

Source: Chesbrough, 2003 [4]

From the perspective of a company which aims for Open Innovation, these principles have to be adapted to the innovation management process within the firm. Real Open Innovation adaptors have to take into account that all of the principles are crucial for long-term competitive advantage.
From the above mentioned principles of Open Innovation the internal as well the external behaviour of a company could be drawn as the following:

Research and Development Activities

Since R&D within a company is expensive and time consuming a company has to make wise decisions on the budget and the R&D strategy for any product development. Sticking to the model of Open Innovation forces the company to decide at what stage external R&D create value for a company and how much internal further R&D will lead to success. Depending on the culture of the company there could be barriers for external technologies arriving from the still existing phrase: “Not Invented Here” (NIH). The innovation management process has to be adjusted, first to the core competences of a firm and second to the financial budget. Therefore multinational companies are still able to finance their R&D in most instances, while small and medium size enterprises (SME's) are characterized by using more external R&D sources, e.g. via collaborations with public research organisations like universities.

IP Management

"In law, intellectual property (IP) is an umbrella term for various legal entitlements which attach to certain names, written and recorded media, and inventions. The holders of these legal entitlements may exercise various exclusive rights in relation to the subject matter of the IP. The term *intellectual property* reflects the idea that this subject matter is the product of the mind or the intellect. The term implies that intellectual works are analogous to physical property and is consequently a matter of some controversy " [20].

IP can be obtained by applying for patents, trade marks, utility models or copyrights. IP right are used to protect the internal generated knowledge of a company, research organization or an individual, the inventor. The invention consists of **patentable subject matter** as the following:

- it is **new** (novelty requirement);
- it **involves an inventive step** or **be non-obvious** (inventive step or non-obviousness requirement);
- it is **capable of industrial application** or **useful** (industrial applicability or utility requirement); and
- it is **disclosed** in the patent application in a clear and complete manner (disclosure requirement) [16]

If an invention meets all the above listed requirements the IP could be used by the owner itself as an internal asset, which demonstrates the Closed Innovation approach, or could be offered for out licensing. In and out licensing of IP demonstrates the Open Innovation strategy of a company. Evidence for the increasing patent licensing revenues is the estimation of Rivette & Kline made already in 2000 [13] that the patent licensing revenues in the United States will be more than $ 500 billion annually by the middle of this decade [6]. The technology licensing is concentrated in a number of industries including chemicals and pharmaceuticals, electronic and electrical equipment, industrial machinery, equipment and computer industries [1].

Networking and Collaboration

To get access to all the smart people in the field a company needs a strong base for networking. Experienced managers and qualified employees use to have networks in their area of expertise. Social and business **networking** is a source of new knowledge from outside and an important resource for the commercialisation of internal knowledge as well [5]. Key benefits of the networking are: firstly, it can save time and money by generating knowledge

from outside the company, secondly, new business partners could be identified and Thirdly, networking may evolve into formal **collaboration** projects [6].
Collaborations from the perspective of a company can be distinguished between inter company collaborations and collaborations with universities. Often SME's are forced to collaborate with others to spread the risk to fund innovations by themselves. Even in larger companies external collaborations have increased too [4]. Without academic research from universities many innovations would have come much later. Common examples are e, g. Google™ - first described by Stanford's Office of Technology and Licensing in 1996 and Gatorade ® - the sports drink is a result of the intensive research concerning the electrolyte loss in the human body caused by football playing. The University of Florida has so far earned more than $ 80 million through royalties and other payments [18].

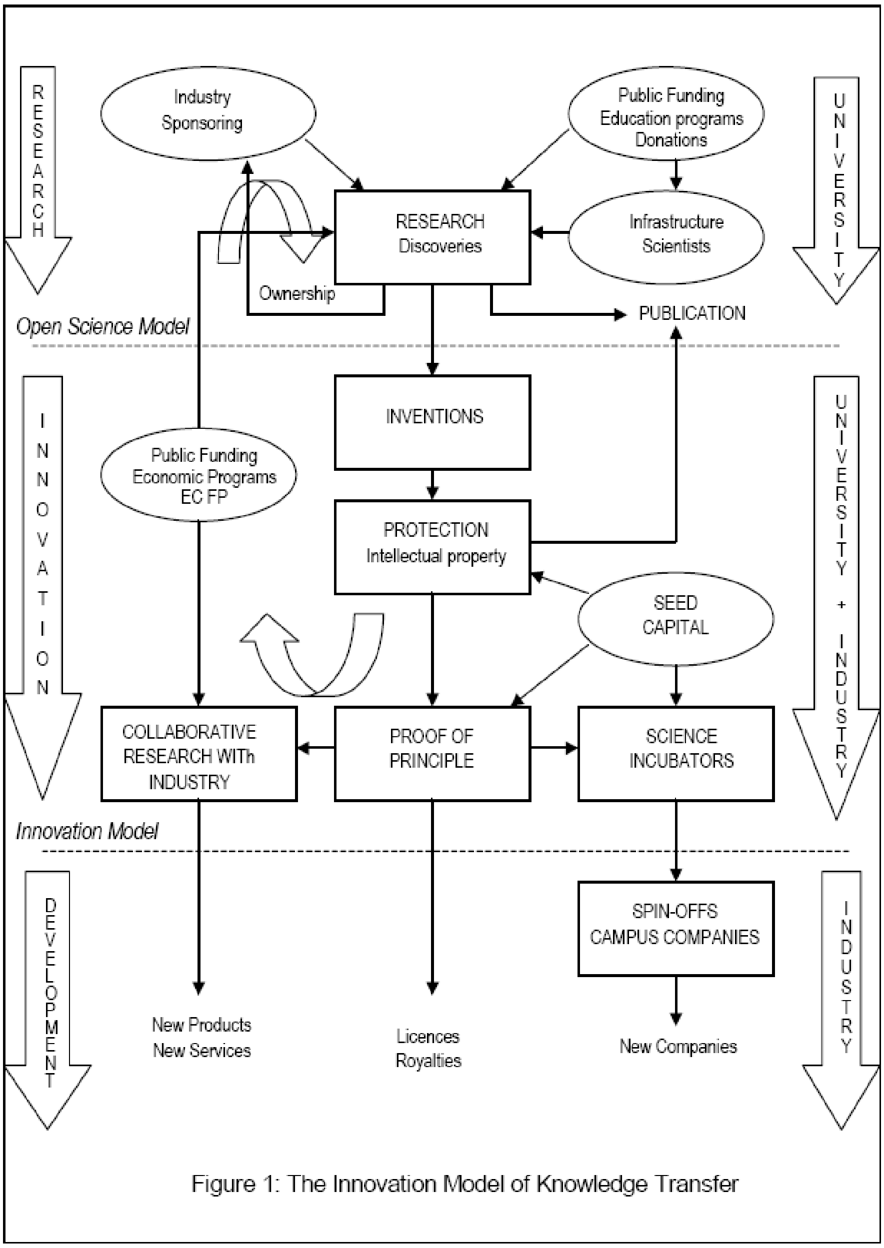
Corporate entrepreneurship
The term entrepreneur was coined in France and means by translation: 'one who undertakes'. The definition is a 'person who assumes the organization, management, and risks of a business enterprise' [15].
Chesbrough [4] summarized corporate entrepreneurial activities as corporate venturing, intrapreneurship, and spinning off new ventures. Corporate venturing is usually practised by larger companies, not at least because of the amount of financial investments into spin offs or other small businesses. Aim of this investment is to get access to innovations and to use external opportunities for new product development. But not only companies use this strategy - universities, research organizations and technology transfer offices are involved in the foundation of start-ups too. Due to the nature of the often early stage inventions and IP rights the creation of a SME is necessary to bridge the gap between early stage R&D and mature product development. Therefore the potential of such new businesses is high, regardless if it is a spin-out of a company or a start-up from a university.
Even so, companies and universities have to prove before starting such new businesses whether the competitive environment, innovative technology, the IP, financial capital and management resources are appropriate to lead to economic success.

3.3 The Innovation Model of Knowledge Transfer

The Innovation Model of Knowledge Transfer explains the innovation management process from the perspective of the Pharmaceutical and Biotech industry. Since both industry sectors are characterised by tending more and more to the Open Innovation approach, R&D from universities and public research organizations is an important external source for the internal product development. In Figure 1 the various processes are shown.
As described in the section **3.2** the four representative characteristics, R&D activities, IP management, networking and collaboration as well as corporate entrepreneurship can be illustrated. This model represents the complex process of

value creation due to knowledge transfer based on the *Open Science Model* and the *Innovation Model.*

Figure 1 Open Science and Innovation Model



Source: European Commission, 2004 [9]

4. Recent Trends in the Pharmaceutical and Biotech Industry

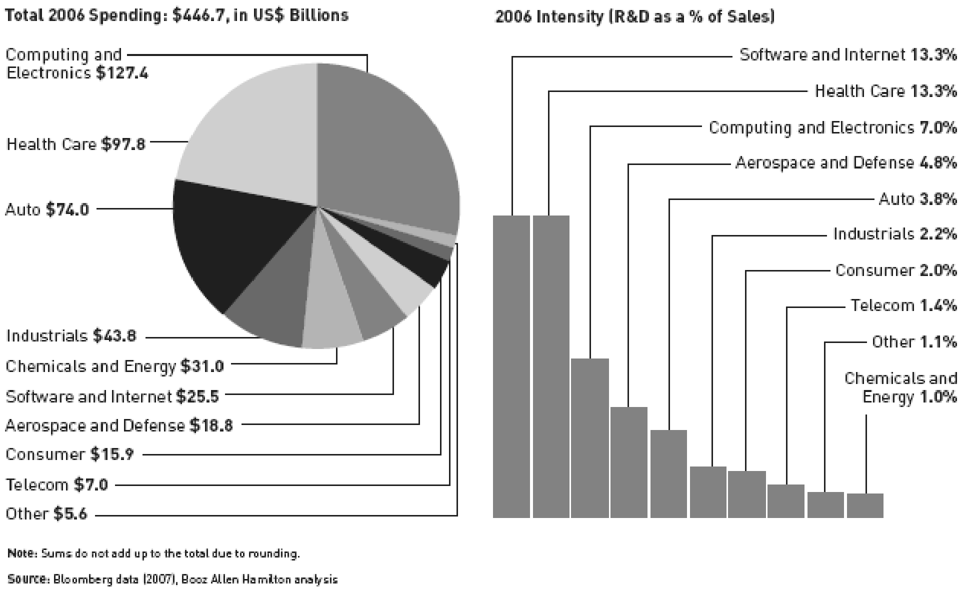
The following section is dedicated to represent recent trends in the Pharmaceutical and Biotech industry. Main focus areas are R&D, IP, networking and collaboration and entrepreneurship. For each area only one significant research source (e.g. reports, articles and interviews) will be represented notwithstanding that there are numerous literatures available. Recent trends meant to show a general tendency in both industries evolving from actual events and movements. All examples are selected from a broad range of secondary research activities and mainly job observation, and make no claim to be complete. The sources are evaluated as representative from the author's point of view in context with this paper.

4.1 Research and Development Activities

Ted Torphy, CSO and Head of External Research and Early Development at Johnson& Johnson Pharmaceuticals made an important statement during the panel discussion concerning the question: "Rethinking R&D: Can Big Pharma address the Productivity Gap through earlier Stage Collaborations?". One of his most substantial arguments was that the industry has to move forward with Open Innovation approaches [7].

R&D activities are identified as the source of innovative products in any industry. The following diagrams in Figure 2 demonstrate the massive investments for R&D in the Healthcare industry**;** in this context the Pharmaceutical and Biotech industry is the major part of the Healthcare industry.

Figure 2 Total Spending on R&D and Intensity as a% of Sales



What is the prospective of Senior Executives of the Life Science Industry?

The whitepaper "The future of the life sciences industries: strategies for success in 2015" developed by Deloitte Touche Thomatsu in collaboration with the Economist Intelligence Unit, was identified as an excellent source for future R&D activities in this industry. Data were generated by a global online survey of 193 senior executives of the life sciences industry as well as roundtable discussion and individual interviews. Here are the key statements from this study. To analyse recent trends in R&D activities in the Pharmaceutical and Biotech industry a close look at the pipelines are necessary. Novartis' CEO, Daniel Vasella stated "Looking at the innovation situation today, we do know that the number of compounds in Phase I (early stage clinical testing) have doubled between 1995 to 2005 across the global pharmaceutical industry, from 1,000 to 2,000 compounds. Phase III (late-stage clinical testing) remains at 400 and we still have to see change here." Other senior executives are convinced that the future of their companies will depend on novel products and services not yet found within their own portfolios today. A strong evidence for the application of Open Innovation is the fact, that 52% of the respondents of the survey expect that by 2015 half of their corporate revenues will be generated by products and services based on external R&D [7].

Regardless the source of R&D companies must improve their ability to translate research ideas into innovative products. Survey participants put great emphasis on long lasting R&D partnerships with other companies and research organisations, e.g universities. To increase the quality of internal R&D the

recruitment of top scientists becomes a crucial factor. To provide the means for improving R&D productivity the senior executives agreed that networking is set to become the hallmark of their life science activities.
Since the Pharmaceutical and Biotech industry is spending a massive amount of money for R&D, cost reduction is crucial to stay competitive. The following recommendation gained from the survey may lead to more efficient product development. Taken the U.S. as an example were medical litigation costs the industry about $ 110 billion per year, increased investments for quality and safety activities and use of data mining and early detection analysis may reduce these spending [14].
The companies are forced to balance between the imperative of fiscal prudence and the need to make investments that improve quality and safety of novel drugs [7].

