Looking for the Healing Innovation Process

An Explorative Study on the Critical Success Factors for Innovation Management in the Pharmaceutical Industry



Master of Science thesis – Management of Technology
Delft University of Technology

Student: *Vincent L. Das*

Student number: *1352040*

Email address: *Vincent.l.das@gmail.com*

Date: *19-01-2014*

Word count: *39,939*

Master: *Management of Technology*

Graduation Committee

Chairman:	*Prof. Dr. C.P. van Beers* *TU Delft TPM faculty, Economics of Technology and Innovation*
First supervisor:	*Dr. R.M. Verburg* *TU Delft TPM faculty, Economics of Technology and Innovation*
Second supervisor:	*Dr.ir. U. Pesch* *TU Delft TPM faculty, Philosophy*
External supervisor:	*Dr.ir. N. Buitelaar, MBA* *Leiden Bio Science Park foundation*

Company

Leiden Bio Science Park foundation
Poortgebouw Noord
Rijnsburgerweg 10
2333 AA Leiden

University

Delft University of Technology
Faculty of Technology, Policy and Management
Jaffalaan 5
2628 BX Delft

Contents

Abstract 9
Samenvatting 10
Abbreviations 11
1. Introduction 13
1.1. The pharmaceutical industry 13
1.2. The innovation process of the pharmaceutical industry 14
1.3. Financial models of the pharmaceutical industry 16
1.4. Problem definition 17
2. Literature review 19
2.1. Innovation performance 19
2.2. Knowledge management 19
2.2.1. Knowledge 19
2.2.2. Knowledge processes 20
2.2.3. Knowledge management in the pharmaceutical industry 22
2.3. Knowledge network 23
2.3.1. Absorptive capacity 23
2.3.2. Knowledge network 24
2.3.3. Knowledge network in the pharmaceutical industry 24
2.4. Motivation 25
2.4.1. Self-Determination Theory 25
2.4.2. Motivation in the pharmaceutical industry 25
2.5. Creative climate 26
2.5.1. Creative individuals, teams and organizations 26
2.5.2. Creative climate in the pharmaceutical industry 26
2.6. Company characteristics 26
2.6.1. Company size 26
2.6.2. Formalization 27
2.6.3. Company strategy 27
3. Methods 29
3.1. Confirming interviews 29
3.2. Interviews 29
3.2.1. Company characteristics 30
3.2.2. Knowledge processes 30
3.2.3. Knowledge network 30
3.2.4. Motivation 30
3.2.5. Innovation performance 30

4. Results 33
4.1. Company characteristics 33
4.2. Knowledge processes 34
4.2.1. Knowledge application 35
4.2.2. Knowledge acquisition 36
4.2.3. Knowledge creation 37
4.2.4. Knowledge distribution 38
4.2.5. Knowledge sharing 39
4.2.6. Knowledge storing 40
4.2.7. Identifying knowledge gaps 41
4.3. Knowledge network 41
4.3.1. From companies to universities 42
4.3.2. From universities to companies 43
4.3.3. Between companies 44
4.4. Motivation 45
4.4.1. Relatedness 45
4.4.2. Autonomy 47
4.4.3. Competence 48
4.5. Innovation performance 48
4.6. Summary results 49
5. Discussion 51
5.1. Phases of Research and Development 51
5.1.1. The learning phase 51
5.1.2. The confirming phase 52
5.1.3. The transitional phase 52
5.2. Innovation strategies 53
5.2.1. Large pharmaceutical companies 53
5.2.2. Small and Medium sized Biopharmaceutical/Biotechnology Enterprises 54
5.2.3. Knowledge institutes 54
5.3. The knowledge reactor model 55
5.4. Other findings 57
6. Conclusion 59
7. Final remarks 61
7.1. Implications 61
7.1.1. Scientific implications 61
7.1.2. Managerial implications 61
7.2. Reflection 62
7.3. Recommendations further research 62
8. Acknowledgements 65

Appendix A : Definition of Small and Medium sized Enterprises 67
Appendix B : What is the Leiden Bio Science Park 69
B.1 Dutch pharmaceutical industry 69
B.2 Dutch clusters 70
B.3 LBSP outline 71
Appendix C : Summaries of the first two interviews 75
Appendix D : Methods and results of questionnaire 77
D.1 Methods questionnaires 77
D.1.1 Dependent variable 77
D.1.2 Independent variables 77
D.1.3 Control variables 77
D.2 Results questionnaire 78
Appendix E Scales used for questionnaire 81
E.1 Introduction 81
E.2 Control variables 81
E.3 Knowledge processes 81
E.4 Knowledge network 82
E.5 Company Culture 82
E.6 Leiden Bio Science Park 83
E.7 Closing remarks 83
Appendix F Coding of the interviewed companies 85
Appendix G : Spearman correlation matrix of the codes used for the companies 87
Appendix H : Interview with the Leiden University Technology Transfer Office LURIS 89
Appendix I : Factor analysis 91
Literature list 93
Scientific literature 93
Non scientific literature 98

Abstract

The pharmaceutical industry has been spending an increasing amount of money on R&D over the years. However, fewer drugs have been approved by the FDA and the EMA recently. This lack in innovation performance is a problem which needs to be solved in order to continue finding medicines for cureless diseases.

Innovation lies at the heart of the problem. It is for this reason that we need to understand more about the innovation management of the pharmaceutical industry. The scientific literature is scattered and a more general list of critical factors would help in improving the innovation performance of these companies. Therefore the main question of this thesis is defined as: "*What are the internal critical success factors for innovation management in the pharmaceutical industry?"*

This thesis includes an explorative research by interviewing fifteen managers of drug developing companies in the Leiden Bio Science Park in the Netherlands. During these interviews the focus was put on five factors; knowledge processes, knowledge network, motivation, innovation performance and company characteristics.

The results show that there is a sharp distinction between large pharmaceutical companies and Small and Medium Sized Biopharmaceutical/Biotechnology Enterprises (SMBEs). These differences are mostly found in the knowledge processes, the knowledge networks and in the motivation of research employees. Also, three R&D phases can be distinguished by looking at the same focus points.

The results presented in this research come from a small dataset. In further research it is recommended to measure the same aspects on a larger scale confirming the findings of this research. Also innovation performance can then be measured more accurately and related to the found critical factors.

Key Words: *Knowledge Management, Absorptive Capacity, Motivation, Innovation Performance, Pharmaceutical Industry, Biotechnology, Small and Medium Sized Enterprises.*

Samenvatting

De farmaceutische industry geeft de laatste jaren steeds meer geld uit aan R&D. Desondanks worden er minder medicijnen goedgekeurd door de FDA en de EMA. Dit gebrek aan prestatie in innovatie is een probleem wat opgelost moet worden zodat de industry door kan gaan met het vinden van medicijnen voor ongeneesbare ziektes.

Innovatie is de kern van het probleem. Daarom is het belangrijk om meer te begrijpen over innovatie management in de farmaceutische industrie. De wetenschappelijke literatuur is verdeeld over verschillende onderwerpen. Een overzicht van kritieke factoren zou daarom kunnen helpen bij het verbeteren van de prestatie in innovatie van deze bedrijven. Het is om deze reden dat de hoofdvraag van dit onderzoek als volgt gedefinieerd is: *"Wat zijn interne kritische succes factoren voor innovatie management in de farmaceutische industrie?"*

Dit onderzoek behandelt een exploratieve methode waarbij vijftien medicijn ontwikkelende bedrijven zijn geïnterviewed in het Leiden Bio Science Park in the Netherlands. In deze interviews is voornamelijk gekeken naar vijf factoren; kennisprocessen, kennisnetwerk, motivatie, prestatie op het innovatieve vlak en bedrijfscharacteristieken.

Uit de resultaten kan worden geconcludeerd dat er een scherpe onderverdeling is tussen grote farmaceutische bedrijven en kleine tot grote biofarmaceutische, biotechnologie bedrijven. Deze verschillen zijn voornamelijk gevonden bij de kennisprocessen, kennisnetwerken en de motivatie van de onderzoekers. Er zijn ook drie R&D fases ontdekt door te kijken naar dezelfde focus punten.

De resultaten in dit onderzoek zijn afkomstig van een kleine dataset. Het is daarom aanbevolen om in toekomstig onderzoek te kijken naar dezelfde aspecten om zo op grote schaal deze bevindingen te kunnen bevestigen. Op deze manier zou de prestatie in innovatie ook precieser gemeten kunnen worden en daardoor gerelateerd worden aan de kritieke factoren.

Abbreviations

ACAP = Absorptive Capacity
CRO = Contract Research Organization
CMO = Contract Manufacturing Organization
EMA = European Medicines Agency E.U.
FDA = Food and Drug Administration U.S.
GMP = Good Manufacturing Practices
IP = Intellectual Property
IPO = Initial Public Offering
ITA = International Trade Administration U.S.
IT = Information Technology
KM = Knowledge Management
KMS = Knowledge Management System
LBSP = Leiden Bio Science Park
LBSPf = Leiden Bio Science Park foundation
LSH = Life Science & Health
LU = Leiden University
LUMC = Leiden University Medical Center
LURIS = Leiden University Research & Innovation Services
NBE = New Biological Entity
NCE = New Chemical Entity
NME = New Molecular Entity
PACAP = Potential Absorptive Capacity
RACAP = Realized Absorptive Capacity
R&D = Research and Development
SDT = Self-Determination Theory
SME = Small and Medium sized Enterprise
SMBE = Small and Medium sized Biopharmaceutical/Biotechnology Enterprise
SSP = Specialized Service Provider
TTO = Technology Transfer Office
VC = Venture Capital

1. Introduction

In this report an explorative research is described for a master thesis looking into innovation management of the pharmaceutical industry. First, an introduction is given on the unique characteristics of the pharmaceutical industry and the underlying problems within the industry. After the introduction, the thesis is continued with a short literature study on innovation management. Then, results of the literature study are summarized into target subjects for this research. The methods and results for these mentioned subjects are described and followed by a discussion. The thesis ends with a conclusion and implications and propositions for further research.

1.1. The pharmaceutical industry

The worldwide life expectancy for humans has been growing over the years. According to the Human Mortality Database the world average life expectancy has been growing from 45 (1950) to 68 years (The Human Mortality Database 2013). It is mainly thanks to the pharmaceutical industry that we were able to decrease the number of deaths and cure or prevent diseases, thereby increasing the life expectancy. Old large pharmaceutical companies have been able to create many blockbuster medicines (large scale used products) which are now spread all over the world. But the pharmaceutical industry is not finished with increasing the worldwide health. There are still many diseases for which there are no treatments available. Some diseases or disorders remained untreated because of the low number of patients to be treated. The so called '*orphan drugs'* (drugs for very rare diseases) have become a new interest of the pharmaceutical industry as to improve worldwide health. All these things motivate that ongoing innovation from the pharmaceutical industry is required.

There are now so many companies involved in the Life Science & Health (LSH) industry that it made formulating a definition of the '*pharmaceutical industry'* difficult. However, a precise definition is needed which can be used for the scope of this research. The definition of the '*pharmaceutical industry*' for this thesis was copied from the U.S. International Trade Administration (ITA):

> *"…companies engaged in researching, developing, manufacturing and marketing drugs and biologicals for human or veterinary use."* (ITA 2010)

This definition contains a broad range of companies because not only the drug developing firms are part of the pharmaceutical industry but also *medical technology manufacturers* and *Specialized Service Providers* (SSPs). Examples of SSPs for the pharmaceutical industry are Contract Research Organizations (CROs) for clinical phase studies or Contract Manufacturing Organizations (CMOs) for manufacturing drugs.

Besides the classic pharmaceutical industry there is now also the growing *biotechnology industry*. Many scientists see the invention of the technologies for recombinant DNA in 1973 (Cohen, Chang et al. 1973) and of the monoclonal antibodies in 1975 (Köhler and Milstein 1975) as the starting point of the biotechnology industry. From this point on, scientist were able to use living cells to produce chemicals (*white biotechnology*), design new crops (*green biotechnology*), purify water faster (*blue biotechnology*) and produce complex biological medicines (*red biotechnology*) by altering and using the internal mechanisms of cells. The terminology of these four colored groups of biotechnology is often used to describe the different focus points. Especially the red biotechnology is of interest for this thesis because it is the biotechnology sector for the health industry. Many medicines are complex proteins or virosomes which can only be produced by using the transcription and translation processes of living organisms. The definition of biotechnology used in this thesis was described by the ITA as:

> *"…technologies that use organisms or its components to make products; or to modify plants, animals and micro-organisms to carry desired traits."* (ITA 2010)

These desired traits are not only restricted to producing wanted compounds but can also refer to the ability of micro-organisms to clean waste water or polluted soil. There is some overlap between the biotechnology and the pharmaceutical industry which seems to have increased over the years (see Figure 1). Old pharmaceutical companies, which have been focusing on chemically synthesized small

molecule medicines called New Chemical Entities (NCEs), start to switch to more complex drugs like hormones or antibodies called New Biological Entities (NBEs). For the realization of these complex compounds biotechnology techniques are required (Lawlor 2013). The red biotechnology seems to have opened new niches and markets. These new biotechnology businesses have also been referred to as *biopharmaceutical firms*, underlining the fact that biotechnology methods are used to develop NBEs (Hopewell 2003). This would indicate that it seems as if there is no difference between the biopharmaceutical companies and the red biotechnology companies. Throughout this thesis the pharmaceutical industry is referred to according to the definition mentioned before. The reader should keep in mind that this means that some biotechnology firms (red biotechnology/biopharmaceutical) are likewise considered inside this industrial sector. Other areas of overlap between the biotechnology industry and pharmaceutical industry are the diagnostical tools used and specialized services like laboratory equipment

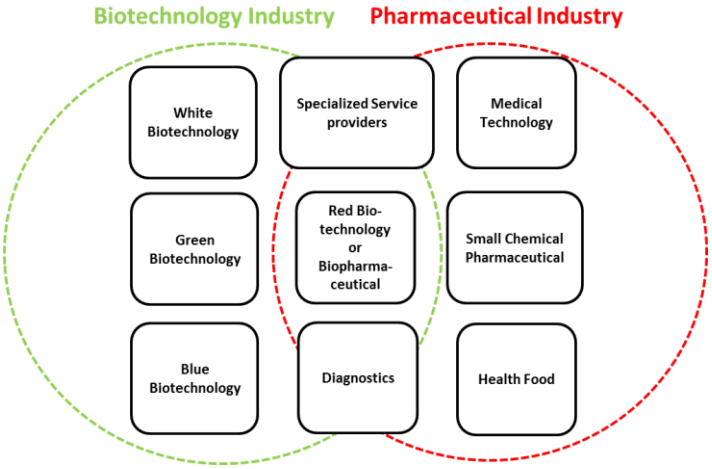

Figure 1 Schematic representation of the pharmaceutical industry and the biotechnology industry which represents the overlapping area of biopharmaceutical sciences/red biotechnology.

1.2. The innovation process of the pharmaceutical industry

Innovation is of great importance for creating a competitive advantage in high-technology companies. (Dyer and Nobeoka 2000). The pharmaceutical industry is considered as high-tech (Hatzichronoglou 1997) and thus innovation plays a key role. In order to remain innovative, pharmaceutical companies focus on research & development (R&D) to improve and increase their product portfolio. Schumpeter defined innovation as:

"…*the setting up of a new production function.*" (Schumpeter and Fels 1939)

Within this definition not only products but also processes and services are considered as innovations. This definition served as a starting point to find a definition that fits the scope of this research. The innovation process of the pharmaceutical industry is unique and requires many coordinated steps over an average cycle period of 15 to 21 years (Ortt, Tabatabaie et al. 2009, Raaphorst 2012, Raaphorst 2013). The complete cycle of potential drug idea generation up to the market introduction can roughly be separated into four stages (Raaphorst 2012); *discovery & development*, *preclinical phase*, *clinical phase* and finally *approval & marketing*.

Discovery & development: This stage starts at pharmaceutical companies, research institutes or universities. Scientists focus on certain diseases by conducting fundamental research. Here they will look closely at certain target chemicals, receptors, proteins or cells to counter the effects of a disease. High-throughput screening is a commonly used technology to increase speed of screening for potential drug candidates (Hertzberg and Pope 2000). Many chemical/biological compounds will pass certain tests until interesting drug agents are found. Companies also need to develop the production process of these compounds and assays to analyze and measure these compounds during this stage.

Preclinical phase: After the first stage the most interesting compounds will continue for further complicated testing on models and animals to see whether the desired medical improvement

can be found. Additionally, some first research in up-scaling production is being done in this stage as well. During these first two stages most of the potential medicines already fail. This reduction in potential drug candidates is schematically represented as the funneling model shown in Figure 2 (Raaphorst 2012).

Clinical phase: After preclinical testing, researchers are more certain about the potential effects of their compounds. This means that trials on humans can be started. Clinical trials are separated in three phases. In case a drug does not pass a phase successfully, the clinical progress is terminated. During Phase I the drug is tested on healthy volunteers to measure the drug activity and the toxicity. In Phase II the drug is tested on a small group of patients of the target disease. In this phase the effectiveness of the drug is investigated. Finally, in Phase III, the drug will be used on a large group of patients to prove effectiveness and see long-term results on a large dataset. The preclinical studies and the three clinical phases are mostly referred to as the '*drug pipeline' (Raaphorst 2012)*.

Approval & marketing: All the results of (pre)clinical studies are combined into a document. This will be sent for approval to regulatory organizations like the FDA (U.S. Food and Drug Administration) or the EMA (European Medicines Agency) depending on which market the pharmaceutical company wants to sell its new drug. These filed documents are inspected to see whether the trials truly prove that the benefits are significantly better than existing treatments and outweigh potential side-effects. After filing and approval, the drug becomes a medicine and can finally be sold on the market.