4.2 IP Management

Because the Pharmaceutical and the Biotech industry are two of the most research - intensive industries, the protection of research results becomes a major issue. Intellectual Property rights are one of the most valuable intangible assets in this industry. Sources for inventions are internal research, public research organisations, universities and small/medium sized Biotech companies as well as medium/large sized Pharmaceutical companies. The transfer of new technologies based on research performed in universities and public sector R&D institutions on one side and commercial applied research and development on the other, becomes often a cost and time consuming process. Evolving IP is crucial for all of the afore mentioned, first, to protect the innovative technologies and knowledge, second, to add value to the company's assets and third to gain revenues due to in and out licensing.

The emerging IP strategy of Novartis

Novartis operates in 140 countries in the world; it has 75 new treatments in the pipeline. Their most revenue generating drugs are Glivec, treatment for leukaemia, gastrointestinal stromal (GIST) tumours and various rare cancer, and Zomenta, a treatment for bone diseases [3].
Paul Herrling, head of corporate research at Novartis explained that there is no commercial return on investment in neglected diseases like malaria at the moment , so no one invests.
Novartis' newly developed model for neglected disease funding is using an innovative IP strategy to overcome the risk associated with any investment in this field and in spite of it to provide a commercial return for the developer. The approach starts with governmental or charity funding of R&D of neglected disease drugs. This investment comes from existing development funds already

reserved for developing countries to ensure that the fund is used according to its moral ethos.
Pharmaceutical companies can provide research proposals, which most worthwhile projects will be selected by an expert panel. After a successful development of a neglected disease treatment the funders receive an exclusive license for all uses of the patent in this area free of charge. In the future the fund would hold many neglected patents and would be responsible for the production of the drugs for the developing countries.
The gain for the Pharmaceutical companies in return to their contribution of skills and technology would be the patent rights to the drugs. For the possible non-neglected diseases treatments evolving from those patents, the companies are allowed to use the patent rights for commercialisation. The incentives could be an improved company reputation gained from the neglected disease drugs as well as the revenues evolving from the new IP.
The IP enforcement strategy of Novartis depends also on the fact, who and where the treatment is needed the most. In case of their novel, patented malaria drug the company remains to not enforce patents of generic companies, if they distribute the drugs at the same quality and lower costs. Novartis does not enforce their non-profit patents in the interest of the consumer in developing countries [3].
Besides Novartis, GlaxoSmtihKline (GSK) and Eli Lilly are also focusing on this future IP strategy based on non-profit development of effective treatments for developing countries. It is mandatory that more companies follow this path, Biotech as well as Pharmaceutical companies.

4.3 Networking and Collaboration

Biopartnering is one of the most feasible approaches of networking and collaboration in between the Pharmaceutical and Biotech industry. Evidence is the growing number of Mergers and Acquisition (M&A) as well as academic collaborations. Since innovative products are the driver for competitive advantage, one can observe a twist within this sector: Pharmaceutical companies are getting competition from Biotech companies. Since innovation seems to be the almost-exclusive territory of the Biotech industry, Roche, GSK, Bristol-Myers Squibb are going out of their usual way and adopt the mentality and tactics of the biotech milieu [12].

Roche’s partnering model – the new industry standard?
Warwick S. Bedwell is the Vice President, Global Head of Business Development and Pharma Partnering for Roche. He described the partnering model and its four phases, which are: “Want, Find, Get and Manage.”
To identify what they “Want” to look for, the Disease Biology Leadership Team defines the scientific innovations which complement or enhance their internal pipeline.

The process to “Find” the appropriate Biotech companies or academic institutions starts with identification of the latter. Next steps are to open up the dialogue and manage the projects and opportunity assessment within Roche.
In terms of “Get” the knowledge, a highly specialized group of negotiators, due diligence directors, lawyers and alliance directors are allows to make a timely and informed decision on the opportunity.
To “Manage” the partnering project, Roche has about 90 people to manage these business development activities in the U.S., Switzerland, Japan, UK and they will be launching an office in China for the Asian market.
Evidence for the successful history of networking and collaboration are Roche’s numerous life extending products, e.g Avastin, Herceptin, MabThera and Tarceva which are the result of the collaboration with Genetech started in the early ‘90s.
Since Roche has 80 active alliances worldwide, other companies could learn from Roche’s collaboration model. The following four approaches are crucial for a successful outcome of partnership. First, Roche respects their partner’s aspirations and vision on one side and beliefs in shared goals on the other side. Second, every partner has to stay autonomic with its own solid management, clear vision and the capacity for shared long-term growth and innovation.
Third, in term of deals, creativity is most important to meet the requirements of both parties.
Fourth, Roche’s alliance management team is accessible to the collaboration partners. Depending on the project key people like managers or scientists ensure that the milestones can be approached.
Bedwell summarized that Roche’s partnering remains a crucial element at the core of their future innovation strategy. This strategy will enable them to find the right scientific opportunities that will lead to differentiated medicines which meet unmet medical needs [10].
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4.4 Corporate entrepreneurship

Pfizers Biotherapeutics and Bioinnovation Center

Corey Goodmen, PhD has taken the opportunity to become President of Pfizer’s Biotherapeutic and Bioinnovation Center. After several years in academia followed by the co-founding of Biotech companies like Exelixis and Renovis, he decided to become an entrepreneur again. However, in this case he joint the biggest and in his opinion, the best pharmaceutical company- Pfizer. His reasons however remain the same, as previously by launches of smaller biotech start-ups, risk, innovation and challenge. The idea behind this centre was to build an organization inside Pfizer with the same strength like Biotech companies – entrepreneurial, small and well connected to academia and biotech.

Goodmen stated that the Pharmaceutical industry is facing two important questions; how to increase the productivity on one side and how to reduce costs for product development on the other? Therefore, all of them are looking for creative new business models.
Pfizer new business model is the Biotherapeutics and Bioinnovation Center, where the spirit and culture of Rinat, a South San Francisco based Biotech Company, which was acquired by Pfizer in 2006, still exists. The new model will benefit from the strength in preclinical development from the biotech side and the financial strength and ability to produce scaling up drugs from the pharmaceutical side.
To stay competitive even Pfizer needs the corporate entrepreneurship as demonstrated in this new business model. Otherwise it could fail in identifying new technologies, making the right business decisions and developing innovative drugs. Goodmen expects his new position to become one of the most creative jobs in his career, last but not least because he has the potential to become one of the innovative, creative thinkers in this industry sector [8].

5. Conclusions

This study shows that Open Innovation approaches are mainly adopted by the Pharmaceutical and Biotech industry, even thought to a different degree.
The key characteristics, namely R&D activities, IP management, networking & collaboration and corporate entrepreneurship are significant indicators for the grade of application of Open Innovation approaches. Despite the fact that every recent trend example represents one of the latter characteristics, all of them are strongly connected with each other.
From the perspective of senior executives half of their income revenues by 2015 are expected to come from external R&D. This will lead to more networking and collaboration with external partners. To get access to external R&D results, companies are additionally forced to in license IP from external sources e.g. other companies or academia. Learning from the success and failure of the adoption of external R&D sources new strategies has to be developed in order to answer the question: At what stage can external R&D create value for a company and how much internal further R&D will lead to success? New approaches in Open Innovation in regard to R&D activities could be reliable methods to minimize the risk of early investments. But nevertheless companies have to ask: What is the best use and value, and how to balance between internal and external ideas?
The innovative IP strategy using governmental funds should become a common approach in other industry sectors as well. A new approach for Open Innovation could be the identification of existing IP which could be used for the provision of vital treatments to penniless developing countries. Even other charitable products, based e.g. on environmentally friendly patents or water-purification technologies could help to provide developing countries affordable products enhancing their quality of life. However, one important question has to be taken

into account in this context: Will the in-licensing and out-licensing process of IP be fast enough to really take advantage?
Regarding to networking and collaboration the described partnering model including its main factors is approved over several years of experiences. Neither company which already has adopted the Open Innovation approach regardless from the sector can avoid or ignore the importance of networking and collaboration. New approaches evolving from this model may take into account the different cultures in the context of global networking and collaboration.
Learning from global acting companies as innovation leaders may assist to overcome those cultural differences. Outcome may be an access to the right partner for collaboration, regardless from which part of the world.
Corporate entrepreneurships like spin-out of big Pharmaceutical companies and start-up of universities are to some extend innovation engines. Creative new business models are necessary to speed up the process from invention, over research and development to an innovative product. These new business models are evidence to the wide adoption of Open Innovation in this sector. But, will this business model be successful in the future? What if Biotech companies remain more innovative due to their independency? Have all the Pharmaceutical companies the financial power to invest in such new models?
Therefore, new approaches in Open Innovation are still in the focus of many studies. Analysing recent trends in the Pharmaceutical and Biotech industry may allow conclusions and recommendations for other sectors, conversely deeper insight and the characteristics of these sectors have to taken into account.

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Appendix B

Case Study Research Proposal LSBU, 2010

RESEARCH PROPOSAL

Case Study

"Open Innovation in Biotech Start-ups"

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Course: 916 MPhil/PhD Business Studies
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NUMBER OF WORDS: 3.649

Contents

1. Case Study Title

"Open Innovation in Biotech Start-ups"

2. Background

This case study will become part of a PhD thesis which focuses on the adoption and the degree of maturity of Open Innovation approaches in the Biotech Industry. The aim of this case study is to gain qualitative and quantitative data in order to be able to analyse all administrative and strategic activities during the formation process of a biotech start-up.

This study will be the most significant part of the data collection. In addition to further research methodologies, such as action research, job observation and in-depth interviews, the case study will be the main resource for data generation. The evolving business strategy for the start-up will be characterized and linked to the Open Innovation approach.

The first outcome of the MPhil/PhD study was the research paper: "How do Recent Trends in the Pharmaceutical and Biotech Industry influence Open Innovation Approaches?" (Kunz, 2009) This paper was presented at the International Conference: "Innovation Enhancing the Quality of Life", in January 2009, at Loyola College, Chennai, India, and at the International Society for Professional Innovation Management (ISPIM) Conference: "The Future of Innovation", in June 2009, in Vienna, Austria. The aim of this paper was to answer the question, if recent trends in the pharmaceutical and biotech industry influence Open Innovation approaches. It starts with the definition of Open Innovation and a comparison of the principles of Closed Innovation versus Open Innovation (see Table 1).

The term Open Innovation was originated and developed by Henry Chesbrough in 2003. He published his research findings about the innovation practices of multinational companies in a Harvard Business School Press book. This book was targeted primarily at practitioners who are involved in the innovation process. Chesbrough's further research led to a broader picture about the innovation process, its impact on the business strategy of companies, the role of research and development (R&D) at non-profit organizations, and the impact of intellectual property rights (IPR). He defined Open Innovation as:

> "…the use of purposive inflows and outflows of knowledge to accelerate internal innovation, and expand the markets for external use of innovation, respectively. Open Innovation is a paradigm that assumes that firms can and should use external ideas as well as internal ideas, and internal and external paths to market, as they look to advance their technology." (Chesbrough et al., 2006)

Despite the fact that Open Innovation approaches have a much longer history than the definition, the paradigm shift is still in process. Industries, especially technology driven ones which are facing a strong competitive environment, are forced to speed up their innovation process. The following table shows six important principles comparing Closed Innovation with Open Innovation.

Table 1 Principles comparing Closed Innovation with Open Innovation

Closed Innovation principles	Open Innovation principles
The smart people in the field work for us.	1. Not all the smart people in the field work for us. We need to work with smart people **inside** and **outside** the company.
To profit from R&D, we must discover it, develop it and ship it ourselves.	2. **Externa**l R&D can create significant value: **internal** R&D is needed to claim some portion of that value.
If we discover it ourselves, we will get it to the market first.	3. We do not have to **originate the research** to profit from it.
The company that gets an innovation to the market first will win.	4. Building a **better business model** is better than getting to the market first.
If we create the most and the best ideas in the industry, we will win.	5. If we make the best use of **internal and external ideas**, we will win.
We should control our IP so that our competitors do not profit from our ideas.	6. We should profit from **others' use of our IP**, and we should **buy others' IP** whenever it advances our business model.

Source: Chesbrough, 2003

Four internal and external business activities which are mandatory for the Open Innovation approach were identified based on Chesbrough's definition of the six Open Innovation principles:

1. Research and Development Activities **(R&D)** - Make; Buy; Make and Buy
2. Intellectual Property management; **(IP)** - In and Out Licensing
3. Networking and Collaboration; **(N&C)** - Formal and Informal
4. Corporate Entrepreneurship and Leadership **(CEL)** – WHO?

The case study will focus on one particular innovative biotech start-up to gain deep insight knowledge of these activities. The link between the four business activities in established companies and start-ups can be described as follows.

Research and Development Activities (R&D)

Since R&D within a company is expensive and time consuming, a company has to make wise decisions concerning the budget and the R&D strategy for any product development. Sticking to the model of Open Innovation forces the company to decide at what stage external R&D create value for a company, and how much further internal R&D will lead to success. Depending on the culture of the company, there could be barriers for external technologies arriving from the still existing phrase: "Not Invented Here" (NIH). The innovation management process has to be adjusted, firstly to the core competences of a firm, and secondly to the financial budget. Multinational companies, therefore, are still able to finance their R&D in most instances, while small and medium size enterprises (SMEs) are characterized by using more external R&D sources, e.g. via collaborations with public research organisations such as universities. An early decision on the balance of radical and incremental innovations adopted into the company has to be made, especially for the young biotechnology industry only active over the last 30 years. (Diligu, 2006)

The Proof of Concept for the core proprietary technology of the case study start-up is financed by the governmental programme "Go BIO" (for more information, see Appendix A). R&D activities as well as the formation process of the start-up are the core activities over the next three years. Since the product development of the so-called "Organ on a chip" technology platform is based on very complex tissue engineering methods, internal as well as external R&D sources will be used.

IP Management (IP)

"In law, intellectual property (IP) is an umbrella term for various legal entitlements which attach to certain names, written and recorded media, and inventions. The holders of these legal entitlements may exercise various exclusive rights in relation to the subject matter of the IP. The term *intellectual property* reflects the idea that this subject matter is the product of the mind or the intellect. The term implies that intellectual works are analogous to physical property and is consequently a matter of some controversy." (www.wipo.int/sme)

IP can be obtained by applying for patents, trademarks, utility models, copyrights, or establishing internal secret know-how. IP rights are used to protect the internal generated knowledge of a company, research organization or an individual, the inventor. The invention consists of **patentable subject matter** based on the following:

- it is **new** (novelty requirement);
- it **involves an inventive step** or is **non-obvious** (inventive step or non-obviousness requirement);
- it is **capable of industrial application** or is **useful** (industrial applicability or utility requirement); and
- it is **disclosed** in the patent application in a clear and complete manner (disclosure requirement). (www.wipo.int/sm)

If an invention meets all the above listed requirements, the IP could be used by the owner itself as an internal asset, which demonstrates the Closed Innovation approach, or could be offered for out licensing. The in and out licensing of IP demonstrates the Open Innovation strategy of a company. Evidence for the increasing patent licensing revenues is the estimation of Rivette & Kline made in 2000 that the patent licensing revenues in the United States will be more than $ 500 billion annually by the middle of this decade (De Jong et al., 2008). Technology licensing is concentrated in a number of industries, including chemicals and pharmaceuticals, electronic and electrical equipment, industrial machinery, equipment, and computers (Huizingh, et al., 2010).

The start-up still has a strong IP portfolio generated by the founder. These patent applications are basic to the core technology. Due to an option contract, including the terms for a licensing contract IP from outside will be licensed in after three years. During this period, up to six new patent applications are planned, and for one, a US Provisional and European Patent application has already been filed. Since the research and development activities will bring out novel scientific and technical solutions in the field of tissue engineering, the new IP will be crucial to back up the market position of the start-up. It is expected that additional IP rights from outside will be needed for the development.

Networking and Collaboration (N&C)

To get access to all the "smart" people in the field, a company need**s** a strong base for networking. Experienced managers and qualified employees are used to having networks in their area of expertise. Social and business **networking** is a source of new knowledge from outside and an important resource for the commercialisation of internal knowledge as well (Chesbrough, et al., 2006) . Key benefits of networking are, firstly, it can save time and money by generating knowledge from outside the company; secondly, new business partners can be identified; and thirdly, networking may evolve into formal **collaboration** projects (De Jong et al., 2008).

Collaborations from the perspective of a company can be distinguished between intercompany collaborations and collaborations with universities and other research institutions. Often SMEs are forced to collaborate with others to spread the risk of funding innovations by themselves. Even in larger companies, external collaborations have increased too (Chesbrough, 2003). Many innovations would have been developed much later without academic research from universities. Common examples of this are, for example, Google™, first described by Stanford's Office of Technology and Licensing in 1996, and Gatorade®, the sports drink, which was a result of the intensive research concerning the electrolyte loss in the human body caused by playing American football. The University of Florida, which created the drink in 1965, has so far earned more than $ 80 million through royalties and other payments (http://aspe.hhs.gov/daltcp/reports/medliab.htm).

The start-up group under research was founded by the former CFO of a biotech company, with a strong business background combined with over 20 years' experience in the biotech and pharmaceutical sector, and a group of researchers from a university. The founder is a specialist in the field of tissue engineering. As a senior manager, he has a strong international network based on long-term scientific and business collaborations.

Corporate Entrepreneurship and Leadership (CEL)

The term "entrepreneur" was coined in France and directly translated means, "one who undertakes". The definition is a "person who assumes the organization, management and risks of a business enterprise" (http://encyclopedia2.thefreedictionary.com/Entrepeneur).

Chesbrough (2003) summarized corporate entrepreneurial activities as corporate venturing, intrapreneurship, and spinning off to new ventures. Corporate venturing is usually practised by larger companies, particularly because of the amount of financial investment needed for spin offs or other small businesses. The aim of this investment is to get access to innovations and to use external opportunities for new product development. However, not only companies use this strategy; universities, research organizations and technology transfer offices are also involved in the foundation of start-ups. Due to the nature of the often early stage inventions and IP rights, the creation of a start-up is necessary to bridge the gap between early stage

R&D and mature product development. The potential of such new businesses is, therefore, high, regardless of whether it is a spin-out of a company or a start-up from a university.

Even so, companies and universities have to prove before starting such new businesses whether the competitive environment, innovative technology, IP, financial capital, and management resources are appropriate to lead to economic success.

Drucker (1993) stated that entrepreneurial management in a new venture has the following four requirements:

1. A focus on the market;
2. Financial foresight, and especially planning for cash flow and capital needs ahead;
3. Building a top management team long before the new venture actually needs one; and
4. The founding entrepreneur has to make a decision in respect to his or her own role, area of work and relationship.

3. Research Aims

Open Innovation is a common term throughout many industries and has become a highly stressed term in connection with innovation management. Numerous publications focus on R&D, IP, N&C, and CEL, but none of the sources studied so far have focussed on the link and causality between **all** four business activities. A start-up from the biotechnology industry, in particular from the tissue engineering field, was intentionally selected for the case study. A well-known, very high demand in innovation and a high level of system complexity, and consequently significant R&D costs, are associated with the biotechnology industry. Tissue engineering is one of the youngest, still rudimentarily, segments of the biotech industry, forcing its entrepreneurs to use the most efficient innovation models in order to secure competitiveness. The study is based on the knowledge of the importance of every single activity in the innovation management process. In-depth analysis and recording of each and every detail related to the process is, therefore, envisioned. Finally, light will be shed in particular on the role and interdependence of R&D, IP, N&C, and CEL during the formation process of a high-tech start-up by combining all the available basic literature on Open Innovation with case study findings. Since the start-up tries to develop and explore radical as well as incremental innovations within its business model, the study might generate new insights into the value of an Open Innovation model for optimizing the risk-benefit-balance for both types of innovation.

The aim of the start-up case study is, therefore, to answer the following questions:

1. What have the four business activities in common, what is different, where is a link, and why?
2. How to handle these activities inside and outside a company in order to gain the most value?
3. Is it possible to create an Open Innovation culture during the formation process of the start-up?
4. What internal incentives could be measured to support an Open Innovation model?
5. What would be the universal characteristics of such a model for the early establishment phase investigated?

Limitation of the case study

The data collection from the case study will focus on one high-tech start-up. A common criticism regarding the study of a single case is that one resource might not be enough to gain data and make conclusions and recommendations for one industry sector.

Therefore, it is expected that certain questions arising during interviews will require further validation. Further research outside the start-up is, therefore, planned. In-depth interviews with a selected number of CEOs from European/German biotech start-ups and SMEs will provide additional source material for the study.

The aim of the CEO interviews is, therefore, to answer the following questions:

1. To what extent are the four business activities already adapted in the Innovation Management process in the biotech industry (SMEs and start-ups)?
2. What would an Open Innovation business model for the start-up phase of a biotech company look like?
3. Are the characteristics and elements of an Open Innovation model specific to the biotech industry?

Answering these questions the key success factors of OI models for the biotech sector should be identified.

4. Research Design and Methodology

4.1 Data Collection Methods

The data collection method will be based on a single case design. The single case was chosen as an appropriate design because it meets the following requirements described by Yin (2009). The single case of the start-up can be described as a critical case in connection with the theory of Open Innovation; therefore it can represent a significant contribution to knowledge and further theory building. Moreover, this case study will also represent an extreme and unique case.

The units of analysis are summarized in the following figure:

Fig. 1 Units of Analysis

Source: Convergence of Evidence; Collecting Case study evidence Yin (2009).

The multiple units of analysis, such as documents, observations, interviews, etc., are mandatory for the embedded design of a case study. These units of analysis can enhance the insight into the case study and can lead to convergence of evidence.

One important unit of analysis will be open-ended in-depth interviews.

Table 2 The key advantages and disadvantages of personal in-depth interviews:

Advantages	**Disadvantages**
Interviewer can observe reactions, and probe and clarify answers	Costly and time consuming
Technique usually nets a high percentage of completed surveys	May contain interviewer bias
Flexibility of location and time for gathering information	Answer has to be coded?
Interviewer can use visual displays Allows for good sampling control Respondents can answer in their own terms Unusual responses are allowed	Recording the answer on a tape!
Respondent's level of knowledge and understanding can be tapped	Time consuming transcription
Useful for exploring new areas	

Source: Adapted from www.quick-mba.com and Brymann et al., 2003

In contrast, structured interviews are determined by a high degree of standardisation or uniformity. This could lead to missing the opportunity of discovering important information owing to the inflexible nature of this type of interview.

Semi-structured and unstructured interviews are the most popular method. This type of interview allows a certain degree of flexibility which is important if new issues arise during the interview process (Grix, 2004). An interview guide is important to this process to ensure that the correct information is gained from the interviewees and the research objectives are central to this.

4.2 Analysis of Data and Interpretation of Findings

The six units of analysis shown in figure 1 will generate mostly qualitative, but also quantitative data, regarding the research objectives summarized due to the four business activities:

1. Research and Development Activities **(R&D)** - Make; Buy; Make & Buy
2. Intellectual Property management; **(IP)** - In and Out Licensing
3. Networking and Collaboration; **(N&C)** - Formal and Informal
4. Corporate Entrepreneurship and Leadership **(CEL)** – WHO?

Due to the embedded case study design using several units of analysis, it is expected that every business activity will be characterized by subunits, for example, R&D-Make will be clearly represented by R&D **I**, R&D-Buy will be R&D **II**, and so on.

One possible presentation of the collected data of the case study can be seen in the following diagram, where 1 to 5 represents the level or grade of importance.

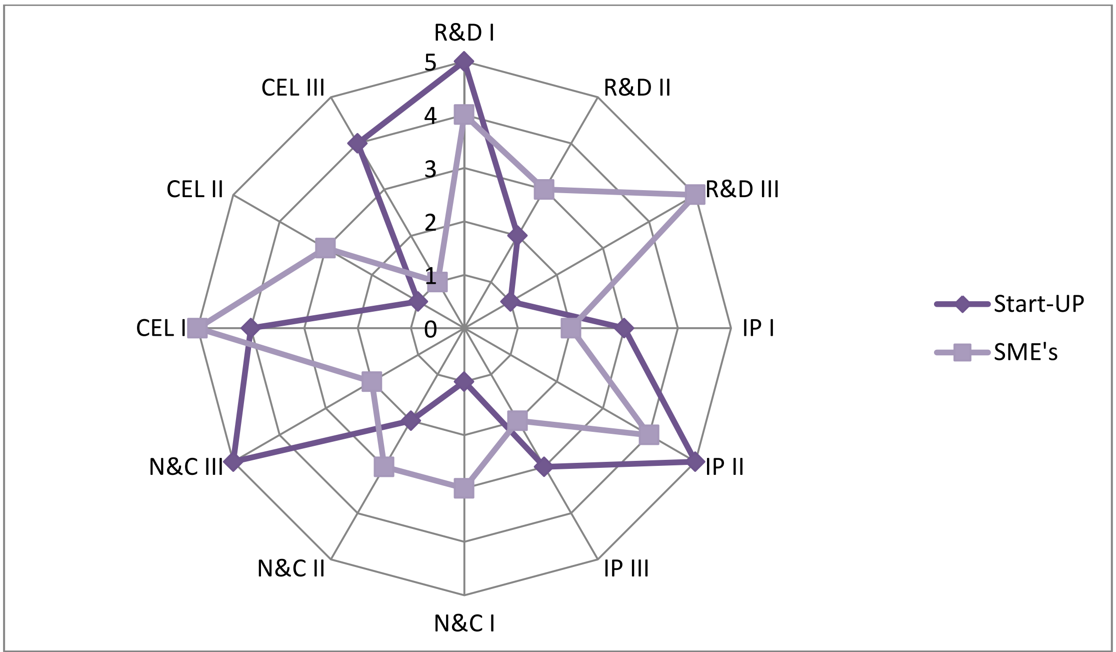

Fig. 2 Example of Analysis of Data

The interpretation of data will also be generated in a comprehensive report form. The generated data from outside the start-up case study can be added at a later time.

5. Conclusions

The start-up case study will be an excellent source for data collection to answer the above mentioned research questions. The meetings with the founder of the start-up, its researchers and collaboration partners will ensure access to all relevant data covering the units of analysis. Since the start-up fulfils the requirements for a single–case design paired with a high-tech product development programme, the results will represent a significant contribution to the knowledge about successful innovation management. The analysis regarding the grade of the adaption of Open Innovation approaches during the formation process of the start-up will allow best practice recommendations for the implementation into the business practice. The outcome of the study should be an Open Innovation business model for high-tech biotech start-ups.

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Appendix C

Pilot Interview Guideline

Personal Information

Name: Profession:

Function: Institution:

Date: Location:

Type of interview: In-depth open-ended Interview

General

Q1: What was your motivation to join the pre founding and formation process of TissUse?