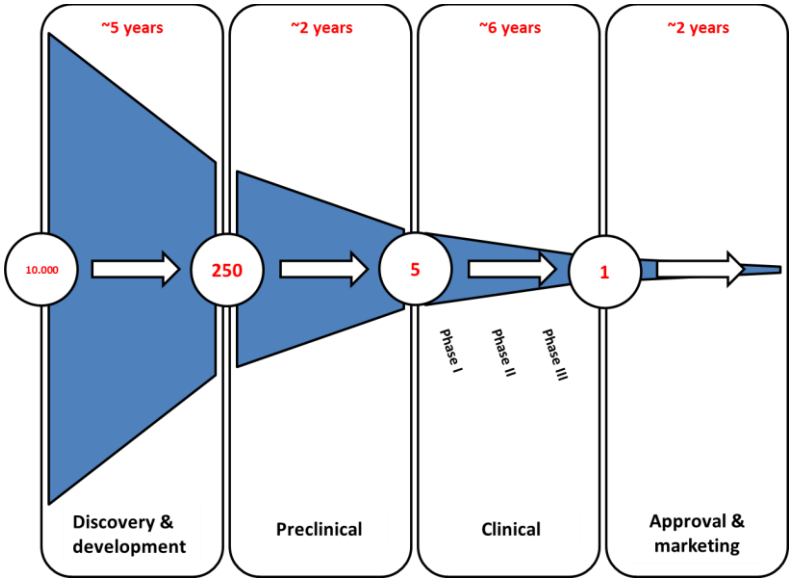

Figure 2 Funnel model for the innovation process of the pharmaceutical industry. The average duration is given on top of every stage. It is estimated that from the 10.000 potential drug compounds only one will make it to the market. Altered model from Raaphorst was used (Raaphorst 2012).

In the above mentioned definition of *innovation* by Schumpeter, the formation of new products, processes and services are included. However, this thesis focuses solely on drug innovation and for this reason *pharmaceutical innovation* will be considered as the formation of new potential medicines. Approval and marketing do not seem to contribute to the formation of new potential medicines and will not be considered here. Thus the focus in this research will be on the first three steps of the innovation process mentioned in Figure 2.

With this definition of innovation in the pharmaceutical industry, the scope of organizations used to study innovation management can be narrowed down. The focus on pharmaceutical innovation for this thesis lies on the actual discovery and development of NCEs and NBEs; the area in which new drugs are searched for and developed until they pass all clinical trials. This includes biopharmaceutical firms (red biotechnology), chemical pharmaceutical firms and knowledge institutes. Pharmaceutical firms are easily targeted by identifying the active drug pipeline. The knowledge institutes are added to the scope as well, because many start-up pharmaceutical firms are based on ideas generated at knowledge institutes.

Technology Transfer Offices (TTOs) are also very interesting because they contribute in transferring ideas of knowledge institutes into the innovation funnel of the pharmaceutical industry by selling or licensing these to commercial companies (West and Nightingale 2009). These TTO's are part of universities and therefore part of the knowledge institutes. Though they are highly involved in the process of innovation, they do not generate new potential medicines themselves and are therefore excluded from this study on innovation management.

1.3. Financial models of the pharmaceutical industry

The pharmaceutical industry does not only have a special innovation process, but also some unique financial models for their R&D. Clinical studies become larger and thus more expensive when a drug continues on the innovation process. However, no revenues can be earned during R&D because no drugs can be sold until they are approved. This means that a company can be without revenues for 21 years (Ortt, Tabatabaie et al. 2009). The closer drug development gets to market introduction, the more expensive their operational costs become. There are mainly five strategies for financing these clinical studies (Kerkhof 2012, Raaphorst 2012, Raaphorst 2013); investment from Venture Capital (VC) and sell rights of the product to large pharmaceutical firms, investment from VC and merge/be acquired by a large pharmaceutical firm, investment from VC and earn back through Initial Public Offering (IPO), earn revenues from services and invest this in own drug development or having enough revenues from other medical products already approved on the market. These revenues allow companies to reinvest in new products for the drug pipeline and to increase their portfolio.

Start-up companies, mostly categorized as biotechnology companies, have access to many grants from universities and governments which allow them to perform discovery research. When these funds run dry, most of the companies have found interesting drugs for preclinical research but lack the financial resources to continue. It is from this point that companies need to attract more investments to start preclinical and clinical research. This gap of finding investors is called the '*Valley of death*' (Rai, Reichman et al. 2008, Raaphorst 2013). VC investors mostly invest in these start-up companies only when they have promising results to show from which high returns can be expected. Therefore, the start-up companies need an exit strategy which will allow the VC investors to earn their invested capital back within a desired time frame. The problem however is that the VC investors force small biotechnology companies to use an exit strategy before their products can be launched on the market (Raaphorst 2013).

The division between the small biotechnology companies and large pharmaceutical companies is being preserved because of these financial strategies. It seems as if financial strategies created a stalemate which does not allow small pharmaceutical companies to fully grow. However, the large pharmaceutical firms are not safe either. Many of these companies were able to create blockbuster medicines in the 1990s, which patents are now expiring. This is called the '*patent cliff*' of the pharmaceutical industry (Abou-Gharbia and Childers 2013). After this point competitors are allowed to produce these blockbuster medicines and compete on the market. The portfolio of these old firms should be correctly balanced and thus they have tried to refill their revenues with newly found medicines.

The patent cliff resulted in some other problems in financial strategies as well. When a patent on a certain medicine runs out, it is relatively easy for a new company to enter the same market. Proof of principle has already been paid for (clinical trials) and medicine production methods are also made public due to the publicity of patents. So some pharmaceutical companies focus on so called 'me-too-drugs'. 'Me-too-drugs', or generics, are medicines which have the same or similar molecular structures as a drug for which the patent expired and can be put on the market relatively cheap without large risky investments. Thus a lot of R&D money is not invested in finding cures for untreatable diseases, but finding new cures for already treatable diseases. The pharmaceutical innovation process is sometimes declared to be 'sick' where it only spends 10% of their R&D money on 90% of the known diseases that have no current treatment (Stiglitz and Jayadev 2010). Stiglitz and Jayadev proposed a new funding system where pharmaceutical companies should pay a fine when there is no added value for their product on the market (Stiglitz and Jayadev 2010). This would stimulate the generation of 'first-in-class' medicines rather than 'me-too-drugs'. This would in addition also stimulate best-in-class medicines over comparable 'me-too-drugs' (Schmid and Smith 2002). These best-in-class medicines allow competition and thus price competition. It can make drugs more

affordable but still does not solve the problem of untreatable diseases. Other scientists see an opportunity for emerging economies (Abou-Gharbia and Childers 2013) because most of these 90% drugless diseases are large national problems in these countries.

1.4. Problem definition

The pharmaceutical industry has been growing for a long time. Although an increase in R&D investment has been measured the last decade (see Figure 3), the amount of new drugs approved by the FDA or the EMA is not growing as anticipated (Cockburn 2004). Many expected that the relation between R&D spending and drug approvals would be linear. When more money is invested into the discovery of drugs, more NCEs or NBEs would be approved. However, Figure 3 clearly shows that this is not the case. This disappointing result has been cracking many scientists' brains. One might say that the further we continue in drug developments the harder it becomes to find new cures because of decreasing potential targets. Whether this process is linear or not, many patients still wait for medicines for their untreatable diseases.

A lot of researchers have looked into the innovation performance of the pharmaceutical industry because they believe that innovation performance must be increased (Yeoh 1994, Cardinal and Hatfield 2000, Cockburn and Henderson 2001, Gassmann and Reepmeyer 2005, Hung, Huang et al. 2005, Sundgren and Styhre 2007, Karim 2009, West and Nightingale 2009, Huang, Lai et al. 2011, Hunter 2011, Zhaohui and Xiaokang 2011, Rocha, Lima et al. 2012). This declining innovation performance is a serious problem for a world with a large need for new medicines. These medicines are needed in order to find cures for untreatable/orphan diseases or to find improved treatments for replacing old medicines, Ironically, one might even say that the innovation process appears to be 'sick' and needs to be 'healed' as to continue developing drugs for orphan drugs and other cureless diseases.

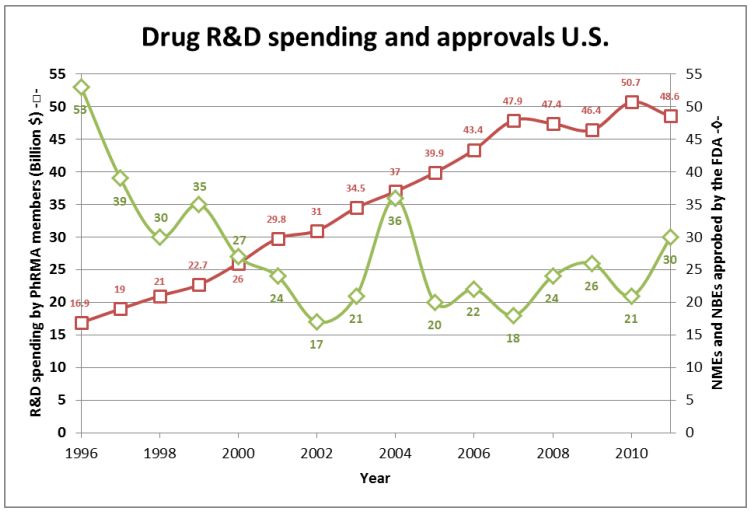

Figure 3 Amount of money spent on R&D by U.S. companies registered at PhRMA (PhRMA 2013) (-□-) and the amount of New Molecular Entities (NME) and New Biological Entities (NBE) approved by the FDA (CDER 2010, Center for Drug Evaluation and Research 2012) (-◊-).

There are two major problems in the pharmaceutical industry which are linked to this low innovation performance. They have been there since the start of the pharmaceutical industry but now seem to have become more threatening due to decreasing potential targets. First of all, it is common in this industry that the percentage of failed projects is high (Hynes Iii 2009, Raaphorst 2012). Approximately 50% of the projects focusing on radical new medicines that start clinical trials do not make it to the market (Schmid and Smith 2002). It was estimated that from all the potential drug projects only 8% result into NCEs or NBEs (Hynes Iii 2009).

Besides the risks involved in this industry there is also a financial problem which was mentioned before in chapter 1.3. All new drugs must go through expensive clinical trials. These clinical trials take up eight years on average (Schmid and Smith 2002, Raaphorst 2012) before drugs are approved by the FDA or the EMA. It was estimated that the development of one NCE would cost over 802 Million US Dollars (DiMasi, Hansen et al. 2003).

The *low success rate* and *high expenses* combined make it difficult for pharmaceutical companies to innovate. The pharmaceutical industry needs an innovation performance pulse. But just investing more money into R&D is not a viable solution, as shown in Figure 3. To understand more on how to create such an increase in innovation performance, one must first understand the innovation process of the pharmaceutical industry. After that, a potential list of important critical factors can be created. Such a list can be helpful not only for managers of existing companies, but also for entrepreneurs who are new to the area of innovation management. It is impossible to prevent projects from failing because of bad results in clinical trials, but it might be possible to increase performance by changing management styles. In order to gain insight in the critical success factors an explorative study was performed which is presented here. The main research question of this thesis was:

"*What are the internal critical success factors for innovation management in the pharmaceutical industry?"*

To come to the conclusion of the main question some sub questions need to be answered. Each chapter of this thesis is dedicated in answering one sub questions which brings us closer to the main goal of this thesis. The sub questions for each chapter can be found in the list below:

Chapter 2*: "What aspects of innovation management, currently mentioned in the scientific literature, are important for the pharmaceutical industry?"*

Chapter 3*: "How to measure the important aspects of innovation management mentioned in the scientific literature?"*

Chapter 4*: "What are the findings in relation to important aspects of innovation management in the LBSP companies under study?"*

Chapter 5*: "What are the trends for the important aspects of innovation management in the LBSP?"*

Chapter 6*: "What can be concluded about the internal critical success factors for innovation management in the pharmaceutical industry according to the results of the LBSP companies?"*

Chapter 7.1*: "What are the implications of the findings of the results of this research?"*

Chapter 7.2*: "What are the strong and what are the weak points of this research on the critical success factors for innovation management in the pharmaceutical industry?"*

Chapter 7.3*: "What research can be recommended for the future to follow up this research?"*

First a literature study on innovation performance and antecedents in the pharmaceutical industry is summarized in chapter 2. In chapter 3 the methods used for this thesis are briefly described. In chapter 0 and 5 results of this research are illustrated and discussed respectively. Chapter 6 contains a brief conclusion followed by the last chapters which contain the implications for scientific research (7.1.1), implications for the industry managers (7.1.2), a short reflection on the research performed (7.2) and future recommendations for further research (7.3).

2. Literature review

The problem addressed in the introduction is the decreasing innovation performance of the pharmaceutical industry. If the critical factors that influence this innovation performance are known, it can be used to increase the medicine output of the industry without wasting more money on R&D.

This chapter discusses the known information on innovation management as it is expected that innovation management will have the tools and controls to influence the innovation performance. The sub question that will be discussed in this chapter is the following:

"What aspects of innovation management, currently mentioned in the scientific literature, are important for the pharmaceutical industry?"

The information presented in this chapter was gathered from scientific publications specifically focused on innovation performance and innovation management in the pharmaceutical industry. From these findings it was decided to focus on five subjects; *knowledge management*, *knowledge network*, *motivation*, *creative climate*, and *company characteristics*. The influence and the reason behind this choice are described in the following. Also several other subjects were found in the literature review but with much less support. It is for this reason it was chosen not to use these topics and to remain focused on the five subjects mentioned above.

2.1. Innovation performance

The main problem addressed in the introduction is the low number of drug approvals of the last years despite the increase in R&D budgets of the pharmaceutical companies. Although a linear relationship cannot be assumed, it is clear that a higher output of new medicines is wanted. This problem is a clear indication of declining *innovation performance* of the industry. Innovation performance seems like an easy factor to measure for a whole industry. However, innovation performance is not a simple indicator to be measured on a company scale. One has to think about the definition of true productive innovation. The scientific literature provides many different approaches in quantifying innovation performance. Some use the number of patents (Lane, Koka et al. 2006), percentage of sales for certain new products (Roper, Du et al. 2008), amount of new introduced products on the market (Roper, Du et al. 2008, Bagnoli and Vedovato 2012), involvement in innovation projects (Keizer, Dijkstra et al. 2002) or use several Likert-scales (Hitt, Hoskisson et al. 1996, Liao, Fei et al. 2007, Wang, Wang et al. 2010, Hurmelinna-Laukkanen, Olander et al. 2012). However, most of these indicators are not fitted to measure innovation performance in the pharmaceutical industry. The innovation cycle of this industry takes a long time (Ortt 2009, Raaphorst 2012, Raaphorst 2013) which means that the results on the market are measured with a long delay. Therefore, solely looking at products approved for the market would not measure product innovation which happened before the market approval. This leads to an inaccurate measurement of innovation performance.This explorative research will therefore look into innovation performance of the pharmaceutical industry to see whether any measurements can make this concept quantifiable.

2.2. Knowledge management

2.2.1. Knowledge

According to the definition presented in chapter 1.2, the setting up new products is called innovation. To create something new one must have access to a knowledge base (Nesta and Saviotti 2005). These new products, processes and services can be created by using new knowledge or by making new knowledge combinations. It can be said that knowledge lies at the heart of innovation. That is why this research is mainly focused on knowledge in the innovation process.

Knowledge has been approached by many as a resource which can create innovation success (Deeds and Decarolis 1999, Dyer and Nobeoka 2000, Swan and Scarbrough 2001, Jantunen 2005, Andriessen 2006). Some make a distinction between explicit and tacit knowledge with explicit knowledge being codified, structured and accessible knowledge which can easily be transferred and tacit knowledge being not easily transferable because it is based on mental modes, skills and experience which makes it difficult to share with co-workers, but not impossible (Nonaka 1995, Weggeman 1997, Andriessen 2006).

Managing knowledge became an important topic, because it was found that knowledge is a valuable resource for a competitive advantage (Dadfar, Dahlgaard et al. 2013). This resulted in a large stream of literature dedicated to *Knowledge Management* (KM). For example there are two different KM strategies found which can be used separately or combined. These strategies are *codified* and *personalized* KM (Hansen, Nohria et al. 1999). Codified KM mostly uses explicit knowledge transfer processes like written documents and reports. The advantages of this strategy are that knowledge can be distributed easily and is accessible by many employees worldwide. However, the main issue of this knowledge transfer is the translation of the tacit knowledge into explicit knowledge. Not all knowledge can be codified, thus the storing of knowledge is not always preferred or possible. The second strategy is personalized KM where personal contact between employees is the main transfer process. Employees and/or scientist should pass tacit knowledge on to each other through internal training, presentations and conversations.

Although KM has been a widely used concept, knowledge itself is often difficult to manage partly due to the tacit knowledge of employees. However, the processes involving knowledge within an organization are manageable and thus people rather talk of *knowledge process management* instead of knowledge management (Weggeman 1997, Andriessen 2006, Verburg and Andriessen 2011). Throughout this thesis, knowledge management was used even though knowledge process management is actually meant.

2.2.2.Knowledge processes

There is not much consensus on the terms used to categorize knowledge management. Braganza et al. refers to knowledge projects, which are actions a company can get engaged in considering knowledge (Braganza, Edwards et al. 1999). These projects can be categorized into *exploring*, *exploiting*, *enhancing* and *expediting* actions. However, others speak of many different knowledge processes like *knowledge acquisition* (Gold, Malhotra et al. 2001, Jantunen 2005, Lin and Lee 2005, Chen and Huang 2009, Huang and Li 2009, Jiménez-Jiménez and Sanz-Valle 2011, Verburg and Andriessen 2011), *application* (Alavi and Leidner 2001, Gold, Malhotra et al. 2001, Lin and Lee 2005, Chen and Huang 2009, Huang and Li 2009, Hung, Lien et al. 2010, Verburg and Andriessen 2011), *capture* (Lee and Hong 2002), *conversion* (Gold, Malhotra et al. 2001), *creation* (Alavi and Leidner 2001, Hung, Lien et al. 2010, Xu, Houssin et al. 2010, Verburg and Andriessen 2011), *development* (Lee and Hong 2002), *dissemination* (Jantunen 2005, Alegre, Sengupta et al. 2013), *distribution* (Jiménez-Jiménez and Sanz-Valle 2011, Verburg and Andriessen 2011), *interpretation* (Jiménez-Jiménez and Sanz-Valle 2011), *processing* (Xu, Houssin et al. 2010), *protection* (Gold, Malhotra et al. 2001), *sharing* (Lee and Hong 2002, Lin and Lee 2005, Oshri, Pan et al. 2006, Chen and Huang 2009, Huang and Li 2009, Verburg and Andriessen 2011), *storing* (Alavi and Leidner 2001, Hung, Lien et al. 2010, Verburg and Andriessen 2011, Alegre, Sengupta et al. 2013), *transfer* (Alavi and Leidner 2001, Oshri, Pan et al. 2006, Hung, Lien et al. 2010), *usage* (Xu, Houssin et al. 2010) and *knowledge utilization* (Lee and Hong 2002, Jantunen 2005, Artz, Norman et al. 2010). As one might notice, there are many terms mentioned above that refer to the similar processes, meaning that there is some consensus on the categorization of knowledge management.

One of the most used and quoted distinction between different knowledge acivities is the one made by Nonaka (Nonaka 1995, Alavi and Leidner 2001, Carlile 2004, Andriessen 2006, Verburg and Andriessen 2006). Nonaka speaks of a knowledge spiral. A person starts with tacit knowledge which is created from experience. Another person can learn this tacit knowledge through a process called *socialization*, which is a master-apprentice relationship. This tacit knowledge can be written down as to potentially teach others which is called *internalization*. It allows other people to communicate the knowledge more easily in the form of explicit knowledge. Exchanging explicit knowledge is called *combination* by Nonaka. And finally there is *externalization* where explicit knowledge is being transformed into tacit knowledge.

Although this model of Nonaka is a very commonly used distinction, it does not contain all knowledge activities considering organizational learning which have been mentioned before. The model of Nonaka is mainly focused on the internal transfer of knowledge within a company. This importance of knowledge transfer has been proven by many (Dyer and Nobeoka 2000, Lee and Hong 2002, Oshri, Pan et al. 2006) to help all individuals to learn. This sharing will ensure individual knowledge to become organizational knowledge when it is accepted by others (Hendriks 1999) and it

will allow to transfer capabilities from one side of the company towards another (Alavi and Leidner 2001). However, there are other processes not mentioned by the model of Nonaka. The four processes, socialization, externalization, combination and internalization (Nonaka 1995) can be expended as proposed by Weggeman (Weggeman 1997, Andriessen 2006, Verburg and Andriessen 2011). He made a distinction between five knowledge processes; *identify knowledge gaps, acquiring/creating knowledge, storing knowledge, sharing/distributing knowledge* and *applying knowledge*. In this thesis an altered version of the five processes described by Weggeman is used by making a distinction between acquiring and creating knowledge and separate sharing and distributing knowledge. This altered model is used because it includes more activities without losing the ability to make clear distinctions between knowledge related activities. Thus it allows us to have a better look into knowledge management of the pharmaceutical industry.

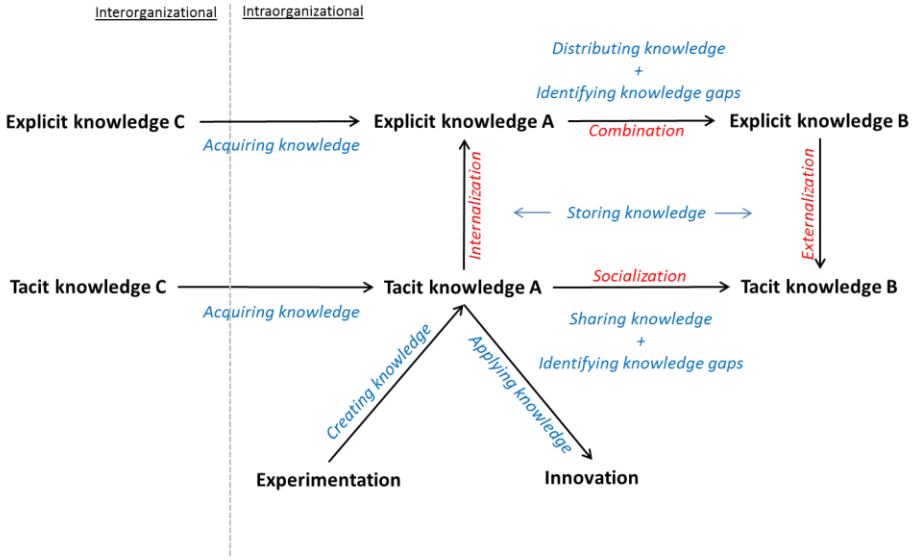

Figure 4 Knowledge processes within an organization (intra) and between organizations (inter). In blue are the seven categories according to Weggeman (Weggeman 1997, Andriessen 2006, Verburg and Andriessen 2011). In red are the four categories according to Nonaka (Nonaka 1995). A and B represent different employees within the same company. C is an employee of a different company.

The seven knowledge processes used in this research are *knowledge application, knowledge creation, knowledge acquisition, knowledge distribution, knowledge storing, knowledge sharing* and *identifying knowledge gaps* (see Figure 4). The four processes described by Nonaka (Nonaka 1995) are similar to three of these processes. *Socialization* is the process in which tacit knowledge is transferred between two or more people. This can be compared to *knowledge sharing*. People can have formal or informal meetings to discuss certain topics and exchange tacit knowledge. *Externalization* and *internalization* processes are referred to as *storing knowledge*. Knowledge is being codified and Information Technology (IT) tools are used to create databases and store knowledge in proper ways (Argote, McEvily et al. 2003). These IT systems are also known as knowledge management systems (KMS). Finally, there is the process of *combination* from Nonaka in which codified knowledge (explicit) is combined. This can be related to *knowledge distribution*.

Besides these Nonaka processes there are other activities a company can get engaged in for the benefit of the organizational knowledge base. External partners can provide useful information in the form of explicit or tacit knowledge, here referred to as *acquiring knowledge*. Strategic alliances are a formal method of knowledge acquisition, but informal discussions and conferences can also be seen as knowledge acquisition activities. Another knowledge input process used, is *creating knowledge*. In this process internal research methods are used to come up with new knowledge. Individuals can create knowledge with experiments and teams can create knowledge by using brainstorm sessions. Additionally there is the use of knowledge to create new products, processes or services. This knowledge process is called *applying knowledge* and thus is strongly correlated with innovation performance. Finally, a company can look forward to what knowledge it requires to create certain products or processes. This process is named *identifying knowledge gaps*. A scheme of all these processes is given in Figure 4, representing the two categorizations of knowledge processes of

Weggeman and Nonaka. It explains the boundaries between inter- and intraorganizational activities and the difference between tacit and explicit knowledge.

2.2.3.Knowledge management in the pharmaceutical industry

Knowledge is essential in the pharmaceutical industry to stimulate drug discovery and development. Not only insights in human biology and microbiology are required to understand diseases, but also knowledge on chemistry and physics are needed for a good understanding of drug properties (Hatzichronoglou 1997). Pharmaceutical firms need a broad range of scientific disciplines and thus a broad knowledge base. All this knowledge is needed to create new products for the drug pipeline. The pharmaceutical innovation process is even more complex because it is not only companies whom are involved but also universities and governments who have their share of knowledge input. Universities supply academic knowledge which is not directly applicable for products. Still, important discoveries of these universities helped developing new products in the past. Governments are involved in legislation. Although they do not supply knowledge for product innovation, they do help the development of the medicine until it is approved for patient usage. Thus knowledge in the pharmaceutical industry is a very broad concept which is not solely focused on product innovation. This makes the topic of knowledge processes more interesting to look into for this thesis. During the explorative research it is expected to find that many companies focus on certain knowledge processes for different reasons.

To increase a company's knowledge base one can absorb new knowledge (Dierickx and Cool 1989, Deeds and Decarolis 1999). The knowledge base of a company is sometimes referred to as a 'bathtub' model where knowledge can flow out (if knowledge becomes irrelevant or people leave the firm) and where knowledge can flow in (through knowledge acquisition and creation) (Dierickx and Cool 1989). It therefore seems as if knowledge acquisition and knowledge creation can play a vital role in the pharmaceutical industry.

Sometimes a pharmaceutical firm might decide to focus on a new area of interest. Through reorganization an attempt is made to create a new R&D division which should focus on a promising area. However, research showed that reorganizations do not work according to expectations (Karim 2009). Reorganizations take more time than expected because new knowledge needs to be created for recognition. Managers tend to forget that path dependency and recognition is important for development (Cohen and Levinthal 1990). Of course some of this knowledge can be acquired by purchase. However, purchased knowledge might still be missing out on contextual information or it might result in problems such as the '*not-invented-here-syndrome'* (Katz and Allen 1982) which is the difficulty employees have when ideas from outside the firm need to be executed. These problems of knowledge creation and knowledge acquisition are interesting aspects to look into.

Knowledge sharing influences innovation of pharmaceutical companies (Sundgren, Dimenäs et al. 2005). This sharing was found to cause a complicated chain reaction in the innovative climate. Sundgren et al. found that sharing had a direct negative effect on a creative climate and a direct positive effect on the learning culture. In competitive firms not many scientists want to share their knowledge internally because it is considered as valuable resource. Many R&D employees are afraid to give too much information because they preferably want to be praised for their individual efforts. This caused a direct negative effect on the creative climate. However, employees do understand that sharing is beneficial for innovation and creativity of the company. Therefore, the indirect effects of information sharing, through the learning culture, seem to overshadow the direct negative effects on a creative climate (Sundgren, Dimenäs et al. 2005).

Dunne and Dougherty looked more closely into KM strategies and found that personalized KM is mainly used in the pharmaceutical industry instead of codified KM (Dunne and Dougherty 2011). Dunne and Doughtery suggest that drug studies are very complex and thus should be transferred in person rather than through documented explicit knowledge. This builds up the collective sense of the scientists. Interpretation of the results is important and should be discussed personally among scientists. This thesis tries to find out if this is the true argument behind the increased focus on personalized KM.

2.3. Knowledge network

2.3.1. Absorptive capacity

In the knowledge based view there are also other innovation management theories among which *absorptive capacity* (ACAP) has gained support over the years. In 1989 Cohen and Levinthal introduced the concept of absorptive capacity (Cohen and Levinthal 1989). Already in 2006, over 900 peer reviewed articles focused on this specific topic (Lane, Koka et al. 2006). Absorptive capacity is described as the ability to absorb knowledge into the organization (Easterby-Smith, Graça et al. 2008). ACAP creates knowledge from external sources (Gold, Malhotra et al. 2001) and has been mentioned many times with the concept of *open innovation* (Chesbrough 2003). It is knowledge acquired from outside the firm that separates itself from learning-by-doing processes which is learning from inside the company (Lane, Koka et al. 2006). Knowledge from outside the firm needs to be transferred and transformed into internal knowledge.

Zahra and George have looked deeper into the absorptive capacity theory of Cohen and Levinthal and distinguished two different types of absorptive capacities (Zahra and George 2002); the *potential absorptive capacity* (PACAP) and the *realized absorptive capacity* (RACAP). PACAP is the theoretical potential a company is able to acquire external knowledge. Zahra and George explain that there are two important knowledge processes involved for PACAP. First, a firm needs to *acquire* external knowledge. Second, *assimilation*, meaning the ability to interpret the information and create understanding, is needed to achieve high PACAP. However, the actual amount of external knowledge exploited for application, the RACAP, is lower than the PACAP. First, the knowledge needs to be *transformed*, i.e. the internalization and conversion of the potential knowledge. Then it needs to be personalized by individuals within the company and they should get familiarized by writing it down as explicit knowledge. Finally, there is the *exploitation* phase which finalizes the RACAP where knowledge is used and applied in developing products, processes and services.

ACAP and KM are two branches within the management literature which both have been discussed separately. Both see knowledge as a resource and focus on a resource-based view (Deeds and Decarolis 1999, Lane, Koka et al. 2006). However, these two scientific theories have many interfaces which have not been aligned before. In 2009 an attempt was made to combine both theories by explaining that knowledge management exists of six different capacities, among which one is absorptive capacity (Lichtenthaler and Lichtenthaler 2009). Knowledge management capacity was seen as an extra seventh capacity which was the ability of a company to combine the six capacities. However, there are more interfaces between the two management theories. When looking at the scheme presented in Figure 5, one can see that the PACAP steps of *acquisition* and *assimilation* are the same as *acquiring knowledge* from the presented scheme of knowledge management processes in Figure 4. The RACAP, according to Zahra and George, exists of *transformation* and *exploitation* which look very similar to *sharing, storing, distributing and applying knowledge* from the seven knowledge processes mentioned in chapter 2.2.2. Therefore, absorptive capacity which is mentioned in the literature is actually a very commonly used combination of knowledge processes.

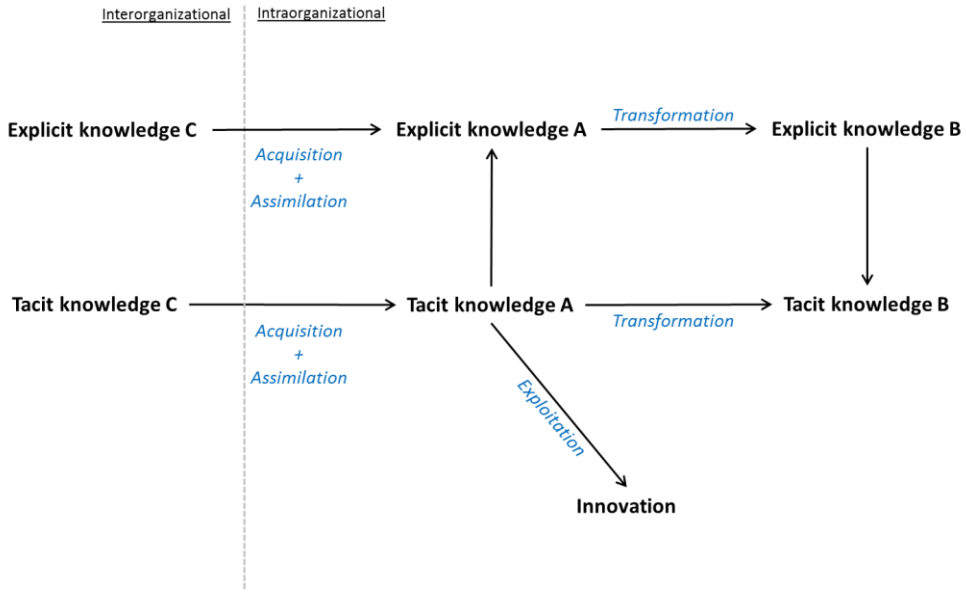

Figure 5 Absorptive capacity within an organization (intra) and between organizations (inter). In blue are four steps of absorptive capacity according to Zahra and George (Zahra and George 2002). A and B represents different employees within the same company. C is an employee of a different company.

The most important step in absorptive capacity, when thinking in terms of knowledge processes, is acquiring knowledge from external partners. Interorganizational relationships help to increase the knowledge base and can thus improve innovation performance (Xia 2013). Linkages between other organizations influence the innovation capability (Dadfar, Dahlgaard et al. 2013). However, to increase knowledge acquisition one needs knowledge relationships on a regular basis which means that the amount and the strength of interorganizational relationships are important as well. For this reason, the scope of this explorative research was expended by looking at the *knowledge network* of the pharmaceutical companies.

2.3.2.Knowledge network

A knowledge network exists of many different partners, such as other companies, knowledge institutes or governmental institutes. The collaboration between industry, government and universities is also referred to as the triple helix (Cooke 2002). It is believed that collaboration between these three partners will result in an optimal level of innovation. Especially the transfer between private and public knowledge organizations needs to be stimulated like the connection between universities and companies. For this reason TTOs have been deployed. These offices aim to stimulate the collaboration by sharing useful technologies, patents and knowledge with industrial partners. Some refer to these TTOs as old fashioned and passive (Barden and Weaver 2010). Whenever companies want new knowledge they need to use their own connections with university experts because that would be a lot quicker.

A network of universities and companies closely placed together can form a cluster. Many small firms spin out from these technology clusters (Gebhardt 2013) which is a side effect of open innovation. Such a cluster network is also beneficial for all the existing companies because their combined strength allows them to attract more investors (Cooke 2002) and public grants (Arechavala-Vargas, Rico-Huerta et al. 2012).

2.3.3.Knowledge network in the pharmaceutical industry

The concept absorptive capacity was encountered many times in scientific literature on pharmaceutical firms (Karim 2009, Biedenbach 2011, Dunne and Dougherty 2011, Arechavala-Vargas, Rico-Huerta et al. 2012, Lowman, Trott et al. 2012, Xia 2013). This means that knowledge acquisition, and thus a knowledge network must play an important role for innovation performance in the pharmaceutical industry.

An interesting finding is that most biotechnology companies are spinoffs from universities (West and Nightingale 2009). These young small firms use their mobility to quickly make a new idea

marketable. Their lack of resources motivates them in succeeding. TTOs often feel threatened by large pharmaceutical companies (West and Nightingale 2009) making small biotechnology companies more suitable for collaborations. The current trend in the pharmaceutical industry is that many of these small companies will be taken over by large pharmaceutical companies (see chapter 1.3) (Hunter 2011). Universities have their specialty in fundamental research, biotechnology companies are better in applying these results and large pharmaceutical enterprises have specialized people in marketing of new drugs (Sternitzke 2010). This collaboration is a pharmaceutical interpretation of *Co-opetition* in which these small companies compete but need to collaborate as well (Quintana-García and Benavides-Velasco 2004).

During the explorative research it is hoped to see differences in contact with companies/universities/institutes between smaller and larger companies. Also, the beneficial influences of a technology cluster on a knowledge network is of interest for this study.

2.4. Motivation

2.4.1. Self-Determination Theory

When speaking of innovation performance it is not only related to the knowledge base of the company. A company exists out of individuals which all contribute to the knowledge base and contribute to the innovation performance. Even if the knowledge management is optimized for a company it might be that the employees will restrict in obtaining full potential performance. The employees thus need to be motivated to use the tools supplied by the managers. For this reason motivation is added to the focus of this explorative research.

Motivating employees is an important and delicate task for all managers. Although many motivational theories exist (Hackman and Lawler 1971, Hackman and Oldham 1976, Latham and Locke 1991, Bandura 1994, Huitt 2004) the *Self–Determination Theory* (SDT) (Ryan and Deci 2000) is chosen for this thesis because it is very often used in scientific literature and contains many categories to describe motivational drive in more detail. The SDT exists of three categories for determining and describing the strength of a certain motivation; *autonomy*, *competence* and *relatedness*. Autonomy stands for the amount of freedom an employee feels in his or her job. The more freedom the employee has in planning, the more he will be motivated to continue working. Competence stands for the challenge of the job and believing in ones capabilities, much like the self-efficacy theory (Bandura 1994). By giving positive feedback and rewarding employee's actions, managers can stimulate the feeling of competence. Finally there is relatedness, which influences the internalization of a certain goal (Gagné and Deci 2005). The more employees can relate to a certain goal, the more they are driven to accomplish that goal. This means that the goal setting theory is entwined with SDT (Latham and Locke 1991).