Q2: What are your expectations about the outcome of your current position of a coach and consultant of TissUse?

Research & Development

Q3: To what extend does the research and development process of multi-organ technologies require the following approaches:

a) Make: R&D in house; with own resources
b) Buy: R&D using external partners; outsourcing
c) Make & Buy: using core competences of R&D in house and using complementary core competences of external partners to save time and money?

IP Management

Q4: What are your suggestions regarding the IP strategy of TissUse to gain the most value from already existing and future property rights?

Q5: How can TissUse optimize the licensing of IP?

Q6: What factors, internal and external could be a threat to the property rights and freedom to operate?

Networking & Collaboration

Q7: How can N&C influence the time to market of complex products and technologies like the multi-organ-chips?

Q8: What are the basic requirements for a collaborative approach in business development?

Q9: Which networking platforms regarding the Pharma and Biotech sector are the best?

Corporate Entrepreneur & Leadership

Q10: How do entrepreneurs influence the strategy of a start-up company?

Q11: How would you describe leadership in context with the company TissUse?

Closing Question

What is your definition of an Open Innovation Business Modell?

Thank you for your time!

Appendix D

LONDON SOUTH BANK UNIVERSITY

Spin-off Interview guide

" Open Innovation in Biotech Start-ups"

Name:

Function: Institution:

Date: Location:

Type of interview: In-depth structured open-ended Interview

General

Q1: What are the 5 most important success factors, considering the development of the GO Bio project /spin-off company TissUse GmbH ?

Q2: Which of these factors are from your perspective specific for Germany?

Research & Development (R&D)

Q3: Can you name 3 highlights of the R&D process regarding the GO Bio project?

Q4: Can you name 3 highlights of the R&D process regarding the spin-off company TissUse GmbH?

Intellectual Property Management (IP)

Q5: What are the suggestions regarding the role of IP from your perspective as a university professor?

Q6: How can the licensing of IP be optimized?

Q7: What factors, internal and external could be a threat to the property rights and

Networking (NET)

Q8: How can networking influence the outcome of the GO Bio project /spin-off company TissUse GmbH?

Q9: Which networking methods do you use?

Collaboration (COL)

Q10: What are the most important, valuable collaborations for the success of the GO Bio project /spin-off company TissUse GmbH?

Entrepreneur & Leadership (EL)

Q11: How do entrepreneurs influence the strategy of a spin-off company?

Q12: How would you describe leadership in context with the GO Bio project /spin-off company TissUse GmbH ?

Closing Question

What is your definition of an Open Innovation Business Model?

Thank you again for your time! Comments and amendments are appreciated.

Appendix E

<u>SMEs Interview guide</u>

" Open Innovation in Biotech Start-ups"

Name:

Function: Company:

Date: Location:

Type of interview: In-depth open-ended Interview

General

Q1: What are the 5 most important success factors, considering the development of your company during the last 5 years until now?

Q2: Which of these factors are from your perspective specific for your country?

Research & Development (R&D)

Q3: To what extend does the research and development process of your core technology/product require the following approaches:

d) Make: R&D in house; with own resources
e) Buy: R&D using external partners; outsourcing
f) Make & Buy: using core competences of R&D in house and using complementary core competences of external partners to save time and money?

Intellectual Property Management (IP)

Q4: What are your suggestions regarding the IP strategy of your company to gain the most value from already existing and future property rights?

Q5: How can your company optimize the licensing of IP?

Q6: What factors, internal and external could be a threat to the property rights and freedom to operate?

Networking & Collaboration (N&C)

Q7: How can N&C influence the time to market of complex products and technologies?

Q8: What are the basic requirements for a collaborative approach in business development?

Q9: Which networking platforms regarding the Pharma and Biotech sector are the best?

Corporate Entrepreneur & Leadership (CEL)

Q10: How do entrepreneurs influence the strategy of a start-up company?

Q11: How would you describe leadership in context with your company?

Closing Question

What is your definition of an Open Innovation Business Model?

Thank you very much for your time!

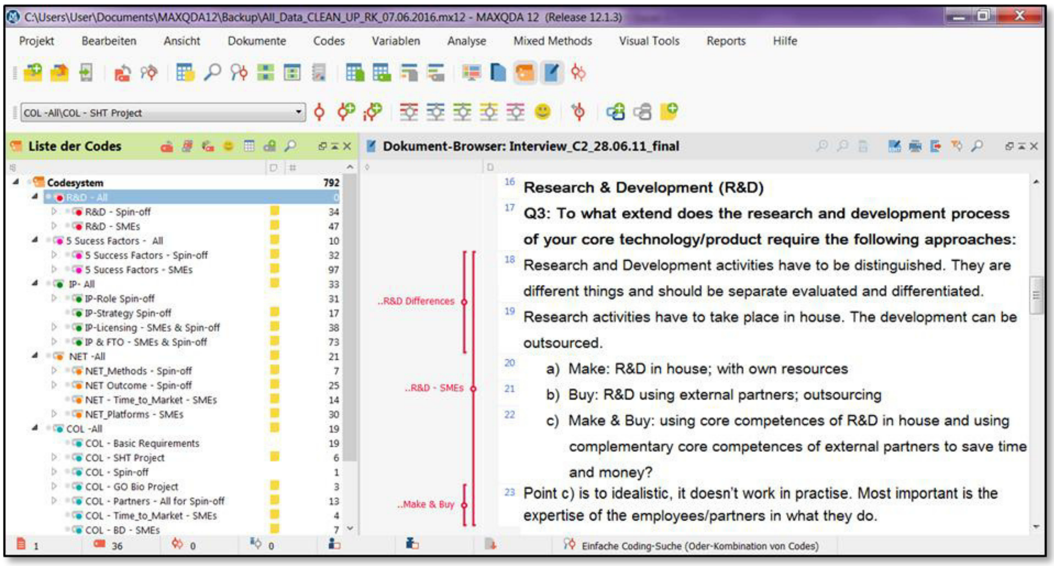
Appendix F

Spin-off Longitudinal Data CollectionExample

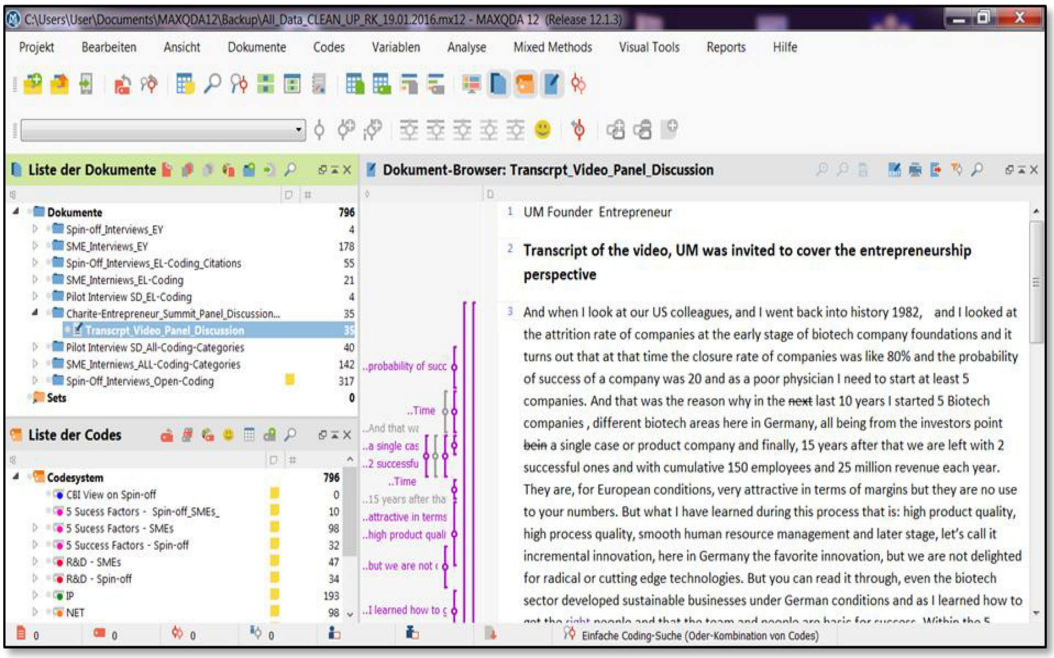
B	C	D	E	F	G	H	I	J	K	L	M	N
Date	**Source**	**Event**	**City**	**Country**	**Activities**	**Nr.**	**R&D**	**IP**	**NET**	**COL**	**EL**	**Evaluation**
Dec.2007						1	1	1	1	1	5	9
11.05.2011						152	2	5	2	4	3	16
14.05.2011						153	4	3	2	5	3	17
13.-15.05.2011						154	5	4	2	3	3	17
15.-17.05.11						155	5	2	2	4	3	16
18.05.2011						156	1	1	2	4	5	13
22.05.2011		**Confidential Information**				157	4	4	3	4	5	20
24.05.2011						158	1	1	1	4	5	12
25.05.2011						159	5	3	2	4	2	16
27.05.2011						160	4	1	2	5	2	14
31.05.2011						161	3	1	1	4	5	14
01.06.2011						162	4	2	2	5	3	16
03.06.2011						163	3	1	2	5	2	13
06.06.2011						164	5	1	1	4	2	13
09.06.2011						165	4	2	2	5	3	16
10.06.2011						166	3	2	2	4	5	16
11.06.2011						167	2	1	1	5	3	12

Appendix G

Example of the Coding Status in MAXQDA, as of 07.06.2016

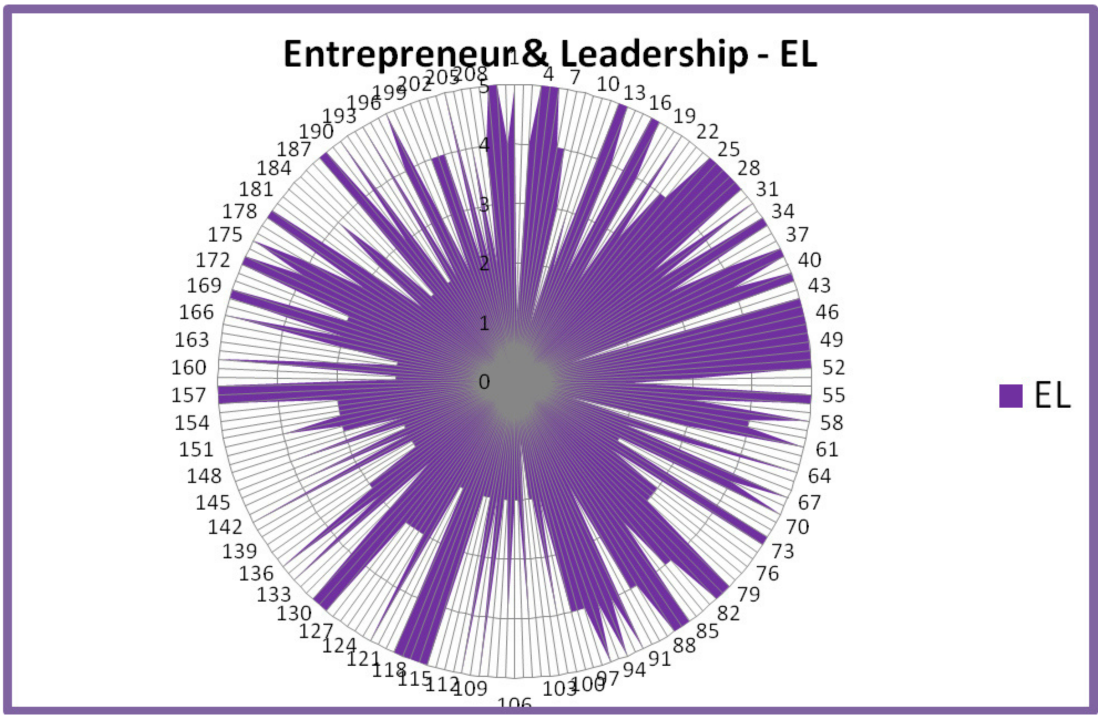


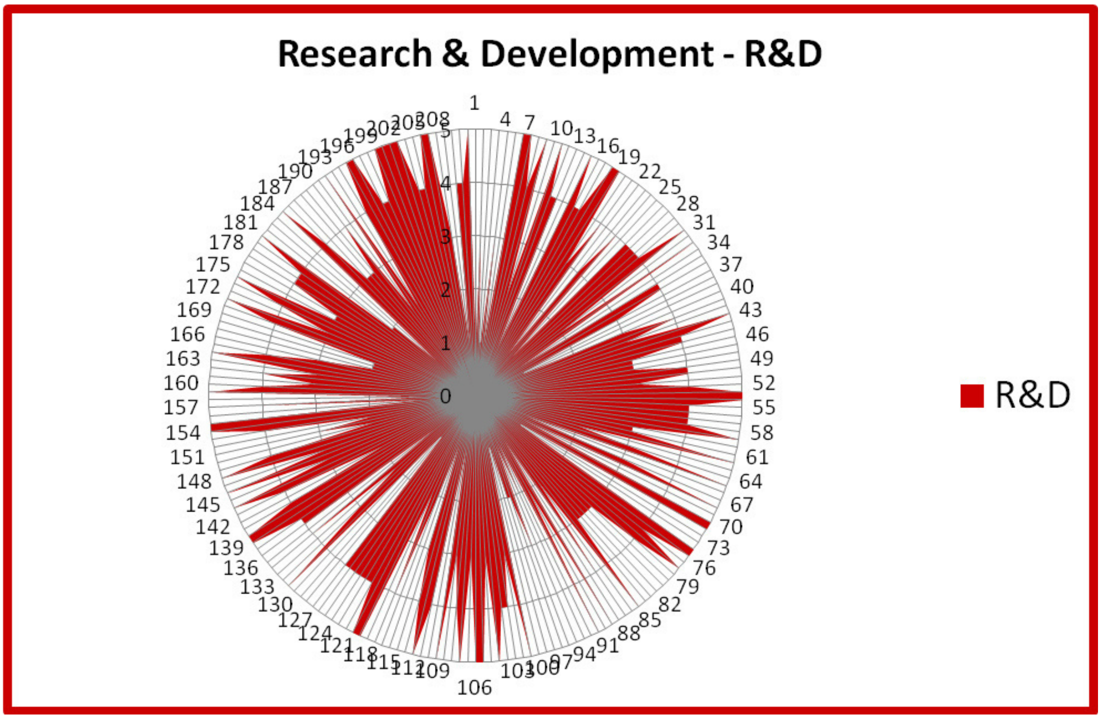
Final Coding Status in MAXQDA, as of 19.01.2016