Besides these three categories, SDT states that motivation can be separated into *intrinsic* and *extrinsic motivation* (Ryan and Deci 2000, Sundgren, Dimenäs et al. 2005), a distinction often used in scientific literature. *Intrinsic motivation* is the drive of an employee to do something for him or herself. The result of the action is the goal itself and thus people feel related to the action. Emphasis is not put on the output of employees, but on the interests of a person. An employee can be stimulated to do work because he or she is interested in finding out more on the topic of research. The scientific curiosity feeds the intrinsic motivation of the researcher.

Extrinsic motivation is the drive of an employee to work because of emphasis being put on achieving external goals. Salary payment and awards are examples of controls which managers can use to stimulate extrinsic motivation. Different kinds of salary payment systems can stimulate R&D employees in different ways, like focusing on quality or quantity.

2.4.2. Motivation in the pharmaceutical industry

Motivation can create a lot of energy. Dwahan et al. made an employee energy balance depending on the daily activities. Some of these activities required energy and some gave energy (Dhawan, Roy et al. 2002). He finally concluded that working in laboratories is creating more energy than it absorbs over time. This means that the motivation for researchers to work in laboratories of pharmaceutical companies is already high.

Some research on SDT has been conducted in the pharmaceutical industry. Intrinsic motivation was found to have a positive influence on a creative climate (Sundgren, Dimenäs et al. 2005). When people see drug research as a goal on its own, they have more positive energy which will increase the creative climate. It is because of this energy that employees can remain focused on finding new drug targets.

Additionally, extrinsic motivation has been found to stimulate a creative climate (Sundgren, Dimenäs et al. 2005, Biedenbach 2011). The pharmaceutical industry contains a special extrinsic motivation. Customers of these companies are patients with diseases which can be life threatening. The products which are developed by these companies can literally changes people's lives. This can boost the motivation of research employees but can also become a high pressure for these people. Extrinsic motivations can thus have a negative influence on innovation performance when an incorrect motivation is being used. This research therefore hopes to find a distinction between certain motivations in the pharmaceutical companies.

2.5. Creative climate

2.5.1. Creative individuals, teams and organizations

Innovation does not only require knowledge and motivation. Gathering and sharing knowledge by employees will not directly result in successful new products, processes or services. These innovations come from a creative process in which new combinations of knowledge are formed. That is why a *creative climate* will help in creating more innovation performance (Amar and Juneja 2008).

Creativity acts on many levels (Woodman, Sawyer et al. 1993). The individual person can have a certain creative mind. However, this individual creativity will always be restricted to the knowledge the individual has. In 1975 Stein proved that teams can create more ideas than the same amount of individuals working separately (Stein 1975). The social context in which brainstorming is put into during team sessions helps in creating more ideas and will boost the innovation performance. Team creativity is not a simple summation of individual creativities. Characteristics like group size, cohesiveness, trust and diversity have been found to influence this creativity (Woodman, Sawyer et al. 1993). Finally, there is the level of creativity in the organization. This is also not just a simple summation of the creativity of the individuals or the teams, but becomes more when certain knowledge is combined.

2.5.2. Creative climate in the pharmaceutical industry

Sundgren et al. found a positive connection between a learning culture, motivation and a creative climate (Sundgren, Dimenäs et al. 2005). This creative climate, on its turn, was found to be connected to innovation performance. Thus creative climate is added to the scope of this explorative research.

Many scientists encountered that the innovation process of the pharmaceutical industry seems to be serendipitous (Schmid and Smith 2002). The creativity process could be responsible for this serendipity effect. The only thing which might help in such serendipity processes is using a large differentiated portfolio of research. However, these strategies only seem to work for large pharmaceutical firms considering they have enough resources to divide amongst multiple projects. Therefore it was thought to be interesting to see if the creative climate differed between certain companies and if it was connected with innovation performance.

2.6. Company characteristics

Companies can also have certain characteristics which are expected to play a large role in the innovation performance. Important characteristics, such as *size*, *formalization* and *strategy*, are discussed in the following text.

2.6.1. Company size

The first theory of Schumpeter (known as Schumpeter I) stated that true innovation comes from small enterprises (Malerba and Orsenigo 1995, Arechavala-Vargas, Rico-Huerta et al. 2012). These companies are creative and flexible and thus can come up with more innovative ideas and products. However, after some academic experience Schumpeter altered his view on innovation (known as Schumpeter II). He then put more emphasis on the large enterprises, for these companies have more

resources and therefore have more capabilities to create new products (Malerba and Orsenigo 1995, Arechavala-Vargas, Rico-Huerta et al. 2012).

The pharmaceutical industry has made a similar division throughout the years when looking at the true source of innovation. In the 1970s the large pharmaceutical companies were considered most innovative (Howells, Gagliardi et al. 2008). Classical innovation models of technology push (Dosi 1982, Nemet 2009) were used to invent new medicines. In their continued search for new small chemical medicines they found many potential drugs which turned into blockbusters. This line of innovation source fits the Schumpeter II theory. But then in the 1990s the small biotechnology companies took over the lead in finding new medicines. With their special capabilities the biotechnology firms managed to produce biological drugs in niche markets (Biedenbach 2011) which created many opportunities and stimulated innovation in the pharmaceutical sector. This development fits the Schumpeter I theory because these biotechnology companies were mostly Small and Medium sized Enterprises (SMEs) (for a definition of SMEs see 0). Company size is added to the explorative study because it is expected to see differences in innovation performance according to the company size. Most of these SME companies are biopharmaceutical or biotechnology companies. Therefore these companies are referred to as Small and Medium Sized Biopharmaceutical/Biotechnology Enterprises (SMBEs).

SMBEs are also found to have problems with intellectual property (IP) (Eppinger and Vladova 2013). All pharmaceutical companies need to protect their knowledge and technologies but SMEs do not have sufficient resources to protect them. Patenting takes time and costs a lot of money. But IP protection is needed whenever SMBEs want to acquire investments of VC. Therefore it was advised by Eppinger and Vladova to look better into professionalization of SMBEs Intellectual Property management (IP).

Finally company size also seems to play a role in the knowledge network. Small companies by definition have fewer employees. As a consequence the knowledge network of small pharmaceutical companies is expected to be smaller on an absolute scale (Hung, Huang et al. 2005, Hewitt-Dundas 2006). But large companies have the risk of having many people from the same network which might diminish the absolute difference in network size.

2.6.2.Formalization

Companies have different structures and different rules which fit their industry and their profile. These controls are part of the innovation management of the company. For this reason some findings of innovation performance in the pharmaceutical industry are related to the organization structure.

An important antecedent of innovation performance is the company *formalization*. Formalization can be seen as the amount of regulations and planned actions which managers make employees do (Cardinal 2001). Also payments, evaluation and reflection of employees can create formalization (Sundgren, Dimenäs et al. 2005). Managers can use these tools to force certain employees into activities the company wants to get done. For instance, formalization can be used to force researchers to use certain knowledge processes (chapter 2.2.2) within the company. Formalization seems to have positive effects on employees in large organizational structures. However, many creative mechanisms are blocked by this formalization (Cardinal 2001). Formalization might therefore significantly contribute to the innovation process of the pharmaceutical industry in both a positive or negative way dependent on the way it is used.

2.6.3.Company strategy

Strategy can also be controlled by managers. Strategic control is focused on long term orientation and in this way differs from organizational control. The Human Genome Project of the 1990's is a good example of a long term orientation beneficial for pharmaceutical firms. The goal of this project was to discover the complete genome of one human. Bioinformatics and genome sequencing techniques were not very well developed at that time which was the reason behind the long project duration of 10 years (Stiglitz and Jayadev 2010). All over the world people were helping in the DNA sequencing process of the first person. To speed up the sequencing, the Human Genome Project worked together with the pharmaceutical industry. In exchange for their contribution some genes would be put available for patenting (Stiglitz and Jayadev 2010). This Human Genome Project contributed to a wave of new medicine discoveries in the start of the 21th century (Schmid and Smith 2002). This boost was needed

because the large pharmaceutical companies knew that around 2010 the patent cliff would have its impact on their revenues (Abou-Gharbia and Childers 2013).

According to Biedenbach there are three innovation strategies to focus on when working in the pharmaceutical industry (Biedenbach 2011). The first is the focus on *dynamic capabilities*. Dynamic capabilities are the ability to adapt to a certain situation. This is important when the market is uncertain like the pharmaceutical industry. Adaptive, absorptive and innovative capabilities all contribute to the mobility of the firm. The second strategy is focused on *project capabilities*. This means that the firm is successful in starting up from scratch and walking through a project until the end. Project management is commonly used in the pharmaceutical sector (Hynes Iii 2009). However, the cycle of one project (i.e. discovery, development and all clinical trials of a potential drug), is estimated to be over 15 years (Ortt, Tabatabaie et al. 2009, Raaphorst 2012, Raaphorst 2013). This makes it difficult to keep using a project management approach over such a long time. Finally, the third strategy for pharmaceutical enterprises is to focus on *multiproject capabilities*. These capabilities are focused on portfolio management where resource division and pipeline management are of great importance. Portfolio management can help in overcoming the serendipity problem of launching a successful medicine on the market (Schmid and Smith 2002). Therefore these multiproject capabilities are also beneficial for pharmaceutical firms, especially the large firms which have more resources to invest into multiple projects. All three strategies have their own benefits during certain phases of a pharmaceutical company. This means that a combination of all capabilities is necessary considering innovation performance, as advised by Biedenbach. However, it is still unknown in what specific phase each capability is most important.

Altogether, the literature study on innovation management in the pharmaceutical industry resulted in a list of seven potential critical factors for innovation performance. It is expected that knowledge will play an important role when it comes down to the innovation performance. Knowledge cannot be managed directly but *knowledge processes* are controllable. It is also expected to see differences for the following seven knowledge processes; knowledge application, acquisition, creation, distribution, sharing, storing and identifying knowledge gaps. It is also anticipated that the *knowledge network* of the pharmaceutical company will have a large influence on these processes and on the innovation performance. *Formalization* and certain *motivations* can be used to stimulate knowledge processes or *creativity*. Finally it is predicted that *company size* and *company strategy* will differ among the companies due to certain circumstances.

3. Methods

In the previous chapter the important subjects for this research have been introduced. This chapter will focus on the different research methods which were used for gaining information on knowledge processes, knowledge network, motivation, company size, company strategy, formalization and creativity. This chapter covers the following sub question:

"How to measure the important aspects of innovation management mentioned in the scientific literature?"

Three separate methods have been used to explore the seven potential critical factors of chapter 2. First, two confirming interviews were performed with experienced managers from the pharmaceutical industry. Then interviews were held with managers from drug discovery companies to collect qualitative and quantitative data. Finally a questionnaire was spread to research teams of these pharmaceutical companies to collect quantitative data for further analysis. Only 20 researchers spread over six companies (40% response rate) took part in the online survey. Unfortunately, this number of responses is not enough to do a reliable quantitative analysis. As a consequence, the methods and results of the questionnaire are removed from the thesis but are put available in 0 for further reading. *Formalization* and *creative team climate* was measured in these questionnaires because research employees can answer with a higher reliability to these certain questions than managers. This resulted in the lack of data on formalization and creative team climate.

The research was performed on companies within the Leiden Bio Science Park (LBSP) because of the opportunity given by the Leiden Bio Science Park foundation (LBSPf). It provided the opportunity to use existing connections with many pharmaceutical companies of the park increasing the potential dataset. A description of the LBSP is given in Appendix B. The companies of interest were selected based on their involvement in discovery and development of drugs according to our definition of *pharmaceutical innovation*, as mentioned in the introduction. Also, the research institutes that perform discovery and development practices within this industry were involved for the interviews and questionnaires. These companies provided support in many discovery and development steps of pharmaceutical companies and are therefore interesting for this research. In the remaining of the thesis the term 'companies' will be used to refer to both companies and knowledge institutes even though knowledge institutes are not actual 'companies' but a different form of organization.

3.1. Confirming interviews

First, two unstructured interviews were performed to confirm two things; to see if the expected seven factors from chapter 2 are indeed important and to see whether important factors are missing. In these two interviews the focus was put on three things; (1) the establishment of the company where the interviewee is currently working at, (2) the origin of innovation within the company and (3) important factors for stimulating innovation within the company. The interviews were held with two (former) CEOs of pharmaceutical companies located in the LBSP. Because of their large experience in managing pharmaceutical companies from startup towards successful output, these two (former) CEOs were a reliable source of information. Many of the factors mentioned in the theoretical framework came back during the exploring interviews, thereby confirming the predictions made in the literature review. Also some indicators for measuring innovation performance were given during the interviews. These indicators will be discussed in chapter 3.2.5.

3.2. Interviews

The next step in this thesis research was gathering data on the pharmaceutical companies within the LBSP. Interviews were held with top managers from these pharmaceutical companies to get valid data of the companies. These interviews provided qualitative data combined with quantitative data. The higher the management function the more accurate he or she could answer the questions. The interviews consisted of five focus points, of which four were selected from the literature review. Each focus point was approached by using some prepared questions which will be discussed below. The conversation was steered to retrieve the underlying reasoning behind the answers. The average duration of each interview was approximately 45 minutes.

3.2.1.Company characteristics

The first focus point in the interview is the *company characteristics*. Several questions were asked to learn more about the company itself, covering topics such as company age, company size and category of the company (pharmaceutical, biopharmaceutical or biotechnology). According to our definition (see chapter 1.1) biotechnology and biopharmaceutical companies are the same. However, it was interested to see whether companies itself have a different view on the definitions of pharmaceutical, biopharmaceutical and biotechnology companies. Managers are more aware of the company structure and see how infrastructure works and how to compare their company with competitors.

3.2.2.Knowledge processes

The second focus point is related to the seven *knowledge processes* (Weggeman 1997). The managers were asked to select three knowledge processes from the list of seven that were most important in their opinion. To help them in choosing their top three, a brief explanation of the processes were given with the help of the image of Figure 4. Also, the motivations behind their choices and some examples of knowledge process activities were asked in order to gain a thorough understanding of their choices. Additionally, the managers were asked to grade their focus on the selected knowledge processes in comparison with other competitors of the pharmaceutical industry.

3.2.3.Knowledge network

The third focus point is that of the *knowledge network*. The knowledge network may exist in or outside the city (Leiden) or may involve universities and/or companies. During the interviews the managers were asked what kind of knowledge transfer takes place between their company and the four external types of organizations. These four categories of external organizations were the Leiden University/Leiden University Medical Center (LU/LUMC), Leiden companies, other universities and other companies. Interviewees were asked to describe and grade the knowledge transfers with organizations by the strength of the relationship compared to relationships of competitors. This grading was done using a 5 point Likert scale (*very weak, weak, average, strong, and very strong*). Whenever a company was not involved in any knowledge transfer with another organization it was scored as *not applicable*.

3.2.4.Motivation

The fourth focus point is the *motivation* of the research employees. The managers were asked what in their opinion the main motivational drives for the researchers are and were asked to explain how these drives motivate their employees. Additionally it was asked what the company does to stimulate their employees and what managerial controls are used to increase their motivation.

3.2.5.Innovation performance

Finally, the managers were asked for some quantitative data which were expected to correlate with *innovation performance* within the pharmaceutical industry. These questions were sent up-front because it was expected that most managers would not have these numbers at hand. There are many different ways of measuring innovation or innovation performance within a company. But solely looking at product market introduction would not accurately measure true innovativeness of a pharmaceutical company (see chapter 2.1). However, it seemed that looking at the drug pipeline would be more fitted for this thesis. The further a drug is in the drug pipeline, the better a company seems to perform on innovation because it has more proof of concept.

Another aspect of innovation performance, which was proposed during the confirming interviews, involves the amount of grants and other external finances. Pharmaceutical companies rely on financing to continue development and clinical trials. When companies are able to persuade investors, it means that the research performed on their products has shown potential and thus can be considered successful innovation. Notice that the amount of external finance and the amount of products in the drug pipeline reinforce each other.

Companies can have different strategies concerning appropriation. Some try to keep knowledge secret until they find something of value. In this case companies will file the invention as a patent. Other firms not only file patents but also share this in scientific journals. This means that the number of patents and scientific publications indicates the effort companies put into innovations as

well as the amount of successful results. The amount of patents and scientific publications were also used as an innovation performance indicator.

The final quantitative measure of innovation performance is the amount of money spent on R&D in 2012 for the whole company and for the department of Leiden (which were the same in many cases).

This now ends the methods chapter for this thesis describing an open confirming interview and closed interviews focused on five topics of company characteristics, knowledge processes, knowledge network, motivation and innovation performance.

4. Results

In the previous chapter methods for this thesis were described which have been applied to the companies of the LBSP. In this chapter the results of these research methods are described by answering the sub question:

"What are the findings in relation to important aspects of innovation management in the LBSP companies under study?"

These findings are mostly quotes from what has been said during the interviews. Also some results were interpretations based on the conversations where literature based concepts were applied on the information given by the manager.

In the LBSP 21 companies met the requirements for pharmaceutical companies (see Appendix B). From the 21 companies that were approached for the interviews sixteen companies responded. Interviews were arranged with all these sixteen companies meaning we had a response rate of 71% which is very high. One of these interviews could not be used because the company turned out to be a service provider rather than a pharmaceutical compound producer. In response the dataset was reduced to fifteen companies. Most of the managers which answered the questions were directors (three CEOs, three CSOs, one COO and one CBO) meaning that they were fully informed about the complete structure and developments of the organization, therefore increasing the reliability of the data. In this chapter the results of each of the five focus points mentioned in chapter 3.2 are presented.

4.1. Company characteristics

There were many different kinds of companies interviewed during the research. The interviews were coded for company characteristics which seem to return in many other interviews. These coded categories were; *activity in certain clinical phases* (preclinical, I, II, III and on the market), *size* (micro, small, medium or large, see 0), *type of company* (institute, private company, public company), *category of company* (pharmaceutical, biopharmaceutical and biotechnology), *IP strategy* (publishing, patenting or both), *age* (younger or older than fifteen years), *location* (in Biopartner Leiden or not) and *spread* (international offices yes or no). The activity in clinical phases, the age, the size and the category of the company data were gathered during the interviews. The type of company, location and spread were found on the company websites or in the annual reports. The coding of the fifteen companies can be found in 0.