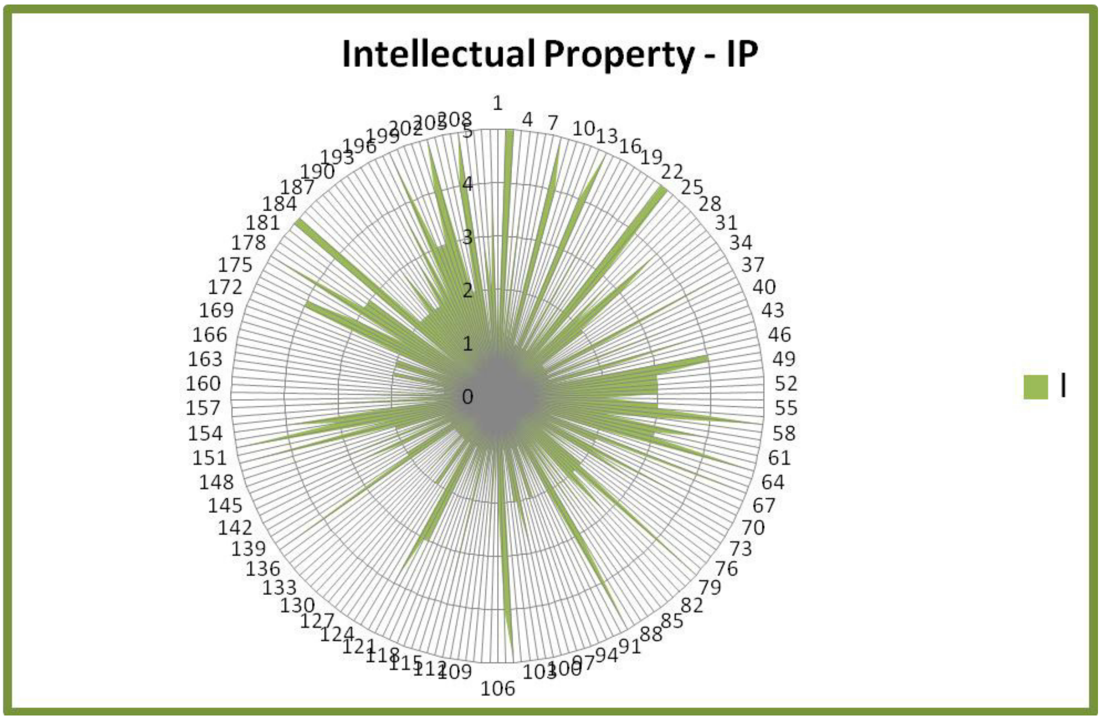


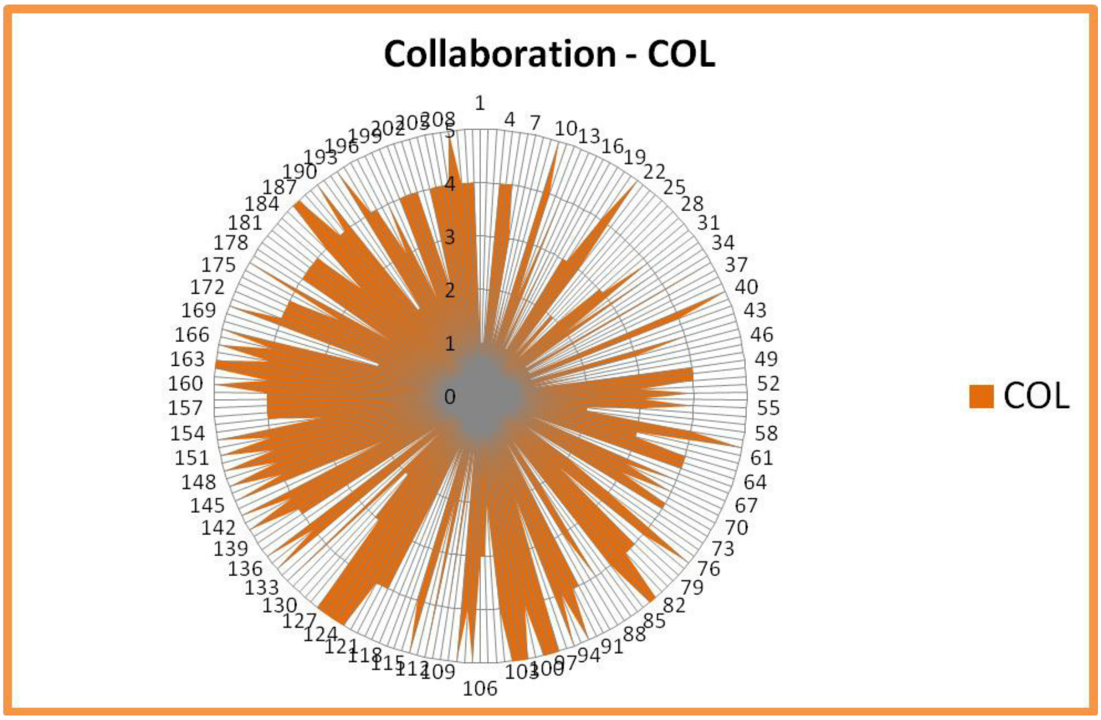
Appendix H

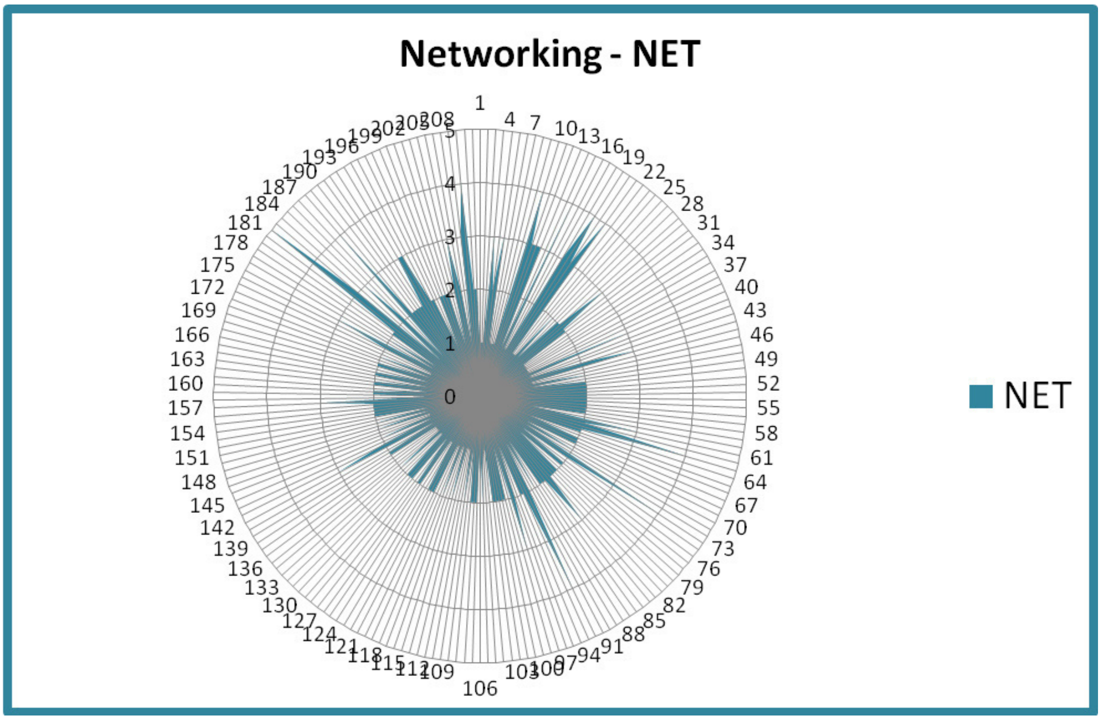
TissUse Longitudinal Data Collection Diagrams for all open innovation activities






Intellectual Property - IP
I


Collaboration - COL
COL


Networking - NET
NET

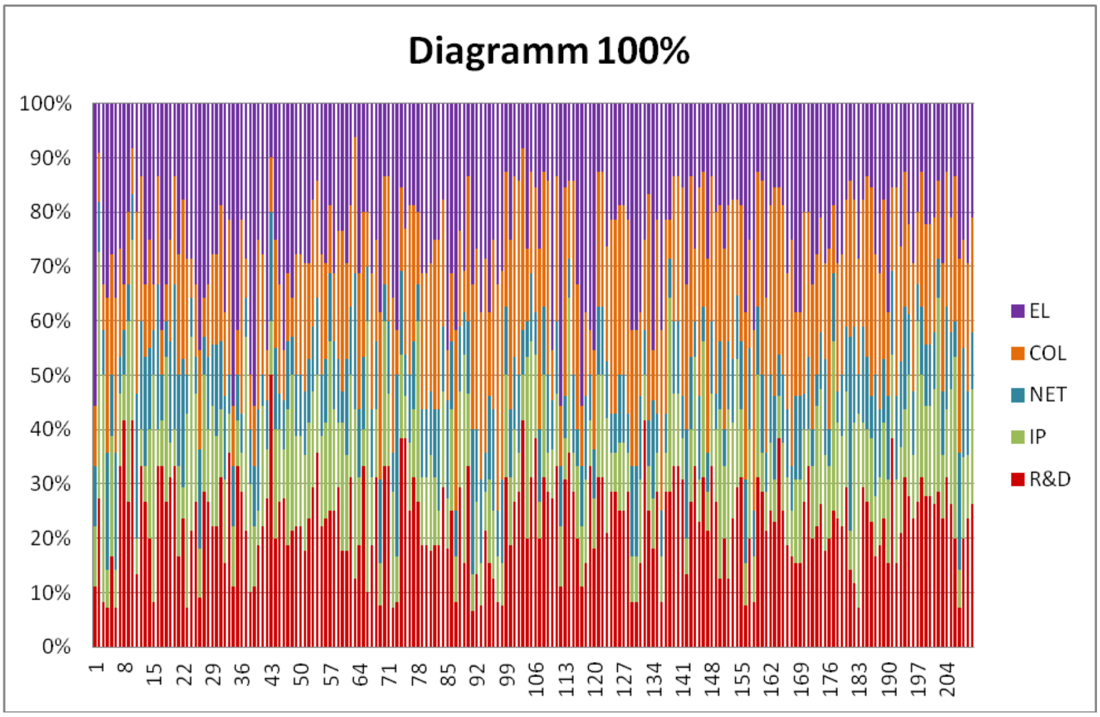


Diagramm 100%
100%
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EL
COL
NET
IP
R&D

Appendix J

CV Uwe Marx, Founder and CEO of TissUse

Appendix J

Curriculum vitae

Dr. Uwe Marx, TissUse GmbH, Germany

After finishing his medical training, Uwe Marx received his doctorate degree in immunology from the Humboldt University in Berlin. Early in his career research activities were focused on protein drugs, such as immunotoxins and fully human monoclonal antibodies towards blood group antigens, HIV and bacterial toxins. Since 1990 he managed a unit for pilot scale manufacturing of human monoclonal antibodies at the Institute for Medical Immunology at Charité hospital in Berlin. At that time he broadened his research activities toward 3D bone marrow cultures for patient specific drug testing. In 1995 Dr. Marx joined the University of Leipzig as head of the department of Medical Biotechnology. His research projects focused on various aspects of tissue engineering, e.g. umbilical cord blood stem cell expansion and in vitro blood vessels for drug screening.
Between 2000 and 2010, Uwe Marx joined ProBioGen – a biotech Company he founded in 1994 - as the Chief Scientific Officer. There he has combined novel technologies for development of high producer cell lines and disposable nature fermentation processes with the long track record of the company's CMO activities. Under his supervision a human lymph node model for in vitro drug testing was developed, patented and introduced into the contract service panel of the Company.

With more than 25 years experience in protein drug development and tissue engineering experience, Uwe Marx has published more than 50 scientific papers. He edited and published in 2007 the scientific book: “Drug Testing In Vitro: Breakthroughs and Trends in Cell Culture Technology” and in 2010 a special issue of the Journal of Biotechnology on “Organotypic Tissue Culture for Substance Testing”. Dr. Marx is inventor in more than 15 patent families as of today resulted in more than 50 granted patents.

During his career Dr. Marx has organized several Meetings promoting modern cell and tissue culture applications, among them the first international Meeting for Hollow-Fibre Bioreactor technology 1992 in Berlin (Germany); the first course for Immunobiotechnology and Tissue Culture 1997 in Beijing (China); the first Tissue Engineering Marathon for junior scientists 1999 in Leipzig (Germany) and the International Symposium “Organotypic Tissue Culture for Substance Evaluation” 2009 in Potsdam (Germany). Dr. Marx is an active member of the working party for Cell Culture Technology of the DECHEMA, the German Society of Chemical Engineering and Biotechnology and member of the Supervisory Board of his spin-off-Companies ProBioGen and VITA34. As an expert he significantly contributed to national survey programs on “German Tissue Engineering activities in worldwide competition” (1997) and “Regenerative Medicine Perspectives in Germany” (2004).

Since April 2010 he is the head of research group "Multi-Organ-Chips" at TU Berlin, aiming for the proof of concept for a cutting edge technology platform for predictive substance testing. It is envisioned to translate positive results into a spin-off of the TU Berlin.

CV as of April, 13th 2011

Source: Data Collection Single Case

Appendix K

"**Radical (Open) Innovation made in Germany: Biotech success stories.**

Rafaela Kunz & Bruce Lloyd, 2017

This paper was presented at The XXVIII ISPIM Innovation Conference – Composing the Innovation Symphony, Austria, Vienna on 18-21 June 2017. The publication is available to ISPIM members at www.ispim.org.

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Radical (Open) Innovation made in Germany: Biotech success stories.

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Abstract: Innovations from Biotechnology are important sources to diagnose, treat and cure diseases. This study aims to explore the pathway of radical biotech innovations, applying the theoretical framework of the Open Innovation phenomenon. First, we identified Research and Development (R&D), Intellectual Property Management (IP), Collaboration (COL), Networking (NET), and Entrepreneurship and Leadership (EL) as the typical Open Innovation activities to investigate. Then, we conducted 6 case studies (1 Spin-off; 5 SMEs) to explore whether Open Innovation is adopted. We further investigated how radical innovative products and services are developed by the spin-off organisation. We found the following concepts (themes): partnerships (for the SMEs) and people (for the spin-off). Sub-themes for all cases are: entrepreneur, technology, idea, technology, knowledge, finance and value. Radical innovative biotechnology products and services, developed by a spin-off organization, are possible in Germany. Mature biotechnology companies have adopted the Open Innovation concept.

Keywords: Biotechnology, Open Innovation, Radical Innovation, Embedded Case Study Design, Entrepreneurship, Partnership, Business Models.

1 Introduction

Open Innovation research provides rich possibilities for discovering new empirical and theoretical developments, based on organizations openness (Chesbrough, 2003; West et al., 2014). In this research study, the adoption and adaption of the Open Innovation concept in Biotech companies, particularly in a spin-off and five small and medium sized (SME) organizations is under investigation to contribute to current research (Vanhaverbeke et al., 2014; West and Bogers, 2014; Dahlander et al., 2016). Aim of the study is to add new knowledge about Open Innovation processes in practice (Laursen and

Salter, 2006; Dogson et al., 2006; Van der Borgh et al., 2012), new theories for open business models (Chesbrough and Rosenbloom, 2002; Chesbrough, 2006) and provide recommendations for innovation strategies (West et al., 2014).

Despite the history of high quality products, grounded in German engineering and the power of the so called Mittelstand (SME's), the typical German innovation is essentially incremental, rather than radical (Allen and Funk, 2008). This paper aims to shed light on this myth, by studying the different stages of the founding process of a biotech spin-off company, led by a serial entrepreneur. This in-depth, longitudinal single case study provides a profound, fine grained inside view into the development of radical innovation in a German ecosystem (Gemuenden et al., 2007).

To broaden the view and be able to draw conclusions for the biotech sector, multiple cases from five successful, mature, dedicated biotech SME's (OECD, 2005), based in Germany (4) and the Netherlands (1) are included in the overall case study design.

One of the most demanding conditions for companies is to innovate and gain competitive advantage in their markets. In the biotech sector, products and services are based on intensive and expensive R&D efforts, with a high risk of uncertainty. These preconditions are applicable to all of the dedicated biotechnology firms, involved in this research study. All six cases involved are fulfilling the following definition according to the OECD (2005):

> "Biotechnology is defined as the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non- living materials for the production of knowledge, goods and services."

Based on the demand for providing more in-depth insight in the adoption of the Open Innovation concept in practice and the comprehensive study of the innovation literature, the research questions were refined to the following:

1. Is the Open Innovation concept adopted by biotech companies?
2. Can Open Innovation enable the development of radical biotech innovation in the specific German ecosystem?
3. How does the evolving business model for an early stage company, pursuing the development of radically innovative products and services, look like?

The causality and interdependency of Open Innovation activities were chosen to provide a holistic view of the adoption and adaption of the Open Innovation concept. The data evaluation aims to identify the success factors for radical innovation in the specific German ecosystem (West et al., 2014). Answering the research questions, if Open Innovation is adopted and adapted and radical innovation is feasible, leads to the identification of the evolving business model (Chesbrough, 2006).

The paper is structured as the following. The literature review provides the background and the evolving theoretical framework for this research. The section research methodology describes the applied embedded case study design, based on the combination of the single and multiple cases approach. In the findings, we present the main insights from the case studies, including answering the research questions. The final section summarises the insights from this research study, discusses the results and provides directions for future research.

2 Open Innovation as Theoretical Framework

The significant hurdles for innovation in biotechnology in general (BIO-TIC, 2014) and for radical innovation in particular, have stimulated the research concerning the question whether cutting-edge technology organizations are possible in Germany (Gemuenden, et al., 2007), and to what extent Open Innovation business models are improving their performance and survival rate (Chesbrough, 2006). The Open Innovation phenomenon has been well investigated and described in the literature since 2003 (Chesbrough, 2010). However, most of the research identified, focuses on established companies. Research-based start-ups are the drivers for innovation (Christensen, 1997). These new ventures are characterized by different starting conditions, which lead to huge variations on the time to market of their first products (Heirman and Clarysse, 2004). Therefore, research about the innovation process of biotech spin-offs and start-ups, and the evolution of their business models needs further in-depth investigation (BMBF, 2010). To clarify the focus of this study, Open Innovation is the theoretical concept for the study and radical innovation is linked to the technology, products and services, the spin-off company is developing. Open Innovation serves as the framework and radical innovation is the goal.

Theoretical Framework

The theoretical framework for this study is based on the Open Innovation phenomenon (Enkel et al., 2009), in particular by focusing on De Jongs et al. (2008) "Policies for Open Innovation" and Lichtenthalers (2011) work: "Open Innovation: Past Research, Current Debates, and Future Directions". The researcher identified these publications as reasonable in two ways: Firstly, De Jong et al. emphasises the 5 key Open Innovation activities: Research and Development (R&D), Intellectual Property Management (IP), Collaboration (COL), Networking (NET), Entrepreneurship and Leadership (EL); Secondly, Lichtenthaler (2011) developed a conceptual framework for Open Innovation, which covers the management of knowledge: exploration, retention and exploitation from the internal and external perspective on a three-dimensional level, namely from the organization, the project and the individual.

By focusing on these 5 key Open Innovation activities, the measurement fulfills the demand for combining different levels of analysis, e.g. organizational level, project level, individual level (West et al., 2014). Moreover, the new theory of the evolving business model and innovation strategy will add new knowledge about the adoption of Open Innovation in general and the framework for radical innovation in particular (Rohrbeck et al., 2009; Huizingh, 2011).

3 Research Design and Methodology

Research Design

The embedded case study design for this research study embraces two basic types of cases: the single-case and the multiple-case design (Yin, 2009). The qualitative case study methodology was chosen in order to generate a rich collection of different type of data in the context of the spin-off biotech company, backed up by the additional data collection of multiple biotech SME's (see Figure 1). Since the dual methodology uses the synergies between the "close-up lens" of the in-depth, longitudinal case and the "wide-angle lens" of multiple cases, this design is compatible to theory building (Leonard-Barton, 1990).

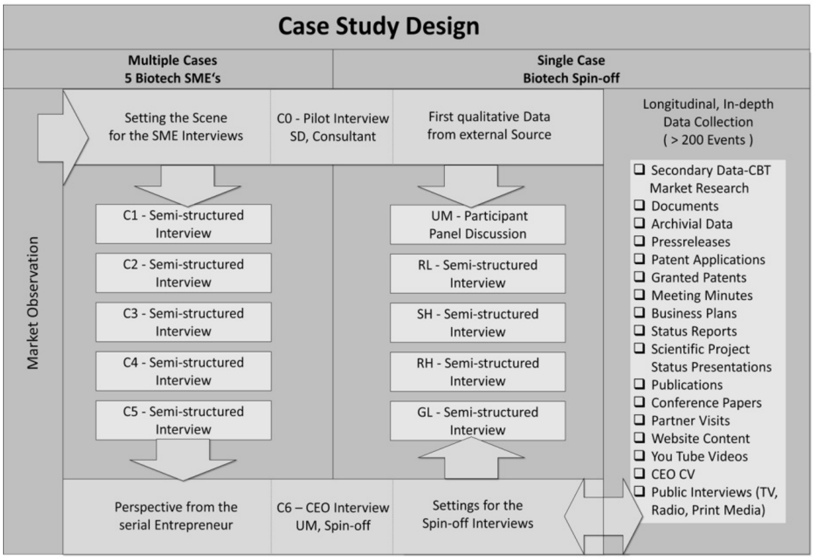

Figure 1: The Case Study Design

Source: Developed by authors, based on the case study methodology (Yin, 2009)

The underlying research methodology is qualitative, inductive and follows the philosophy of an interpretivist epistemology (Klein and Meyers, 1999). The overall data collection includes 11 semi-structured interviews and on-site observations (primary data), and the longitudinal, in-depth data collection of 210 events for the spin-off and websites and published material from the SMEs (secondary data). These different types of data are important to triangulate the sources of information (Kelle, 2001).

The pilot interview was conducted with an US Biotech Consultant (C0), who was actively (by contract) involved in the spin-off pre-and founding phase. The following 5 semi-structured interviews with the SME managers (C1-C5) were complemented by market observation. The next interview was conducted with the spin-off CEO (C6) in order to prepare the 4 semi-structured interviews with the spin-off team leader, members and shareholder (GL; RH; SH; RL). The participation of the spin-off CEO in a documented panel discussion during an international entrepreneurship summit was included in the interview data as a valuable source of information. For the single case, the interviews were complemented with observation and participant observation, and the unique, in-depth longitudinal data collection that illustrates the different stages of founding the spin-off company.

The Cases

The single case (C6), the biotech company TissUse GmbH is a unique, rare source of comprehensive data, since the longitudinal data collection is covering the time frame from 2007 - 2013. Hence, longitudinal case studies are extensively described in literature; they often lack the different stages of newly founded companies. For this case study, the researchers were able to collect data, not only from the prefounding phase, but they were able to accompany the founding phase and early years. No comparable case study could be identified during the ongoing literature review for such a close up view on a university spin-off organisation. Based on the novelty of the envisioned cutting-edge product and services of this spin-off organisation, the focus was set towards radical innovation. More than one and a half decades ago Leifer et al. (2001, p.102) defined radical innovation as the following:

> "A radical innovation is a product, process, or service with either unprecedented performance features or familiar features that offer significant improvements in performance or cost that transform existing markets or create new ones."

The multiple cases (C1-C5) are selected biotech companies which are considered as comparative studies. Each case was carefully selected to either be able to predict similar results, which means a *literal replication*, or predicts contrasting results, which implies a *theoretical replication* (Yin, 2009). The grade of innovation or innovativeness is not easy to measure. Besides definitions of innovation claimed early by Schumpeter (1934), the *Oslo Manual* was considered as an appropriate definition in regard to the selected companies (OECD, 2005). In the framework of this research study design, innovations must contain three types of novelty:

- New to the firm - diffusion of an existing innovation to a firm;
- New to the market - the firm is the first to introduce the innovation to its market;
- New to the world - the firm is the first to introduce the innovation to all markets and industries.

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1 The Dutch biotech SME was chosen, to complement the sample from a European perspective, notwithstanding, that the main focus is the German spin-off biotechnology company.

The selected cases will furthermore serve as valuable sources to gain more insight about the Open Innovation phenomenon by evaluation the 5 keys activities in a retrospective manner. To be comparable to the single case, the spin-off, the multiple cases must meet at least one or more of the following characteristics:

- Dedicated biotech company founded in Germany/Netherlands[1] and older than five years (OECD, 2005; biotechnologie.de, 2011);
- Former spin-off or start-up, based on the IP of innovative technology, product or service;
- Earned governmental funding at the founding stage;
- Winner of a national or international "Innovation Award".

The involvement of the companies does not claim to be representative of the German or Dutch biotech sector, but they are representative samples to complement the in-depth single case study. Some of the cases are spin-offs from universities or research organisations and are, therefore, identified as representative cases for the successful new product development (NPD) based on knowledge generated due to institutional or public scientific research. Since all companies have developed new products, technologies or services and sell them today, they were characterized as examples for successful technology transfer from academia to industry.

Methodology

Consistent with the requirements of grounded theory (Cobin and Straus, 2008), the data were analyzing as they were collected and further evaluated by applying an iterative process. This enabled the researchers to identify emerging theoretical arguments, which were used to categorize the raw data into concepts about the adaption and adoption of the Open Innovation phenomenon (see Fig.2).