The category of company was differentiated into pharmaceutical, biopharmaceutical and biotechnology companies according to the selection of the managers. The reasoning behind the manager's choice was surprisingly very different. Some used size as a distinction, some used the kind of products made and others used the kind of techniques used. This distinction was especially difficult between biopharmaceutical firms and biotechnology firms, confirming our findings in chapter 1.1 that there perhaps should not be made any distinction between these two types of companies. From this point in the thesis we started referring to two types of companies; pharmaceutical companies and biopharmaceutical/biotechnology companies.

IP strategy was determined by looking at the difference in amount of patents and publications a company filed since 2010. It is more expensive to patent certain inventions than to publish this same knowledge. Also a certain patent may contain multiple scientific findings worth publishing. This difference was taken in considerate when determining the IP strategy. For the distinction in IP strategy the amount of patents were subtracted from the amount of patents. But the number of patents was doubled in measuring the difference as to compensate the higher expenses of the patenting

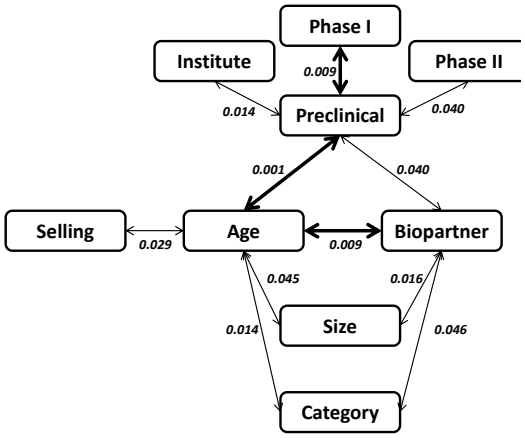

Figure 6 Spearman correlations between the coded groups. The numbers are the significance level of the bivariate correlation. Only correlations with a significance level under 0.05 are represented in the figure. Correlations with a significance level below 0.01 are represented by thicker lines.

procedure. Whenever a company had more patents filed 'patenting' was chosen as IP strategy, when there were more scientific publications accepted 'publishing' was chosen as IP strategy. Whenever the difference was below 2 (after doubling the amount of patents) the strategy of 'both' was chosen.

We coded 'young companies' when companies were below 15 years old, and 'old companies' when they were fifteen years or older. This boundary was chosen because the time it would take for a company to discover a new drug and get it approved for the market will at least take over fifteen years (Raaphorst 2012, Raaphorst 2013).

All companies were located within Leiden and within the LBSP. Within this park there are a few incubator/accelerator buildings called Biopartner Center (Biopartner Leiden 2013). These facilities are specially made for small young start-up companies in the LSH sector. The companies that had their offices and research facilities within these buildings were coded as 'Biopartner'.

The correlations between two codes were analyzed to see whether certain groupings were connected and to see how diverse the interviewed companies actually were. The table with bivariate correlations can be found in 0. A Spearman correlation method of SPSS (version 20.0) was used because parametric analysis methods could not be used with a small dataset of fifteen measurements. Of the 78 correlations only eleven were found to be significant which are schematically drawn in Figure 6 meaning that the companies were very diverse. This means that only 14% of the correlations were significant and that the codes used to group the fifteen companies were unique. In the continuation of this research each coded group should be used separately.

However, the few significant correlated coding groups did already reveal something about the fifteen companies. The distinction between large pharmaceutical firms and the SMBEs already becomes clear during this coding because age, size, category of company and the location within the Biopartner buildings were found to be significantly correlated to each other. Thus SMBEs are small young biotechnology companies within the Biopartner buildings and on the other side there are the large old pharmaceutical companies which have products on the market for revenues.
Also, in chapter 2.6.1 the problem of IP protection in small companies was mentioned (Eppinger and Vladova 2013). But according to these results the company size was not significantly correlated (Sig=0.132) to the IP strategy of a company. This result is contradicting the findings of Eppinger and Vladova.

4.2. Knowledge processes

The seven knowledge processes were briefly explained to the managers during the interviews using the image of Figure 4. They were asked to choose the three most important processes for their company. All managers replied that they were actively involved in all knowledge processes. But by forcing the managers to choose three processes they had to think of their main knowledge activities and combine this with the seven knowledge processes. Whenever they chose a certain knowledge process it would mean that the company is more focused on activities of this knowledge process. The results are shown in Figure 7. Knowledge acquisition, creation and sharing are the most important knowledge processes for the pharmaceutical industry according to this thesis. When we look further at the choices of the managers it can be seen that there are quite some differences between the choices and combinations which means that the difference in choice is most probably linked to particular causes and not due to random choices.

A first interesting finding is that during all interviews knowledge acquisition or knowledge creation was mentioned by the managers. Additionally both knowledge creation and knowledge acquisition are combined with knowledge sharing five times, resulting in the two most popular combinations of processes. Both knowledge acquisition and knowledge creation are processes to increase a company's knowledge base (Deeds and Decarolis 1999). The fact that both these knowledge processes have been chosen implies the importance of increasing the 'bathtub' of knowledge in the pharmaceutical industry (Dierickx and Cool 1989).

A final interesting finding is that knowledge distribution and knowledge storing are never chosen together within a top three during the interviews. Whenever explicit knowledge becomes important for a company it would be expected that both these knowledge processes would be combined. If you want to spread documents containing valuable knowledge it would be smart to invest in knowledge storing activities as well. These findings suggest that apparently there are not so many pharmaceutical companies which are mainly focused on all the explicit knowledge processes.

The codes of company characteristics created in chapter 4.1 were used to group companies and to see if characteristics can be linked to choice of knowledge process focus. For each of these coded groups a percentage for focused companies and unfocused companies was calculated. This calculation (cross tabulation) was done for every knowledge process and for every company characteristic. The groups were analyzed further whenever these percentages differed significantly. A cut-off point of 40% difference was used to filter out the significant different groups. The results for each knowledge process are given in the following part.

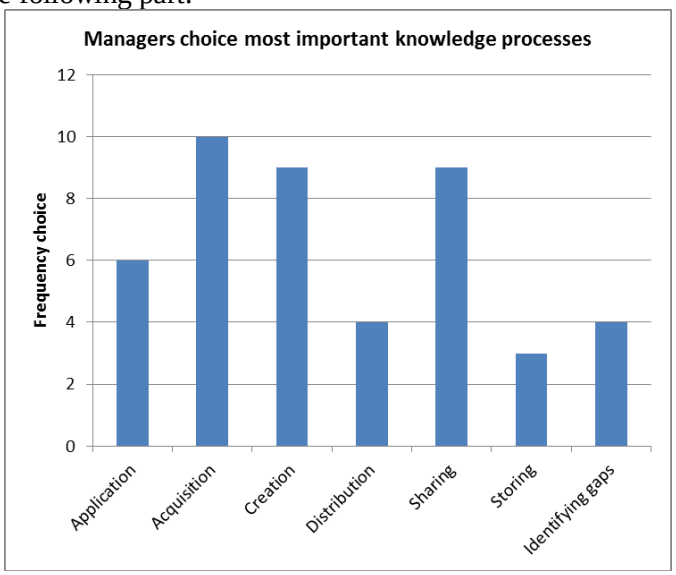

Figure 7 Response of the interviews with the fifteen companies. Each manager was asked to choose three knowledge processes which seemed most important for their company.

4.2.1.Knowledge application

Knowledge application is chosen by 40% of the managers. Most of the managers choose this knowledge process because they spoke of the importance to focus on the output of the company. Just a few pharmaceutical firms have products on the market which allows them to earn revenues. All the other companies want to focus their R&D on finding products so they can finally earn back invested money. When the fifteen companies are split into selling and non-selling organizations, a difference is found in the percentage of companies that selected knowledge application as one of the three most important knowledge processes (see Figure 8). None of the selling pharmaceutical companies chooses the knowledge application process, while 55% of the non-selling companies choose knowledge application. This proves the argument that companies who are still solely in development are significantly more focused on getting their products on the market. These managers are more aware of the financial struggle and cannot afford to waste R&D money on not applicable knowledge. These managers thus have to be careful whether to continue into certain paths even though they do not know the outcomes.

Another important finding of knowledge application is the importance of analytical procedures. Several managers mentioned that whenever companies are working on radical new medicines, they often needed to create their own diagnostic tools which are eventually used during (pre-)clinical trials. One would expect that the pharmaceutical companies would only have to look for new products, however most of this research is performed on such a new area that no qualitative measuring tools exist. This finding is a unique result for the pharmaceutical industry. Additionally most of the pharmaceutical companies use one or multiple platform technologies. The manager of company 11 explained that these platform technologies cannot only be used by the company for internal drug development but also as a service. By licensing their platform technology, companies are able to earn revenues, according to the fourth financial model mentioned in chapter 1.3, which can be used for investments in their own product pipeline. Especially non-selling SMBEs need this extra income to invest in their own research. The importance of a technology platform was also found in the scientific literature (Dadfar, Dahlgaard et al. 2013). Thus knowledge in these companies is not only applied for new drugs but for measurement and platform services as well.

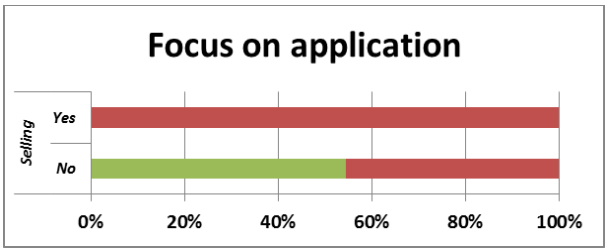

Figure 8 Difference in focus on application between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.2.Knowledge acquisition

From all the responses, knowledge acquisition is the most popular choice. Over 66% of the managers select this knowledge process as being one of the most important for their company. According to the managers, the main reason why companies focused on knowledge acquisition is because they need expert knowledge for certain activities. Experts are needed because the current knowledge base of a company is not enough for application. More knowledge is required for application which can be acquired (externally) or created (internally) (Andriessen 2006).

We interpreted from the interviews some advantages and disadvantages of knowledge acquisition. A first advantage of knowledge acquisition is that in a short amount of time knowledge can be added to the current knowledge base. Experts at other companies or at universities can carry a lot of knowledge directly into the company through actions like training sessions, discussions, presentations and document transfer. Pharmaceutical companies rely on the experience employees can have. Company 10 explained this in the following statement:

"We had a lot of experience in the field, which caused the fast progress of our first drug. We have a very small, but very efficient group of people here in the offices. Some (positive) things can be said for people who have been in these companies before, done similar steps before and learned from their mistakes. Most of the people have had experience with drug approval in the past. You want to recruit and attract people that have done this before."

The second advantage of knowledge acquisition is because it is relatively cheap. Whenever a company wants to do certain experiments it must buy the equipment and needs to learn how to work with the equipment. This can be done cheaper when you use the equipment and expertise of other organizations. This is not just limited to competing companies but can also be done at universities. Although universities are not so much interested in application of knowledge for commercial ends, they can still benefit in cooperating with industrial partners like creating results for learning and scientific publications. Some grants are focused on these collaborations in which both the universities and the pharmaceutical companies can benefit. These grants make knowledge acquisition a relatively cheap solution for the increase of a company's knowledge base.

A final advantage of knowledge acquisition is the ease of use. Many specialized knowledge is provided in the form of services. A good example of such complicated services is the manufacturing of drugs by CMOs. Drugs need to be produced under severe clean conditions with an extensive administration called Good Manufacturing Practices (GMP). This knowledge is often acquired from other companies because it is easier to hire these companies than learning it internally by doing. The learning-by-doing method would mean that a lot of time and money is wasted on production until the facilities meet GMP conditions.

However, when a certain company is able to acquire certain types of knowledge it means that competing companies will also be able to acquire the same knowledge. Thus the value of acquired knowledge is lower than internally created knowledge because the chance of creating a competitive advantage is lower. That is why many of the companies only outsourced less important/central research to external parties.

An interesting result when looking at the characteristics of the knowledge acquisition focused companies is that SMBEs seemed to focus more on knowledge acquisitions than large pharmaceutical companies (see Figure 9). Managers who categorized their own company as a pharmaceutical company are found to choose knowledge acquisition less (25%) than self-declared

biopharmaceutical/biotechnology companies (90%). Additionally, all Biopartner companies stated that acquiring knowledge is one of the most important knowledge processes where only 55% of the companies outside the Biopartner buildings mentioned knowledge acquisition as an important focus. The reason behind this difference can be explained. The advantage of being a large pharmaceutical company is that you already have many relationships with worldwide experts. These bonds have been forged over time and eventually become of true value. Therefore a strong focus on acquisition is missed out by the large pharmaceutical industry because they have the feeling that the most important knowledge has already been acquired.

A final result on knowledge acquisition is the distinction between knowledge institutes and companies. Companies seem to be more focused on knowledge acquisition (75%) than knowledge institutes (33%). Institutes rather focus on knowledge creation internally instead of creation externally because they want to train their own people with learning-by-doing.

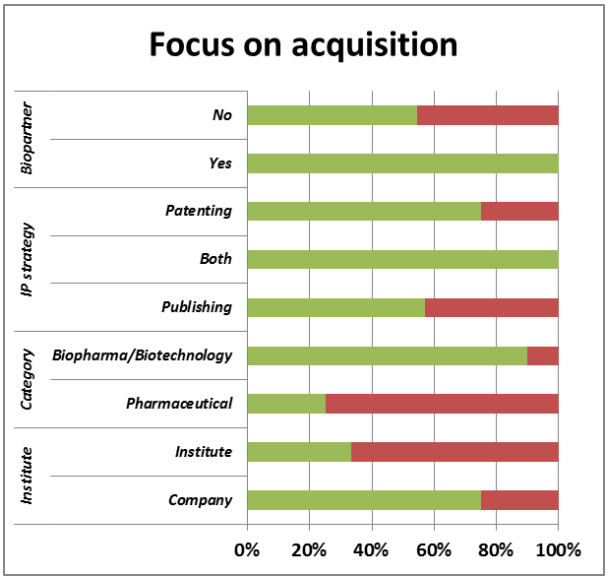

Figure 9 Difference in focus on acquisition between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.3.Knowledge creation

Besides knowledge acquisition a company can increase their knowledge base through the knowledge creation process. Company managers respond positively for knowledge creation in 60% of the interviews. Many managers argue that knowledge creation is important for IP protection. This knowledge creation increases the competitive advantage because the information is not so easily accessible by others through acquisition. Whenever a company outsources research to other firms or to universities they allow a great risk of losing competitive advantage. This was stated by the manager of company 9:

"Creating knowledge is important, that's what we do. Everything is done internally; we do not use literature targets. So acquiring knowledge is the least important process for us. If you want real innovation then it will have to come from knowledge which you create yourself. Otherwise you can only do a little incremental innovation. We are here with a fundamental new approach with new effects and new features. "

IP protection therefore is difficult to combine with publishing in scientific journals. This was often mentioned during the interviews. Interestingly the results, shown in Figure 10, showed that all three IP strategy groups have the same percentage of knowledge creation focused companies (50-57%). Thus it seems from these results that the choice for focusing on creating knowledge and the IP strategy does not influence each other. Similar results are found between IP strategy and knowledge acquisition (see Figure 9).

Knowledge creation also has significant results for the coded group of location implying that again there is a distinction between large pharmaceutical companies and the SMBEs. However, this time the large pharmaceutical companies are more engaged in knowledge creation and the SMBEs are less focused on knowledge creation. From the Biopartner companies only 25% of the companies are focused on knowledge creation compared to 73% of the other companies (see Figure 10). From the interviews a main reason could be interpreted which was focused on financial resources. The underlying argument behind these differences is that the SMBEs do not have many resources. Thus Biopartner companies are forced to choose to acquire their knowledge instead of creating it internally. On the other hand, the large pharmaceutical companies do have the financial resources because of the revenues of pharmaceutical products. This allows them to invest in the research facilities and equipment as a long term investment.

Again the knowledge the knowledge institutes show interesting results for this knowledge process. Where institutes do not focus on knowledge acquisition; it now seems that the institutes all focused on knowledge creation while 50% of the pharmaceutical companies are focused on knowledge creation. The increase of tacit knowledge of the knowledge institute employees was mentioned as one of their eventual goals. Governments finance these institutes as to invest in these people's education. Therefore these institutes need to increase the tacit knowledge base by letting the researchers do experiments themselves.

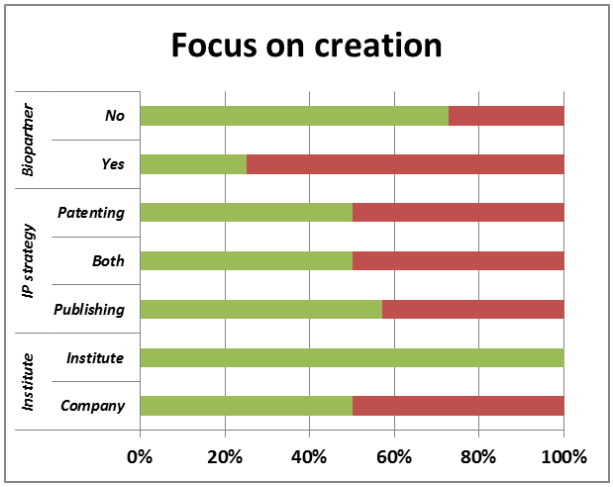

Figure 10 Difference in focus on creation between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.4.Knowledge distribution

Only 27% of the managers responded during the interviews by choosing knowledge distribution as one of their main focuses. Interestingly, the two largest pharmaceutical companies of the LBSP choose knowledge distribution. They stated that the main reason behind their choice is that distribution becomes important when knowledge needs to be transferred through a large company quickly. This knowledge transfer among many employees is easier done on explicit level. On can also think of knowledge distribution to allow communicating better when certain divisions are separated. For example, company 2 has a physical separation of buildings between the quality assurance and the manufacturing divisions. It is not allowed for all personal to walk into the manufacturing division because of the strict GMP qualifications. Distribution of documents allows the employees to spread knowledge between the divisions more, even though these divisions are physically separated for personal contact.

The manager of company 9 makes a distinction between the learning phase and the confirmation phase through which pharmaceutical projects go in their company. First potential drugs are tested in models and preclinical studies to learn about the diseases and their compounds. The manager called this the *learning phase*. Afterwards the drugs can continue in the pipeline with clinical tests which should only confirm the expectations of the model, hence the *confirming phase*. The manager of company 9 argues that distribution becomes more important during confirmation phase because the written results of the clinical studies, which are reports from hospitals and CROs from

over the world, need to be distributed quickly for data analysis. This argument is confirmed when looking at the companies choosing knowledge distribution. A small difference is found between companies selling products (50%) on the market and companies that did not (18%), confirming that knowledge distribution becomes important in later stage of clinical studies (see Figure 11).

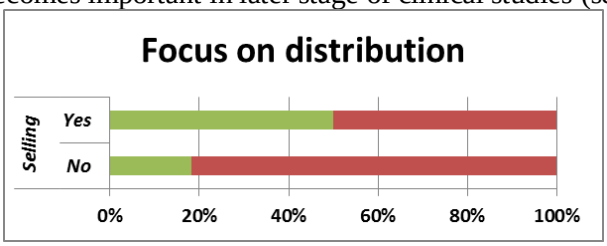

Figure 11 Difference in focus on distribution between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.5.Knowledge sharing

Tacit knowledge is very important for many pharmaceutical companies. Therefore 60% of the managers reply positively to focus on the knowledge sharing process. Distribution of knowledge is the explicit transfer process which is chosen by 27% of the companies, a significant lower value. This indicates that more companies focus on the transfer of tacit knowledge than on explicit knowledge. The pharmaceutical companies use multidisciplinary knowledge and thus the information becomes rather complex for this high-tech industry. One might imply that because of this complexity scientists and researchers need to share knowledge personally rather than impersonal.

Another interesting result is that non-selling companies (73%) are focused far more on knowledge sharing than selling pharmaceutical companies (25%). These findings are similar with the results of knowledge distribution because the non-selling companies are less focused on knowledge distribution than selling companies (see Figure 11). It was interpreted from the interviews that the focus of speed lies different between the learning and the confirming phase. Companies want to progress quickly. During the confirming phase you want to generate new ideas and understanding quickly. To stimulate the creativity of this progress, managers let their employees transfer knowledge in person because people will therefore understand more easily. However, when finalizing clinical trials become important, creativity is not required anymore. The new products need confirmation which has a different process focus. Now it becomes important that analysis of the clinical studies are studies quickly. A different sort of knowledge becomes important which is not so much related to product innovation anymore. The manager of company 14 referred to this as follows:

"Companies that are on the market want to transfer as much explicit knowledge as possible through knowledge acquisition of consultants in order to get things done. It's like a cyclic process, you start with tacit knowledge that is stored and shared and eventually through explicit knowledge a new product can come out. However, for us it is important to focus on explicit knowledge to continue business as we are a selling company. "

Most companies are actively trying to increase the sharing of knowledge through weekly presentations, meetings and also through informal procedures. It is interesting to see that micro (0%) and small sized companies (33%) are less focused on sharing knowledge than medium (100%) and large sized (75%) companies. These results are presented in Figure 12. Managers of small and micro sized companies spoke of an informally based structure in which managers know what researchers do and employees know what colleagues are currently working on. To find the right internal expert is rather easy because everybody knows each other. Large companies, however, often can lose sight of internal knowledge base and knowledge sharing needs to be actively stimulated to find these internal experts. Technology nowadays can help in facilitating personalized knowledge sharing even if distance is large like using a KMS like a 'yellow-pages' model. The fact that we found that large companies focus more on knowledge sharing can be interpreted that managers are aware of this problem and start focusing more on the sharing of knowledge. Additionally, there is again another company characteristic indicating a distinction between the large pharmaceutical companies and the SMBEs; all pharmaceutical firms are found to focus on knowledge sharing while biopharmaceutical/biotechnology companies (40%) are focused less on this knowledge process.

Knowledge institutes also seem to rely more on sharing of tacit knowledge (100%) compared to the companies (50%). In these institutes employees are stimulated to share their knowledge through the academic world. However these researchers look for themselves what partners are suitable for sharing. Certain relationships cannot be forced upon these people because they are more independent and more stubborn. They want to use their personal knowledge network rather than being forced to cooperate with somebody they do not know just because it is an expert. The findings shown in Figure 9, Figure 10 and Figure 12 indicate that there are quite some similarities between KM strategies of large pharmaceutical companies and knowledge institutes considering their focus on knowledge acquisition and knowledge creation.

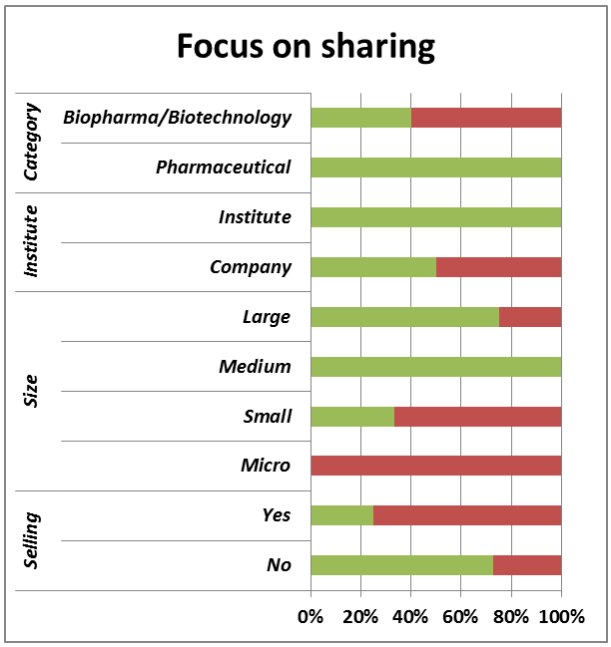

Figure 12 Difference in focus on sharing between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.6.Knowledge storing

Knowledge storage was expected to be important in the pharmaceutical industry because knowledge is very important in the innovation process and thus it would be a waste if any of it would get lost. However, this is not found to be of main interest of the managers. The results of the interviews show that only 20% of the managers think knowledge storage is an important knowledge process making it the least important knowledge process of the pharmaceutical industry. It can be interpreted that in the pharmaceutical industry not much focus lies on creating a sufficient KMS.

The few companies that do mention knowledge storage were referring to the importance of storage for clinical studies. Doing clinical studies is very expensive. It would be a waste if certain experiments were done repeatedly within a company because people did not record data and results properly. So storage during model experiments and preclinical studies need to be documented well. Once certain drugs pass these experiments they can go to clinical studies; phases which all people remember very well. So it is in the starting phase where knowledge storage should play a role. This importance in preclinical studies is given in the results of Figure 13.

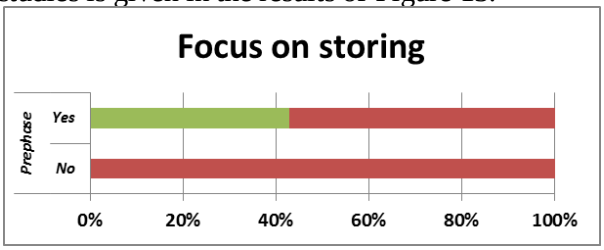

Figure 13 Difference in focus on storing between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.2.7. Identifying knowledge gaps

Only 27% of the managers respond with identifying knowledge gaps as one of the most important knowledge processes within their company. The main reason behind focusing on these gaps is for making strategic choices. According to the manager of company 4 employees forgot to see the gaps and the problems in their daily jobs over time. Therefore identifying knowledge gaps becomes a real important process for the old large pharmaceutical companies. A small difference is found between international companies (43%) and local situated companies (13%) and between selling (50%) and non-selling companies (18%) indicating a slight proof for this theory (see Figure 14).

A final interesting result is that all the managers that mentioned finding knowledge gaps as an important focus point also mentioned knowledge acquisition as an important focus point. When a company is aware of certain gaps it is able to fill these gaps through knowledge creation or knowledge acquisition. Apparently, knowledge acquisition conceived to be a better strategy to fill the knowledge gaps compared to knowledge creation according to the findings of this research. The reason why identifying knowledge gaps is always combined with knowledge acquisition is not yet understood but might be because of the ease and speed of filling the gap. Most of the times when a knowledge gap is identified it is because they run into it as a problem. The first reaction of the company is to solve this problem as quickly as possible and therefore knowledge creation would seem as a bad solution.

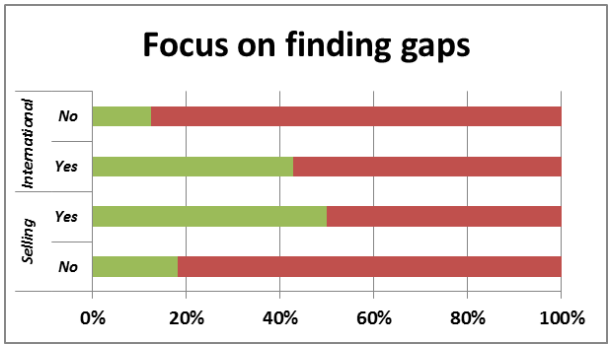

Figure 14 Difference in focus on finding gaps between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to the knowledge process.

4.3. Knowledge network

During the interviews each manager was asked to grade the strengths of their knowledge network. A distinction was made between relationships with companies and universities and between relationships with organizations in and outside Leiden. The results of the responses can be found in Figure 15. At first glance not much can be said about the knowledge networks of the pharmaceutical industry. Most of the companies seem to have an average-to-strong relationship with all universities and all companies, despite the location. Also managers were found afraid to value their knowledge relationship as very weak; most probably because they do not like to speak so negatively about their own company. Whenever the managers are dissatisfied with a certain connection, they prefer to choose the relationship to be weak or non-existing. Additionally, one can see that certain companies have no interaction with the LU/LUMC (29%) while fewer managers responded to have no interactions with other universities (7%). It was explained during the interviews that the LU/LUMC does not have expertise on all medical areas. Therefore, some companies need to look outside Leiden where the chance is higher to have experts ready for knowledge acquisition.

To create a better understanding of the results, the coded groups of chapter 4.1 are used again for cross tabulation. The most deviating results are discussed in the following part where again a cut-off point of 40% difference between certain groups responses is used. For this analysis the responses of the managers are grouped into negative (“Very weak”, “Weak” and “No interaction”), neutral (“Average”) and positive responses (“Strong” and “Very strong”) to create a better understanding.

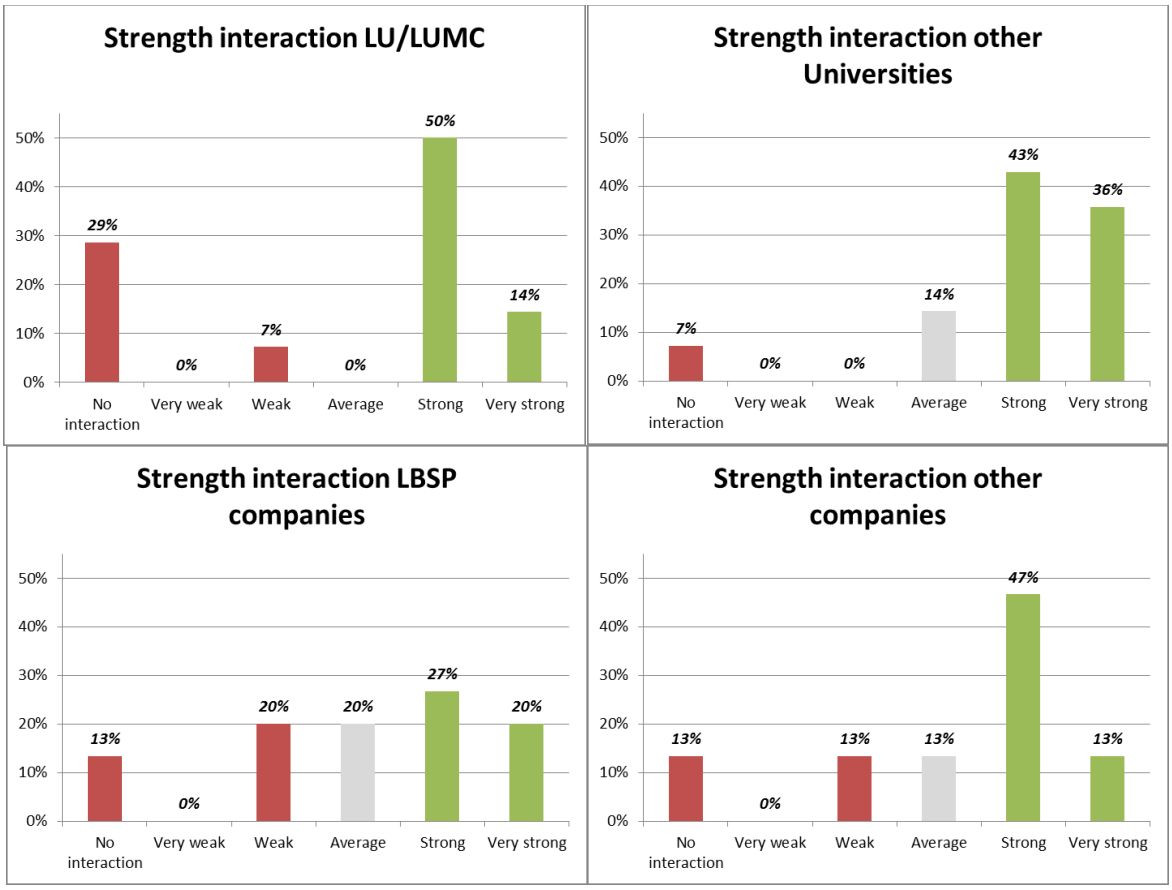

Figure 15 Strength of knowledge networks of pharmaceutical companies graded by the managers. Top left: with Leiden University, top right: with Other Universities, bottom left: with Leiden companies, bottom right: with other companies. The green bars indicate positive relationships, the red bars indicate the negative relationships and the grey bars are for neutral strength relationships.

4.3.1.From companies to universities

Managers explained that the main reason why pharmaceutical companies reach out to universities is to acquire expert knowledge. Universities have loads of experts on certain fundamental areas related to the pharmaceutical industry. There are grants and funds which stimulate the cooperation between pharmaceutical companies and universities like the Collaborative Funding Grant (North Carolina Biotechnology Centre). It is because of these funds that companies tend to cooperate more with the universities because research then becomes cheaper. The manager of company 9 described this relationship as follows:

"Compared to 25 years ago the Dutch academic world was different. Cooperation with industry is currently not considered as dirty but rather as a good thing. Where once many professors were adamantly opposed to cooperation, you do not see that anymore. That is because it has become clear that the ivory tower of academia should be accessible. This consciousness has permeated through the Dutch academic world. The outside pressure in favour of greater cooperation, like stimulating subsidies, has certainly contributed to this. "

It was found that most of the companies start the relationships with universities on an informal base. Companies know what they are looking for and are able to find the experts at universities through the internet. Distance does not become an obstacle because of this. People can easily send emails or perform videoconferences to decrease the threshold. But universities are mostly used for providing results of small research assignments. Less important research is outsourced because central research is valuable for the company and leakage of this knowledge could have a negative impact on their competitive advantage. The fact that a certain company is able to approach a university means that competing companies can do the same. Thus companies consider it safer to propose small collaborative research projects.

When looking into the coding of companies' knowledge networks, it is found that companies which have a product in the preclinical phase or in clinical phase I have stronger connections with universities (Figure 16). These findings suggest that universities are seen as important knowledge sources for their fundamental knowledge during early product studies. Also, universities have a lot of expensive equipment which can be useful during early drugs tests.

SMBEs also seem to be more involved with the universities compared to large pharmaceutical firms. Young companies have significantly stronger connections with LU/LUMC and other universities compared to old companies (Figure 16). Additionally, the location of the company shows that SMBEs are more involved with universities. There are three possible underlying arguments which can be thought of. It might be a result of the fact that young companies are mobile and eager to learn about their future products while large pharmaceutical companies already have acquired experts within their company and thus do not need to look for external experts. It might also be due to the fact that large pharmaceutical companies are frightening for the universities (West and Nightingale 2009). A final reason behind this difference in connection strength is that most of the SMBEs are spin-off companies from universities. Naturally their scientific knowledge network lies still with the universities.

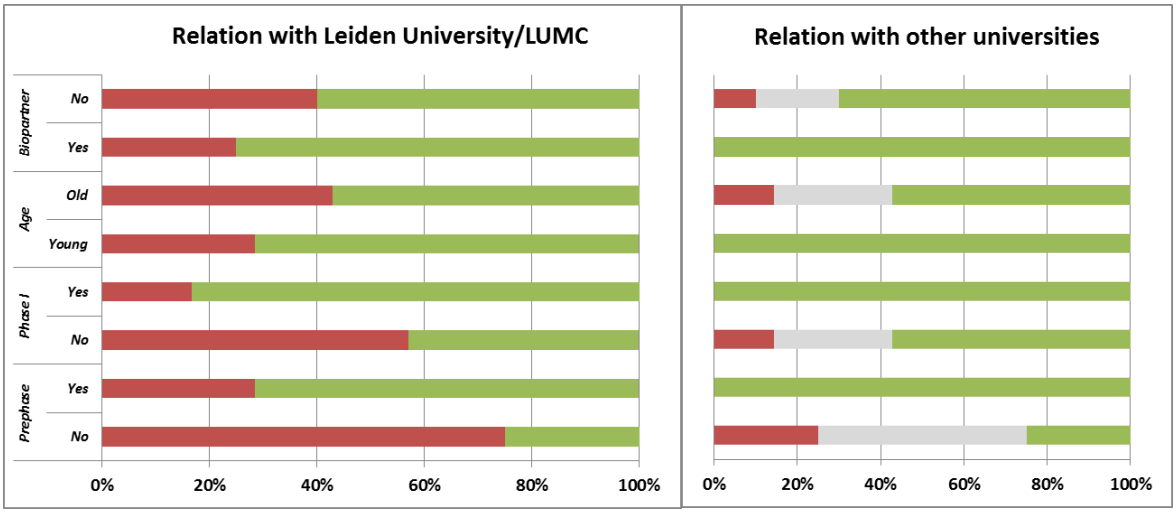

Figure 16 Difference in strength of relationships with Leiden University/LUMC (left) and other universities (right) between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively and grey is percentage answering neutral about the strength of the relationship.

4.3.2.From universities to companies

Many companies of the LBSP complain about the Leiden University Research & Innovation Services (LURIS), the TTO of the LU/LUMC. The complaints gathered during the interviews were mostly about negotiations when contracts for licensing were being made. Where TTOs expect to ease the transfer of technologies, it turned out that LURIS was making the transfer more complicated. Some companies try to avoid LURIS as much as possible and directly contact the inventor of the technology at the LU/LUMC. This confirms the findings of Barden and Weaver whom stated that TTO were to old fashioned (Barden and Weaver 2010). However, due to legislation LURIS has to be involved as all results from university research is intellectual property of the university (see 0).