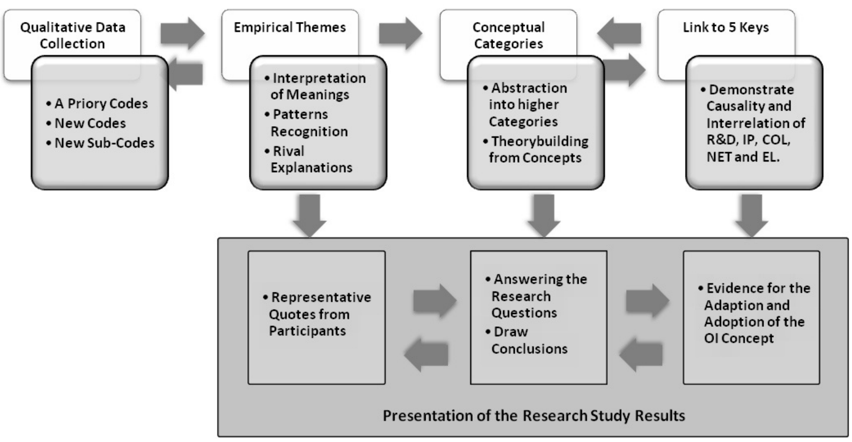

Figure 2: The Data Evaluation Process
Source: Developed by authors.

For the longitudinal data collection, a comprehensive database was built up. The comprehensive material provided by the spin-off company (see Figure:1) was analyzed by content analysis and finally evaluated by ranking the different events in regard to their importance to one of the 5 key Open Innovation activities. This analysis provided a semi-quantitative evaluation to draw conclusions about the activities of the spin-off at different stages of their founding process.

All interviews were transcribed (1 was translated from German into English) and achieved written approval by all interviewees. For coding the data from all interviews, the qualitative data analysis software MAXQDA[12] was applied. Extensive content analysis, coding and constant comparison, adapting grounded theory methods led to empirical themes (Corbin and Strauss, 2008), which were further evaluated into the new central concepts (theme) and the conceptual categories (sub-themes). Eisenhardt (1989) emphasises that theory building from case study research is appropriate to provide “freshness” to a topic which has already been researched. The aim of this study is, therefore, to provide new “fresh” theories regarding the Open Innovation concept in conjunction with radical innovation. Because it is possible to fit the theory behind the Open Innovation phenomenon to the many details of the particular cases, the creation of complex new theories becomes possible (Eisenhardt and Graebner, 2007). The embedded case study design was chosen to guarantee replication and comparability between the data collection from the single and the multiple cases (Yin, 2009).

There is a clear demand for new management theories (Suddaby et al., 2011). For every case type, a substantive theory is developed. Substantive theory is characterized by being grounded in the study of one area of investigation and one specific population (Griffith, 2012). The area of investigation for the single case is the formation of a biotech spin-off company and the "Human-on-a-Chip" project[1], the population is the entrepreneurial founder and his team. For the multiple cases, the area of investigation are the five mature biotech SME's, the population covers the participating CEO's, and managers. The following section is describing the findings from the embedded case study.

4 Findings

The answer to the question, if the Open Innovation concept is adopted and adapted by the participating biotech companies is yes. After analyzing and evaluating all data from the embedded case study, the insights in the innovation management practices of the single and the multiple cases suggesting, that their innovation strategies and business models are grounded in the principles of Open Innovation.

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[1] The technology platform "Human-on-a-Chip", developed by TissUse GmbH is emulating the human biology to provide preclinical insight on a systemic level. The "Multi-Organ-Chips" (2-OC; 4-OC) are already on the market, with the aim to predict toxicity, ADME profiles and efficacy in vitro to reduce and finally replace laboratory animal testing. Source: https://www.tissuse.com/en/

Even at the early stage, two years after founding the spin-off company, the participants had a clear view on their business model and the research study results confirming, that Open Innovation concepts are implemented from day one. The spin-off CEO emphasized in his definition of an Open Innovation business model the importance of IP management with the focus on licensing.

> "[Applying an Open Innovation business model means] license-out and license-in on fair conditions all those technologies from my company and the partners." (Interview, Spin-off, UM)

Another team member of the spin-off company strengthens this statement by the following quote:

> "With our IP we are definitely following an Open Innovation model. We have international collaboration partners. We would not only improve and advance our model just by internal research and keeping it locked away from the rest of the world. We will get experienced people to help if needed and the other way around."
> (Interview, Spin-off, RH)

Surprising was the fact, that two of the five SME managers were not familiar with the term Open Innovation and the underlying phenomenon. In contrast, one manager summarized his view on an Open Innovation business model in a comprehensive manner:

> "From the business perspective it [Open Innovation Business Model] has to cover the following requirements:
> - The science has to be better.
> - Open to innovation.
> - Open to change.
> - Open to criticism.
> - Every closed system doesn't work!" (Interview, SME-C2)

These quotes are illustrative examples of the case study participants own view on the Open Innovation concept. The findings based on the data evaluation led to a more fine grained picture about the single case, backed up with the findings about the multiple cases.

The Single Case

Since the overall case study of the spin-off biotech organization covers the large timeframe, from 2007, by mentioning the idea of the radical innovation, the "Human-on-a-Chip" in a book (Marx and Sandig, 2007) until early 2017 (including observation data), this unique case study adds value to the academic and professional understanding of innovation management (Dodson, et al., 2006). The dense, comprehensive data collection of 210 events is covering the timeframe of seven years, from 2007 to 2013. The spin-off interviews, panel discussion and longitudinal data collection are providing in-depth inside information about the innovation strategy of the newly founded organisation. As of today, the spin-off company is having two products, the 2-Organ-Chip (2-OC) and 4-Organ-Chip (4-OC), and services around their platform on the market.

The extensive evaluation of the coded data using MAXQDA[12] led to a semi-quantitative evaluation of the different evolving themes, concepts and categories. This enable the researchers to apply a ranking and compare the ranked categories of the multiple and the single case (see Figure 3). The variation of the data analysis added value to the results and is consistent with triangulation of the data analysis methodology (Kelle, 2001). These findings are embedded in the developed theory and business model for the single case, based on the identified abstracted central concept of **People**.

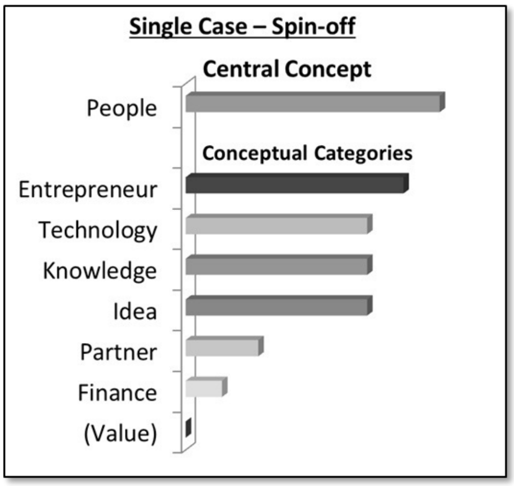

Figure 3: The Spin-off Concept & Categories
Source: Developed by authors.

To develop a theory for the radical innovation strategy, the core concept **People** must be linked to the conceptual categories, which evolved from the data evaluation of the single case. Not surprisingly, the same conceptual categories are identified for the multiple cases, but with different weighting. Nevertheless, the conceptual category **Entrepreneur** plays an important role. This is not surprising in context with this study, but, from the interview data, conducted with the spin-off team, the role, influence and attitude of the entrepreneur gained after *people* in general the highest relevance. Especially as an extract from the interview data, participants have very often stated the importance of the entrepreneurial spirit of the CEO, even if the question was not particularly related to his role and influence. With strong emphasis on the *Entrepreneur*, the other categories are **Technology**, **Knowledge**, **Idea**, **Partner**, **Finance** and to a minor extend **Value**. The conceptual category value plays only a minor role here, since the spin-off was only two years old, when the interviews were conducted, so, the value of the envisioned technology, products and services, was to immature to be discussed at this point of time. Nevertheless, the process of creating value is obvious, even for the spin-off company, but the awareness for it, is at the very early stage. In this context, value creation is an ongoing process, with the goal of building the "Multi-Organ-Chip".

People

The broader meaning of people in context with the spin-off organization is human capital in its function as employees, respective team member. In a team of 15 people, and with the complexity of the "Human-on- a-chip" project, the specific expertise and experiences of every single team member is of great importance. This is illustrated by the statement, that people with a *certain and the right background and skills* are needed (Interview, Spin-off - GL).

Mutual trust due to a personal relationship, competencies and special knowledge, i.e. in IP management are also prerequisites for success.

> "People - the fact that I know Uwe [UM] for more than 20 years. Silke [SH] worked for Uwe many years and therefore I know that she is the right person for IP." (Interview, Spin-off - RL)

Another important human capital related success factor is the attitude of the single team members. Here a highly motivated team is envisioned. The fact, that the majority of the team members is between 25 and 30 years old, is another success factor.

> "The environment of the TU Berlin - many students, young people with ideas and power are the perfect environment for success." (Interview, Spin-off - RL)
> "All the involved people are highly motivated." (Interview, Spin-off - GL)

Regarding the highly motivation of the team members, the researcher herself experienced this during an IP related meeting. The researcher was very impressed by the high confidence, motivation and professionalism in which the inventors/scientists presented their ideas. They took full responsibility for their results and discussed questions very openly and with profound scientific knowledge.

The Entrepreneur

There is no doubt about the strong influence of every entrepreneur in a newly founded company. Nevertheless, for the spin-off company, especially the interview participants emphasized this in a repetitive manner. Therefore, without a dissentient vote, the commonly agreed success factor is the CEO UM. His leading role is emphasized by the following quote:

> "A good CEO [UM] with experiences. Most of the founders do not have enough experiences in science as well as business. It is not enough to be experienced in one of the areas." (Interview, Spin-off - RH)

Here the importance of the entrepreneur, as the scientific and business leader at the early stage of the organisation is demonstrated from a team member's view.

As already cited under the core concept people, in addition, the long-term personal relationship between RL and UM is one crucial success factor. The influence of mutual trust and believing in the others strength is important to start a high risk program, like the development of the " Human-on-a-chip".

Technology

The idea and realization of the radical innovative technology of the "Human-on-a-chip" is from the scientific and the economic perspective, the competitive advantage of the spin-off company. Therefore the chip-technology itself, with all its complexity is an important success factor.

The chip-technology is the building block for the product and market positioning of the company. With this new to the market technology, animal testing can be exchanged by emulating the human body and its functions in the field of substance testing.

Success factors are not limited to specific facts or circumstances. In context with the technology, the process of technology transfer was mentioned here:

> "The transaction of the GO-Bio project into TissUse GmbH, that means the market positioning and the product positioning." (Interview, Spin-off - RH)

This statement emphasizes the importance of the transfer of a governmental funded project into a commercial organization. The technology transfer is the underlying process here, the enabler are the entrepreneur and his team. Interestingly, at this early stage, this team member is valuing the transformation of the scientific project into a business as one already existing success factor. This statement demonstrates the strong commitment and identification with a successful journey towards the radical innovative technology in a commercial environment.

Idea

Every great invention is based on an idea. In case of the spin-off company the entrepreneur and CEO UM had this idea for several years and mentioned it in a co-edited book already in 2007 (Marx et al, 2007). But nevertheless, the team members are committed to this idea and the importance for success, as stated by one participant:

> "The idea behind the project, the idea which is marketable and which gives financial success." (Interview, Spin-off - GL)

This quote also implies that there is commercial value in the idea, when it is mature and ready for the market. UM's role as the head of ideas and the driver behind the program was mentioned by the team members several times. In regard to the entrepreneurial role the following quote is supporting this:

> "The driver, head of the idea is Uwe [UM], who brings all the important people together." (Interview, Spin-off - GL)

Another evidence for the confidence of the team members that the chip-technology will succeed. The source of ideas is in addition linked with the young team of students with *ideas and power* (see People).

Partner
The complex and unique chip technology needs a strong network of partners with expert knowledge. Therefore the closest collaboration, the Technical University Berlin (TUB) is one *basic* success factor:

> "The basis is the Institute of Medical Biotechnology with all the infrastructure." (Interview, Spin-off - GL)

The network of external partners and investors (at this point of time the BMBF) are contributing to the envisioned success.

> "TissUse's investors and collaboration partners." (Interview, Spin-off - RH)
> "The network, without it, the GO-Bio project would not be possible".
> (Interview, Spin-off - SH)

Finance
Without seed funding, especially in the science and technology based biotech sector, there is no commercial success. One of the big advantages of spin-off company is the non-diluting governmental funding of the "Human-on-a-chip" project (approx. 3 Mio €). This enabled the entrepreneur and his team to start developing the technology as a research group, with no influence of external shareholders. In this case the investors are represented by the BMBF and their respective project managers. The scientific requirements and market opportunities for winning the funding of the GO-Bio project are high. Gaining this funding after a two phase evaluation process, is a privilege in the German biotechnology community (Strey, 2015).

The 5 Open Innovation Activities
The semi-quantitative analysis of the longitudinal data collection (210 events) led to the conclusion, that there is a good balance between the 3 key Open Innovation activities; EL 25%, R&D 24%, and COL 23%, followed by IP 16% and NET 12% (see Figure 4). Over the time period of the longitudinal framework, these analysing are implicating the adaption of Open Innovation in general, with minor emphasis on the role of Entrepreneur-and Leadership. This resonates with the findings from the interview data and panel discussion analysis.

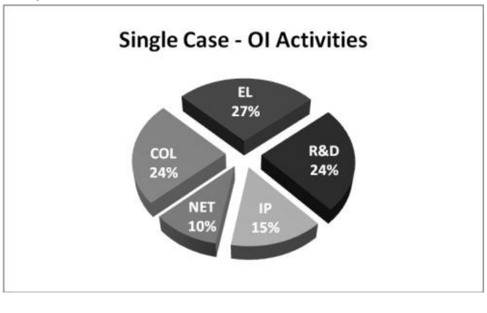

Figure 4: The Spin-off longitudinal Data Evaluation
Source: Developed by authors.