Because of the many complaints about LURIS, it was decided to do an extra interview with one of the employees of LURIS to see how the TTO system works. A short summary of this interview can be found in 0. One important finding of the interview is that LU/LUMC never wants to sell a technology and will always choose to license it. The university is afraid that companies might buy a valuable patent for society which then will not be used. Recent cases have proven that some pharmaceutical companies keep beneficial products from reaching society. For example, Jansen-Cilag and Sandoz kept cheap painkillers for cancer patients from the market to earn more revenues (Dagblad 2013). However, it can be expected that companies are not tempted to license certain technologies if they run the risk that competitors can also license the same patent. For this reason companies can sign for an exclusive license which allows only them to use the technology. However it can become possible that companies are using this exclusive license to shield certain technologies from reaching the market. This rule of the LURIS for not allowing to sell any patents makes negotiations very

complex. Another interesting finding was the way LURIS treated spin-offs. There wasn't always an existing customer for all technologies of LURIS. In this case LURIS looked for an entrepreneur who would want to continue with the technology on the market. Most of these entrepreneurs came from the university itself. However, when this person was starting to write the business plan for this new spin-off company, LURIS would see it as a customer and terminated all support for this individual so it could try to build up a reasonable license contract for this new customer. It is for these two reasons, forceful licensing and lack of spin-off support, that technology transfer from universities to companies was not stimulated and the start-up of new companies was also deregulated.

On the other hand the interviewed knowledge institutes complained about the fact that not enough interaction exists between them and the companies inside the LBSP (see Figure 17). As can be seen in this figure, 67% of the interviewed institutes indicate that the strength of the knowledge transfer with the companies in the LBSP is not sufficient even though they were closely located to each other. The companies score 67% of having a positive relationship with the LU. Earlier it was mentioned that there are companies with connections to other universities and not to the LU. The main reason behind this difference is the lack of expertise at the university. It might also be that the troubles with LURIS causes companies to think there are enough connections with the LU/LUMC but actually the university is able to supply much more knowledge for the companies in the LBSP.

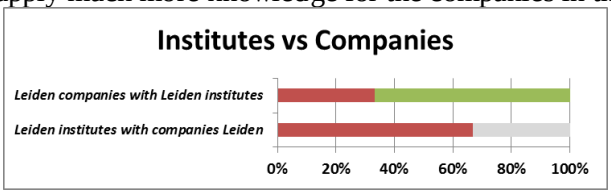

Figure 17 Difference in strength of relationships between the Leiden University institutes and the Leiden companies. Green is the percentage of organizations answering positively, red is the percentage answering negatively and grey is percentage answering neutral about the strength of the relationship.

4.3.3.Between companies

An interesting result found during the interviews is that the knowledge interactions with other companies are mostly formed because they need services from these other companies. Companies with fewer resources hire more CROs for specific specialized services. CROs are used for supplies, machines, analytical research and clinical research. Whenever a company is active in one of the clinical studies, it will be forced to use certain specialized services. This theory is supported by the results of the interviews as presented in Figure 18. All phases show an increase of company involvement in and outside the area.

The decision on where to acquire these services is based on the distance/fit ratio. Pharmaceutical companies cannot afford their products to have any pollution. Clinical studies have strict regulations of the EMA and the FDA. Most of the companies perform a worldwide search for the best distance/fit offer for these services. The most fitted company with experience in similar tasks might be located far away. A tradeoff between transportation cost and a fitting company for the service needs to be made. The importance of this distance/fit ratio is proven by the results of the interviews in Figure 18. The small firms are more involved with local companies, because many services can be done by local companies. Local company services have very low transportation costs. The results on location and age show that SMBEs are more involved with local companies while international companies show to have stronger connections with companies outside Leiden (see Figure 18). These international companies have the advantage that other settlements also have companies nearby which means that they can choose from more potential partners with the same distance/fit ratio. On the other hand, large pharmaceutical show to have less strong positive connections with companies inside and outside Leiden. This coincides with the findings of increased knowledge creation. Large pharmaceutical firms were found to do more services internally with knowledge creation. This off course acts out in the strengths of the connections with companies. Again the coding factors of age and location show significant differences with SMBEs which can be seen in Figure 18. As the manager of a typical SMBE company (company 5) explains:

"Contact with companies in LBSP is good. Mostly these are the people who have more experience than us. That is why we have chosen LBSP. I noticed that there is a concentration of good businesses

in Leiden. If you are situated around the corner, it's a lot easier to talk, to explain a problem or to have a look at a sample, than when you have to send it to Belgium or America. "

The benefit of the LBSP is that many activities allow companies to get in contact with each other and remain updated with their development on an informal basis. However, it was mentioned during the interviews that mostly non research-relevant topics are shared among companies like the benchmarking of wages for certain employees and the struggles of filing at the EMA and FDA. Another benefit of the LBSP, which was discussed during many interviews, is that many employees switch between LBSP companies on a regular basis. Because of this a tight LSH knowledge network is created which goes beyond company boundaries. During the interviews it was even mentioned that people within the LSH network recognize one another and speak to each other on scientific congresses.

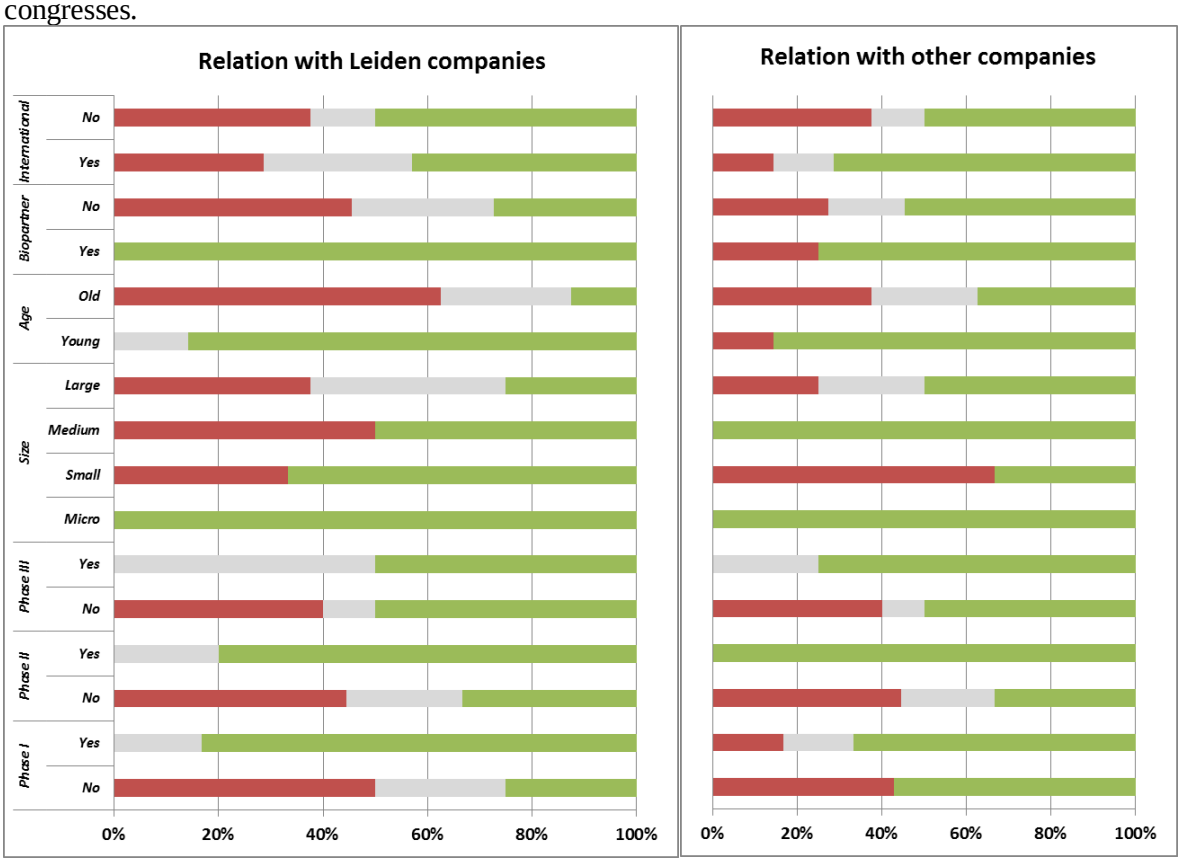

Figure 18 Difference in strength of relationships with Leiden companies (left) and other companies (right) between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively and grey is percentage answering neutral about the strength of the relationship.

4.4. Motivation

Another topic questioned during the interviews was how the managers motivate their research employees. All managers mentioned different focus points. However, all agree that it is one of the most important tasks during their job. The different approaches are separated into different categories of the Self-Determination theory (SDT) (Gagné and Deci 2005) which explains motivation by the level of *relatedness*, *autonomy* and *competence*. Within these motivations other motivational arguments were coded for further analysis.

4.4.1. Relatedness

The first dimension of the SDT theory is the relatedness of an employee which determines the internalization of the motivation. This dimension makes the distinction of the motivation being *intrinsic* or *extrinsic* (Gagné and Deci 2005).

4.4.1.1. *Intrinsic motivation*

In total 60% of the managers mention intrinsic motivation as one of the main motivational drivers for their research employees. Five of these managers mention scientific curiosity as an important driver. They explained that most of the researchers have a scientific background and therefore have a natural hunger for doing research. This was confirmed during the cross tabulation when looking at the knowledge institutes (see Figure 19). This curiosity still remains when the people are hired by the pharmaceutical companies, although research then becomes more focused on knowledge application instead of knowledge creation. It was also found that public owned companies were using intrinsic motivation less as a drive then private owned companies.

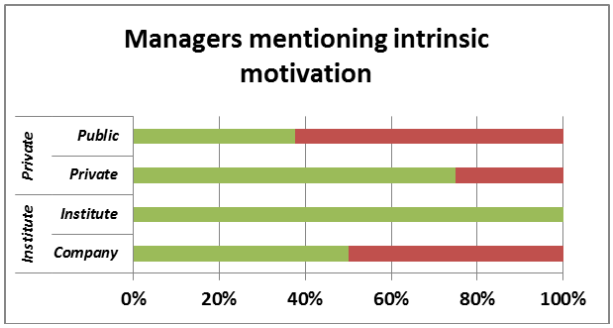

Figure 19 Difference in mentioning intrinsic motivation between certain groups of organizations. Green is the percentage of organizations answering positively, red is the percentage answering negatively to this form of motivation.

4.4.1.2. *Extrinsic motivation*

During the interviews it was found that most of the arguments used to explain the motivational drive of their employees were feeding the extrinsic motivation. All managers mention a certain form of extrinsic motivation during the interviews. The three most used extrinsic motivations are helping *patients*, earning *money* and earning *scientific rewards*. The number of interviews mentioning one of these extrinsic motivations is given in Figure 20.

Ten managers suggested that researchers are constantly aware of the impact of their work on society. The companies use regular meetings with patient groups, chose patient ambassadors and hang motivational posters with patient stories in and around the work environment. Although it would seem that the distance between research and actual helping *patients* is very large due to the long project cycles (Ortt, Tabatabaie et al. 2009, Raaphorst 2012, Raaphorst 2013), the impact of the results is found to be so strong that researchers do feel the motivational drive. By sharing the progress of the drug development in clinical trials, researchers can become more aware of their contributions to these patients. The strange thing is that companies which are far in the clinical trials are using patient groups less as a motivator (see Figure 21). One would expect that employees see the results of the drug and the impact of their research during these clinical studies. However, 100% of the application focused companies are using patient motivation far more than other companies (50%). This means that it is in early research that this motivation of helping patients is needed the most. Another interesting result is that SMBEs are using patients more as an extrinsic motivator than large pharmaceutical companies. A significant difference is found between the Biopartner companies (100%) and the other companies (60%) as can be seen in Figure 21. A final interesting result for patient motivation is that privately owned companies are using patients more as a motivational drive than public owned companies.

A classical extrinsic motivation is *money*. The managers are diverged on this method of extrinsic motivation. During six interviews it was found that money is used as a motivator to stimulate the researchers. Examples were incentives like stock options and bonuses when targets are reached. However, four managers explicitly mentioned that money is not a motivation which works for research

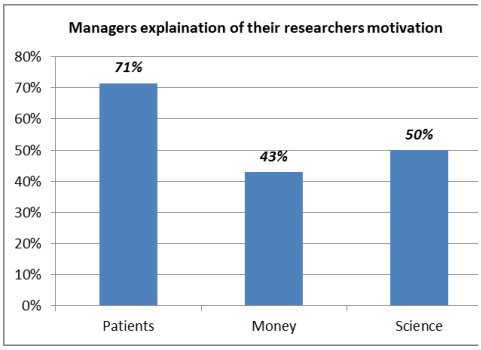

Figure 20 Response of the interviews with the fifteen companies. Each manager was asked to give the main motivators of their research employees.

employees within the pharmaceutical industry. According to them the only thing that needs to be done is to pay just above average to keep employees within the company. Again the results for SMBEs and large pharmaceutical firms are found to differ for this factor. Also selling companies use are better able to use money as a motivator (75%) while other companies find it more difficult to pay awards and bonuses (30%). Over 63% of the knowledge creation companies use money as a motivator while 17% of the other companies use monetary measures. This fits the description mentioned earlier; that large pharmaceutical firms are more focused on the knowledge creation process (chapter 4.2.3). Another interesting finding on monetary awards is that all knowledge institutes do not use this kind of motivation. Also, when looking deeper into these companies the results of Figure 21 show that 25% of the privately owned pharmaceutical companies suggest money to motivate their employees while 63% of the publicly owned companies use money as a motivation.

Not only money can be used as an extrinsic motivator but *science* itself as well. Some managers mention that publications in scientific journals and going to congresses are also seen by many research employees as an award for their work very much related to the scientific curiosity. However, the awards represent a certain appraisal and respect which means it is not fully internalized making it intrinsic motivation. Managers explained that employees are only allowed to make a publication or to go to the congress if they have some interesting results to present. In Figure 21 the differences can be seen between different kinds of company ownerships. All knowledge institutes use science as a motivator. It is 75% of the public owned companies that use this same motivator while only 25% of the private owned companies use science as a motivator.

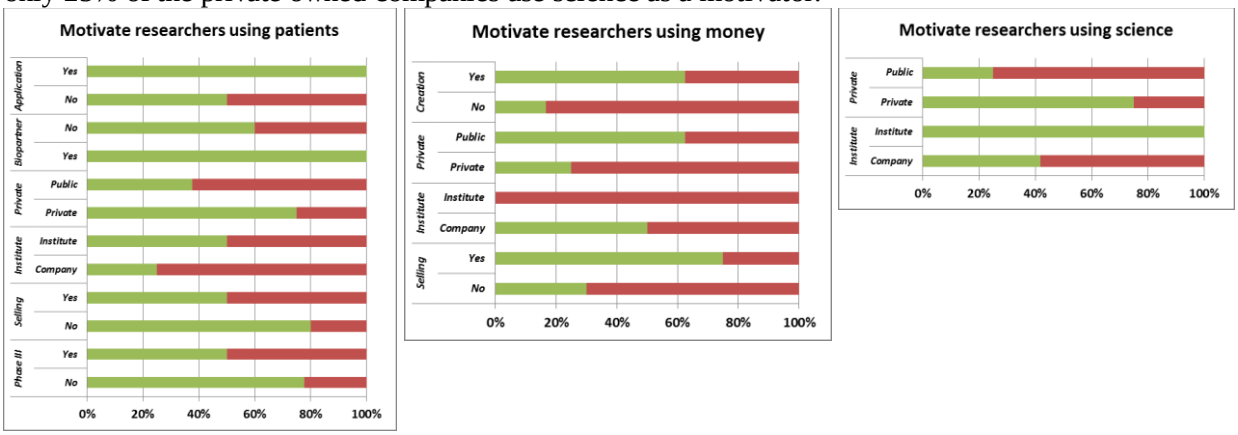

Figure 21 Difference in mentioning extrinsic motivation between certain groups of organizations. Left is the extrinsic motivation of helping patients, in the middle is the motivation of money and on the right is the motivation of science. Green is the percentage of organizations answering positively, red is the percentage answering negatively to this form of motivation.

4.4.2.Autonomy

From the fifteen interviews four managers responded that the researchers at pharmaceutical organizations are very much motivated by freedom in their jobs. This can be related to the autonomy concept of the SDT. Freedom is easily given at small companies; a lot of different tasks can be done which has to be divided over a small group of employees. The small companies are also very transparent which creates the feeling of having more freedom and understanding more of the strategies being chosen.

It was not mentioned during the interviews but one might expect that the danger of giving employees more autonomy is that employees can get off track. Additionally, some researchers don't like to have that much freedom and require more guidelines. Thus a balance needs to be found between freedom to arrange their planning and steering the direction in which research needs to be done. Also autonomy has to be balanced with curiosity. Too much freedom and too much scientific curiosity can lead to unusable research results while the company is looking for knowledge application. Managers should try to prevent this from happening without compromising the motivation of the employee.

4.4.3. Competence

Finally there is the last category of motivation according to the SDT. Competence is best described as the motivational drive of employees to be challenged. Two of the managers mentioned that their researchers are mainly driven by challenge. Therefore, they try to guide their employees with progress evaluations to let the researchers accomplish their goals. Company 7 even has a special evaluation method in which it is forbidden for managers to use aggressive emotions to pressure the researchers. It seems as if competence is not the main focus point of motivation in the pharmaceutical industry.

4.5. Innovation performance

Innovation performance is difficult to measure, especially in the pharmaceutical industry. Therefore, nine different variables were asked to be answered by the managers in order to explore innovation performance in this industry. These nine items are: the amount of *products in certain phases* of the product pipeline (preclinical, I, II, III and on the market), the amount of *patents filed since 2010*, the amount of *scientific articles published since 2010*, the *financial support granted since 2010* and the amount of *money spent on R&D in 2012*. This information was gathered from the fifteen companies during the interviews. Because the amount of results was too small no statistical analysis could be performed to obtain reliable results. However, some exploring results could be summarized to see if these items measure similar scales which could indicate innovation performance. However, these findings need to be interpreted carefully because of a higher chance of random relations in the findings.

First a factor analysis was performed using SPSS. This factor analysis was started by analyzing the Scree-plot of the nine items to see what the best amount of factors would be to look for (Cattell 1966). The resulting graph can be found in 0. The point of inflexion is found at four factors meaning that the nine items could reasonably be reduced to four factors. However, when the Kaiser's criterion (Kaiser 1960) would be used, in which factors need an eigenvalue of at least 1, it would seem that three factors would be a better fit for the dataset. Therefore the analysis was continued looking for three underlying factors.