The Entrepreneurs own Perspective

Implementing the data from the panel discussion:"How to Structure the Financing of your Start-up - Venture Capital and Other Options for Founders"(Charité Entrepreneurship Summit, 2011), where the CEO of the spin-off emphasized his own transformation from an *Creative Inventor* into the *Inventive Practitioner,* added significant value to the research study. The following Figure 5 is illustrating a snap shot of the German biotechnology sector, focusing on the specific capital demand and the requirements for the profile of an entrepreneur at the early stage of founding. The diagram is based on the CEO's personal draft, which he prepared for the talk.

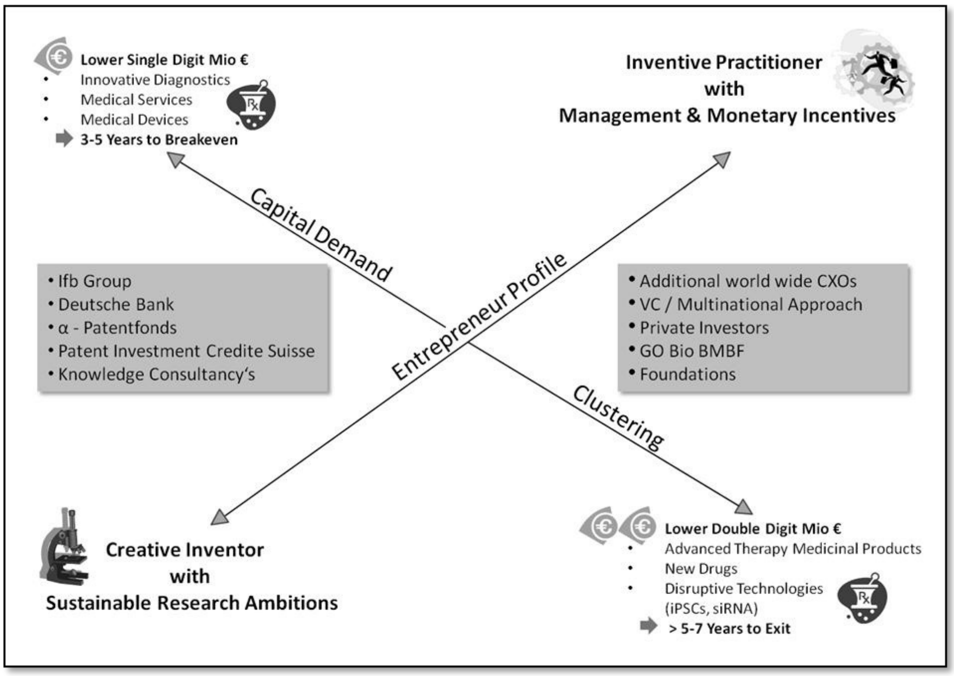

Figure 5: Entrepreneur Profile & Capital Demand

Source: Developed by authors, based on spin-off CEO's draft.

The following quote from this panel discussion emphasizes, that the German biotechnology sector is not used to radical innovation:

> "But what I have learned during this process [founding 5 biotech companies]; that is high product quality, high process quality, smooth human resource management and later stage, let's call it incremental innovation, here in Germany the favorite innovation, but we are not delighted for radical or cutting edge technologies."
> (Charité Panel Discussion, Spin-off, UM)

Furthermore *getting the team and the importance of the team and the people for success* was mentioned by the CEO. The content analysis of the talk and the draft leads to new perspective towards the qualities of the Entrepreneur for pursuing radical innovation, in a German ecosystem.

The Multiple Cases

The overall abstracted central concept for these multiple cases is **Partnership,** based on the term **Partner**. All other categories are related to it, the term partner and its meaning in correlation within and outside their organizations was frequently mentioned by all participants. Not only the frequency of appearance, but also the constant data evaluation of the empirical themes, based on all SME data, led to the conclusion, that the logic and consistent, central concept of the multiple case study is partnership (see Figure3).

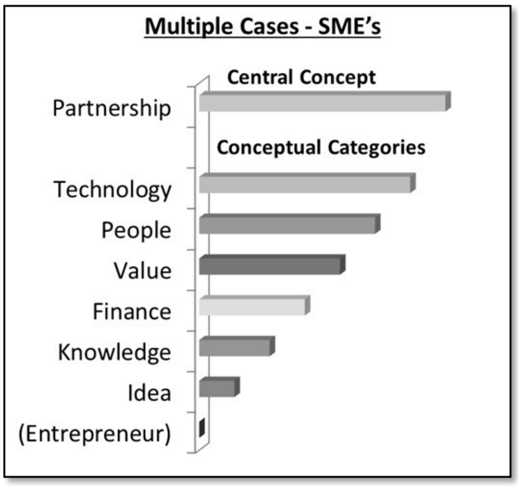

Figure 3: The SMEs Concept & Categories

Source: Developed by authors.

Partnership

Partnership in context with this part of the research study can be defined as the driving force for value creation trough innovation. Partnerships can be established at different levels, i.e. between individuals, between individuals and organizations and between organizations itself. More precisely, the individuals can be managers, employees, team members or private persons. The organizations can be companies, public or private research organizations, finance companies and institutions, universities, national or international regulatory institutions, national or international governmental and society organizations. This complex dimension demonstrates the abstracted level of partnership in an OI ecosystem, characterized by requiring the perfect orchestration of all capabilities (Torkkeli and Mention, 2015).

The following Table 1 is summarizing the correlation between the categories and the specific implications for the 5 key Open Innovation activities.

Table 1 Multiple Cases - SME's - Central Concept: Innovation Partnerships

Conceptual Categories	*5 Key Open Innovation Activities*				
	R&D	*IP*	*COL*	*NET*	*EL*
Technology	▪ Technology type & developmental status counts for external complementary or additional technology ▪ All approaches are possible- make, buy, make & buy ▪ Demand for distinction between **R**esearch and **D**evelopment as different activities	▪ Start with profound IP protection ▪ High quality IP protection to gain FTO ▪ Demand for multilayer protection ▪ Out-&Cross Licensing Opportunity	▪ Demand for trustful relationship ▪ Value the partners technology like you own ▪ Threat of negative reputation of COL partners due to litigation	▪ Technology type & developmental status defines best suitable NET platforms	▪ Technology leadership in the market due to technical edge
People	▪ Demand for highly qualified people - experts in their fields ▪ Importance of internal innovation culture	▪ Threat of leakage of confidential information ▪ Demand of legal frameworks for information exchange between partners (i.e.CDA, NDA)	▪ Demand for open minded, creative thinkers, who likes to share ▪ Importance of personal relationship in partnerships	▪ Enabler to find the right people for COL ▪ Existing network - source for new partnerships ▪ Importance of face-to face, in person meetings	▪ Importance of internal leadership - the autocratic leader ▪ Internal champions at different stages of the value chain ▪ Demand for different leadership types over the product life cycle
Value	▪ Importance of faster time to market ▪ Enhanced value of R&D outcome due to buy and make & buy approach	▪ Value from shared IP - enhanced quality ▪ Value from in-, out- and cross licensing - monetary	▪ "David versus Goliath" situation ▪ Mutual knowledge of partners strengths and weaknesses	▪ Importance of NET as a key activity ▪ Demand to identify potential future partners	▪ Importance of leadership as key activity ▪ Role model function of the leader ▪ Demand for different leadership types

		■ Early focused FTO strategy due to high quality IP supported by expert attorneys ■ Signaling effect of granted patents	■ Demand of legal framework & project plan with clear goal definition ■ Importance of security and trust between partners		■ Leadership role of the whole project team
Finance	■ Influence of high risk of R&D outcomes	■ Avoidance of overestimated income perceptions from licensing	■ Importance of future financial value gained from COL ■ Importance of financial, management and time resources		
Knowledge	■ Own expertise drives the type of external demand ■ Demand for constantly observing the market for external useful knowledge	■ Knowledge is the core of IPRs ■ Demand for knowledge about the IP process ■ Importance of knowledge what FTO means ■ Demand for constant learning process about own and others IP	■ Advantage of knowledge sharing between partners of different size and culture ■ Importance of strategic fit ■ Demand for profound COL project plan	■ Demand for NET to identify the right partner ■ Role of NET to get to know the right partner ■ Opportunity to share knowledge	■ Internal leaders provide the knowledgebase ■ Demand for constant development of internal capabilities
Idea	■ Demand for legal framework for idea sharing between partners	■ IPRs protect the idea behind the invention ■ Awareness of potential thread of external ideas of non-partners	■ Demand for open attitude towards own and external new ideas	■	■ Leadership function to motivate employees and partners to create new ideas and share them ■ Value of leadership qualities throughout the whole team

Source: Developed by authors.

5 Conclusions and Discussion

The overall data evaluation of the spin-off organization, including stepping back from the data, and approaching the data collection from different perspectives, led to the conclusion, that the right people and the entrepreneur are the building blocks for developing radical innovation in a German ecosystem. Especially in the interviews, not depended from the content of the questions, the participants mentioned with great emphasis the role of the founder and serial entrepreneur UM (CEO). His positive influence was present and described in regard to all five key Open Innovation activities. Therefore this conceptual category gained more importance comparing to the others.
The three research questions are answered in more detail in the following section.

To what extent is the Open Innovation concept adopted by biotech companies?
The outcome of the data analysis of the *multiple case studies* inferred that the Open Innovation phenomenon was not recognized by all participating companies. During the interviews, it was possible that the interviewee did not answer the closing question: “What is your definition of an Open Innovation Business Model?”, since he or she was not familiar with this term. Even so, from the multiple units of analysis of the same case, the evaluation of the data inferred that this particular company has adopted the Open Innovation concept. In summary the Open Innovation concept is adapted and adopted by the biotech SME's.

A new theory for **Innovation Partnerships** is created by linking the conceptual categories: Technology, People, Value, Finance, Knowledge and Idea with the 5 key Open Innovation activities R&D, IP, NET, COL and EL (see Table1).

The lesson learned about the biotech SMEs, is that they are examples for the successful adaption of Open Innovation, consciously and unconsciously. Their innovation strategy is on one side driven by their specific technology, and from the other side, strongly depended from the market need. Therefore the adoption and adaption of Open Innovation is an ongoing process, which needs more investigation, depended from the stage of the value chain.

What we can learn further from the participating SME managers is that theoretical phenomena like Open Innovation are there, but in their practical NPD process, the most important stakeholder is the patient.

Can Open Innovation enable the development of radical biotech innovation in the specific German ecosystem?
The outcome of the overall *single case data* evaluation suggests that it is possible to develop radical innovative products and services in a German ecosystem. Applying the concept of Open Innovation from "day one" was the starting point for this spin-off organization. Over the research study, the first impressions of the unique, open-minded personality of the serial entrepreneur and founder (UM), and his global vision remained as one of the most important success factors (Nambisan and Baron, 2013). Therefore, besides the central concept **People**, the most important conceptual category is **The Entrepreneur**.

We can learn from this spin-off company, that radical innovation needs the right people and an experienced entrepreneur. But these requirements are often fulfilled in start-up companies. What distinguishes the success from the failure? One of the most important success factors extracted from the overall study is that the entrepreneur is the person, who is selecting the right people at the right time. Impressive is here, that the spin-off team of 15 people has nearly no fluctuation (1 person left, 1 person founded a new company). Making the radical innovation *their project* from the early beginning is the best way to succeed in the competitive field of the "Human-on-a-Chip" project.

Nevertheless, this unique case has its limitations, since only one spin-off organisation was under investigation. The results from this case, developing a radical innovation should be compared with others, from the biotech sector, or from other high-tech sectors. Even so, since the "close up" view on this particular case is valuable, the results from the study are adding new theoretical and practical insights to the body of knowledge.

How does the evolving business model for an early stage company, pursuing the development of radically innovative products and services, look like?

The most important outcome from this study is that the evolving business model is not a static one. The different developmental stages, especially for a spin-off organization are demanding ongoing business model innovation, with strong tendencies to a platform design. As a technical innovation driver the spin-off company benefits from the adoption of Open Innovation, by actively forcing the in-and outflow of knowledge.

As the CEO defined his definition of the business model, he is willing to exchange valuable assets like intellectual property with external partners. All participating team members emphasised the importance of openness to collaboration and networking partners (Downs and Velamuri, 2016).

The theory for the specific business model, the causality and interdependence of the evolved conceptual categories: Technology, Knowledge, Idea, Partner and Finance, and their role in context with the 5 key Open Innovation activities are actually under further evaluation. Recent analyses are indicating that there are tendencies towards a business model *beyond* Open Innovation.

The intended knowledge contribution will be applicable to the biotech sector, in particular to the German biotech sector, as the outcome of the embedded case study research allows direct comparisons and conclusions. Since the study focuses on the socio-economic conditions and environment to develop radical innovative products, technologies and services, general conclusions and recommendations to other sectors and policy makers are envisioned too (Etzkowitz and Leydesdorff, 2000).

The outcomes of this study will add new knowledge and a better understanding, how spin-off organizations and SME’s adapt and adopt the Open Innovation concept. The findings, how radical innovations are transformed into novel technologies, products and services are valuable contributions to the body of knowledge in innovation management. Since the researcher conducted the study from the practitioners’ point of view and the demand for connecting theory with practice, both areas will benefit from the outcome of this research study.

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