Next a factor rotation of SPSS (FIELD 2005) was used to see how the nine items are related to the underlying three factors. The results are given in Table 1. The first factor is found to correlate highly with the amount of products in clinical phase III and the amount of products registered on the market. Also the amount of scientific publications and the amount of patents seem to correlate highly with factor 1, which was found to be related to innovation performance by Nesta and Saviotti as well (Nesta and Saviotti 2005). Thus small proof is found that factor 1 represents the innovation performance score of confirming phase (see chapter 4.2.4). Whenever products are in clinical phase III or on the market it is confirmed that the predicted result of a drug are correct. To put it more delicately; it means that the confirming of the things learned (preclinical, clinical phase I and II) is being confirmed (clinical phase III and market approval). Also scientific publications and the amount of patents are forms of confirmations of predictions.

Factor 2 was found to correlate more with factors belonging to companies which are in early development of their product pipeline. Beside early development funding, which is mostly given to developing companies without any revenues, seems to correlate with this factor. Therefore, indications are found that factor 2 is a score of a successful learning phase (see chapter 4.2.4). Whenever companies were able to find good targets for preclinical phases and were able to raise funds with help of their findings it would mean that the learning phase had been successfully conducted.

The third factor is very interesting because it correlates highly negative with spent money on R&D and correlates positively with the amount of patents filed. Additionally, clinical phase II is represented in this factor. This might be the result of the small group of measurements but it might also indicate the transitional innovation performance between the learning phase and the confirmation phase. We call this the *transitional phase* in which innovation performance could also be measured.

Unfortunately not all companies provided answers to all the questions during the interviews. When the new factors are calculated for each company only 5 results can be computed because of the missing values in other companies. This means that unfortunately no further research can be performed with the three new performance factors.

Table 1 Factor rotation analysis (varimax) for reduction to three factors. The numbers are the coefficients to transform the items into the three component factors. Correlations above as 0.5 or under -0.5 were marked green.

Rotated Component Matrix[a]

	Component		
	1	2	3
Products preclinical phase	-.009	1.000	.015
Products clinical phase I	.343	.922	-.150
Products clinical phase II	-.347	.694	.582
Products clinical phase III	.983	.148	.002
Products on market	.990	-.139	-.020
Patents filed since 2010	.585	-.181	.760
Scientific publications since 2010	.994	.069	.020
Funding since 2010	-.090	.990	-.099
Spent money on R&D in 2012	.086	.049	-.931

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
a. Rotation converged in 3 iterations.

4.6. Summary results

The results of this research have extensively been described in this chapter. We will summarize the results in short before the analysis of the results is discussed in the next chapter.

The companies which were being interviewed were very diverse. However some related characteristics are present within the companies interviewed which can best be described as the separation between SMBEs and large pharmaceutical companies.

A summary of the results on the knowledge processes is given in Table 2. It is found that knowledge acquisition and knowledge creation were had opposing company characteristics. SMBEs are more focused on knowledge acquisition while large pharmaceutical companies and knowledge institutes are more focused on knowledge creation. Another interesting result on knowledge processes is the separation between knowledge distribution and knowledge sharing. Knowledge sharing is found important in early stage of discovery and development where knowledge distribution became important in late stage discovery and development of pharmaceutical products.

	More focused on process	**Less focused on process**
Knowledge application		Selling
Knowledge acquisition	Biopartner, biopharma/biotech	Not Biopartner, pharma, institutes
Knowledge creation	Not Biopartner, institutes	Biopartner
Knowledge distribution	Selling	
Knowledge sharing	Pharma, institutes, large	Biopharma/biotech, small, selling
Knowledge storing	Prephase	
Identifying knowledge gaps	Selling, international	National

Table 2 Summary results interviews on knowledge processes.

The knowledge network also differs among the companies of the LBSP. Large pharmaceutical companies do not have strong connections with universities or companies as the SMBEs. And SMBEs often choose to cooperate with local companies as distant companies. That is why international companies have stronger ties with other companies outside Leiden and national companies have stronger ties with local companies. Additionally, connections to universities appear to be stronger during early discovery and development. All these results are summarized in Table 3.

	More positive relationships	Less positive relationships
LU/LUMC	Prephase, phase I, young, Biopartner	Old, not Biopartner
Other Universities	Prephase, phase I, young, Biopartner	Old, not Biopartner
Companies Leiden	Phase I, II, III, small, young, Biopartner, national	Large, old, not Biopartner, international
Other companies	Phase I, II, III, young, international	Old, national

Table 3 Summary results interviews on knowledge networks.

Finally the motivation of the researchers of the pharmaceutical companies was compared. All managers spoke of extrinsic motivation and many spoke of intrinsic motivation. The type of organization plays an interesting role in the important motivational drive that is present within the organization. Knowledge institutes finally show to differ from the large pharmaceutical firms because it is mainly focuses on intrinsic, scientific and patient motivation. The results of Figure 21 show the opposite result for knowledge institutes and public owned companies when looking at the financial and scientific motivators. When a company has the financial resources for monetary awards these can easily be used for their employees. However, other companies need to use other rewards which are not expensive but researchers still see it as a great value. Apparently science is a great replacement for monetary awards. Public owned companies are on the opposite which mainly use monetary motivation to control the researcher's performance. Publically owned companies are found to be in between of these extreme groups. Another important difference in motivational drive is between the SMBEs, which rather focus on patients, and large pharmaceutical companies, which rather focus on monetary rewards. All these results are summarized in Table 4.

	Using certain motivator more	Using motivator less
Intrinsic motivation	Institutes, private owned	Companies, public owned
Extrinsic patients motivation	Knowledge application, Biopartner, institutes, private owned	Selling, phase III, not Biopartner companies, public owned
Extrinsic money motivation	Knowledge creation, selling, companies, public owned	Institutes, private owned
Extrinsic science motivation	Institutes, private owned	Companies, public owned

Table 4 Summary results interviews on motivation.

5. Discussion

The goal of this thesis was to learn more about innovation management in the pharmaceutical industry by exploring certain antecedents of innovation management. By looking at five of these antecedents, *company characteristics, knowledge processes, knowledge network, motivation* and *innovation performance*, interesting results can be filtered out of the interviews. In this chapter an answer is searched for the sub question:

"What are the trends for the important aspects of innovation management in the LBSP?"

During analysis three phases of R&D were found specifically for the pharmaceutical industry. Also the distinction between large pharmaceutical firms, SMBEs and knowledge institutes were found having their own innovation strategy in many aspects. The knowledge processes gave some interesting results for the 'bathtub' model which can be expanded (Dierickx and Cool 1989, Deeds and Decarolis 1999). During the analysis some interesting findings were found which all shall be discussed in the following.

5.1. Phases of Research and Development

During analysis of the results it is found that companies in the pharmaceutical industry behave in different manners during the different phases of clinical trials. Three phases are identified during the analysis of the results.

5.1.1. The learning phase

The innovation process begins in the *learning phase* where new biological or chemical compounds are being searched for. These companies focus more on sharing tacit knowledge. This sharing of tacit knowledge is beneficial for innovation (Dunne and Dougherty 2011) and so will result in new compounds for preclinical studies. The personalized transfer of knowledge will allow employees to understand new concepts faster, which is important during this phase of discovery and development. Also knowledge application is more important during this phase. The eventual goal is very far ahead due to the long project cycles. But this does not mean that research employees can look into any topic they want to. All knowledge gathered must be useful for application or else valuable resources are wasted on unusable results.

Additionally companies in the learning phase have stronger connections with universities. These universities are a cheap source of fundamental knowledge which can be very valuable for learning companies. This fundamental knowledge can then internally be used to create valuable knowledge for application allowing it to become a competitive advantage. Also the patients for the disease which they are working on are brought closer to the researchers as to motivate the research being done. Employees become aware of the value their work brings by trying to understand the suffering and pain of the patients.

During factor analysis the innovation performance of this learning phase (factor 2) is found to be represented by the amount of products in preclinical phase, phase I and phase II. Also, in chapter 4.1 the correlations between the coded characteristics indicated that these clinical phases are connected. The amount of funds is connected to this learning phase because funding is the most used finance model of starting pharmaceutical businesses (see chapter 1.3) (Raaphorst 2013).

This learning phase has some characteristics similar to other concepts found in literature. It seems to correlate with personalized KM strategy defined by Hansen et al. (Hansen, Nohria et al. 1999). Although a company mostly uses both personalized and codified knowledge transfer activities, the focus on the learning phase lies more with the personalized KM. This result also seems to coincide with another theory found during the literature review. Biedenbach mentioned that pharmaceutical companies have three separate capabilities; dynamic, project and multiproject capabilities (Biedenbach 2011). The learning phase has similarities with dynamic capabilities where it is important to focus on adaptive, absorptive and innovative capabilities. One must learn many things from in and outside the company and should be adaptive enough to react to these findings. It is especially important when the market is uncertain and during early discovery in such long projects many things are uncertain.

5.1.2.The confirming phase

The second clear phase of research and development of the pharmaceutical industry found is the *confirming phase*, mentioned by company 7. During the confirming phase the results of the clinical studies need to be gathered. It is here that companies want to confirm the prediction made by experimental models and preclinical work. This confirmation comes from clinical studies which prove the drugs work on real patients. Hospitals and CROs gather data from the patients and send these documents to the pharmaceutical firms. These documents are stored and distributed within the company allowing the company to progress towards filing and market introduction. It is in this phase of R&D that explicit knowledge becomes more important. Written knowledge eventually needs to be transferred to the EMA and FDA to facilitate they understand the implications of the clinical research. That is why knowledge distribution becomes so important during the confirming phase. Now, the focus does not lie on learning and understanding diseases as fast as possible but on spreading and understanding the results of the clinical studies. This difference in focus changes the difference on level of knowledge.

Another change is found in the motivational drive of the employees. Whenever drugs continue the drug pipeline patients become less important for motivational drive. There is not much which can be done to improve the lives of the patients because the product has already been developed and now is only being tested. Managers should use other control mechanisms to make sure that the quality and the speed of the employees are up to standard.

Also for this phase a separate factor was found during the factor analysis of the nine innovation performance measures. The amount of products in the clinical phase III and products on the market played an important role. Some might find it odd that products on the market have anything to do with confirming a product. However, the products on the market are found to be an indicator of performance meaning that this product has actually passed all clinical studies. It was mentioned in the previous chapter that knowledge application was less important for selling companies. Thus organizations which are in the confirming phase do not need to focus extra on application anymore because they already have a product which is close to application. This knowledge process becomes important again whenever the company starts working on filling their drug pipeline and increasing their portfolio.

Where the learning phase could be matched with personalized KM the confirming phase rather seems to correlate with a codified KM strategy (Hansen, Nohria et al. 1999). Again the findings of Biedenbach could be applied to the findings of this research. The confirming phase has many similarities with the project capabilities of Biedenbach (Biedenbach 2011). During the confirmation phase the drug approval becomes a project which needs to go through clinical studies in a certain amount of time. It now becomes focused on milestones and deadlines with multiple partners who need be managed accordingly.

5.1.3.The transitional phase

The factor analysis also shows a third phase of research and development which points out a certain *transitional phase*. It is in and around clinical phase II where companies need to change their R&D process. During this transitional phase companies should stop doing fundamental research and start focusing on clinical trials, hence the negative correlation with R&D costs. Further evidence of this third R&D phase is missing so not much can be said about this transitional phase.

Table 5 gives a summary of all the R&D phases. The fact that three different scales of innovation performance are found means that companies can be engaged in many of them to certain degrees at the same time. A company can be focused on the confirming phase while looking for new drug candidates in the learning phase for other diseases. There is a rational order to go through the phases but companies can choose to be active in several innovation phases at the same time. Therefore the model is not cyclical but linear where multiple lines can be activated. Small companies do not have the financial resources to focus on many of these aspects at the same time and thus will be found actively involved in one of the three phases. The more financial resources a company has, the more it can diverse their focus on multiple phases to fill their product pipeline. This also coincides with results from Biedenbach. The ability of being active in multiple phases seems to have many similarities with the multiproject capability theory (Biedenbach 2011). The more resources a company has, the better it

should look for how to divide these resources over projects and still keep innovation performance high.

Table 5 Summary of characteristics of the different research and development phases.

	Learning phase	Transitional phase	Confirming phase
Knowledge processes	Sharing and Application		Distribution
Knowledge network	Universities		
Motivation	Patients		No patients
Performance factor	Factor 2	Factor 3	Factor 1
Clinical phases	Preclinical, Phase I and Phase II	Phase II	Phase III and Selling
Focus points	Quick learning for new discoveries	Stop learning start confirming	Quick distribution of clinical study results
Hansen et al. KM strategy	Personalized		Codified
Biedenbach Strategy	Dynamic capabilities		Project capabilities

5.2. Innovation strategies

During the analysis of the results the separation between the large pharmaceutical firms and the SMBEs was encountered many times. The company characteristics of both groups create a sharp line between the two which allows summarizing some of the most interesting results. Also knowledge institutes were found to have a distinctive innovation strategy.

5.2.1. Large pharmaceutical companies

The first group of companies in the pharmaceutical industry is the large sized pharmaceutical group. The age of these companies lies above fifteen years which also means that they can already have medical products selling on the market. These revenues allow them to work and focus differently from the other group of companies. Large pharmaceutical firms have their own buildings and own research facilities and do not rely on incubator buildings like Biopartner. Additionally, the financial resources allow the large pharmaceutical firms to cooperate with companies far away from their facilities if it means that they can cooperate with better fitting organizations. The financial resources allow large pharmaceutical companies to have a large product portfolio and an extended drug pipeline.

Large pharmaceutical companies need an input of new knowledge which they rather choose to create internally as opposed to acquiring them from external parties. As a consequence their development will be slow, difficult and expensive but in return will create such unique results that it will have high value on the market and increase their competitive advantage. These companies create knowledge internally and thus are focused on knowledge creation. The large pharmaceutical companies do not focus as much on acquisition anymore and cooperate less with other companies. These companies think to already have the experts internally and this can make these companies weak and blind for radical changes in the market.

Another disadvantage of these large pharmaceutical companies is that there are many employees who each have their own specialisms and their own knowledge base. The sharing of this knowledge is difficult and companies can become blind for knowledge gaps. That is why many of these companies are trying to focus more on knowledge sharing and findings knowledge gaps compared to the SMBEs. The fact that they have to focus on this is because SMBEs have the advantage of being able to oversee everything more easily due to their small size.

Large pharmaceutical companies also do not use patient motivation so much as others. This lack of patient motivation probably comes from the increased drug portfolio. They focus on many diseases to generate stable income for the future (multiproject capability). Whenever a company is working on one disease area it is rather easy to keep contact with one patient group. However these large pharmaceutical firms would have to focus on multiple patient groups of all their portfolio diseases. This becomes so time consuming that other motivational drives are used which can be applied to all company researchers like monetary awards. This also is more fitting to the profile considering these companies have the financial resources to do so due to their revenues.

The description of this group of companies is one that is familiar in many industries. It seems to coincide with the Schumpeter II theory (Malerba and Orsenigo 1995). Schumpeter II theory explained that the true source of innovation comes from large companies which have the resources to

pay for many projects and thus are in favor of the serendipity effect (Schmid and Smith 2002). Large pharmaceutical firms also have many resources to pay for internal research. It will take more time but the awards for it are greater, creating a better competitive advantage.

5.2.2.Small and Medium sized Biopharmaceutical/Biotechnology Enterprises

The second group of companies is the SMBE. These companies lack in financial resources because most of them are young spin-off companies which do not have any approved products on the market. They afford to do research because of grants, VCs and revenues of services. These companies are small and try to create new niche market products to protect themselves from competition. The lack of financial resources forces them to look for shared facilities. Incubators and accelerators are good examples of governments supporting these companies.

Instead of buying expensive equipment for research they have to buy knowledge from CROs and universities which is cheaper, easier and faster. These companies are more focused on knowledge acquisition, meaning that SMBEs focus more on absorptive capacity (see chapter 2.3.1). This should bring the problems for absorptive capacity along like not-invented-here syndrome (Katz and Allen 1982) and path dependency (Cohen and Levinthal 1990, Karim 2009). Fortunately, according to this research these problems do not seem to play a significant role for the pharmaceutical industry. Already many tasks are being outsourced in this industry to CROs and CMOs and thus R&D personnel are familiar with handling external knowledge. But the downside of this strategy is that all competing companies can use the same measures. A unique competitive advantage is thus seldom created. Additionally, SMBEs are small and thus do not have to focus so much on knowledge sharing as large companies. It is considered natural in small companies that colleagues speak to each other in person. In SMBEs employees know what everybody does, has been doing and therefore where their expertise lies. All findings and all questions are answered more quickly if you speak to them directly, compared to larger companies.

When cooperating with universities these SMBEs are able to use funds to pay for the research being performed. The fact that all companies are located in a cluster means that they already cooperate in attracting more funds to the area (Arechavala-Vargas, Rico-Huerta et al. 2012). This finding of collaboration between SMBEs and universities was already described by West and Nightingale, in a Swedish research of the pharmaceutical industry by McKelvey et al. and now is confirmed again in this thesis (McKelvey, Alm et al. 2003, West and Nightingale 2009). There are many possible reasons for explaining this tight collaboration, like the low costs, the origin of the company and easy approach by SMBEs. From this research no conclusions can be drawn about the true reason behind this collaboration. SMBEs were also found to have a larger company network because they have to acquire more knowledge from outside the firm. SMBEs tend to collaborate with closely situated firms because it reduces the transportations costs and increases the ease of approach. Scientific clusters like the LBSP are therefore a good example of regions where SMBEs should settle.

SMBEs use the target disease patients as motivator more than large pharmaceutical firms. These firms are mostly focusing on a few disease areas. Thus these few diseases are easily used as a motivator for the company by building a relationship with these one or two patient groups. In their turn patient groups help in funding and shortening the clinical study time. SMBEs however cannot use monetary awards for they need to reduce their expenses. Most of the employees who apply for a job are aware that small companies do not have much to spend on financial awards.

Where the large pharmaceutical companies most fitted the Schumpeter II theory it rather seems that the SMBEs mostly fit the profile of the Schumpeter I theory. His first theory stated that the small companies are the most innovative ones because they are able to be mobile and need to focus more on surviving (Malerba and Orsenigo 1995). They can come up with many unique solutions with a real entrepreneurial spirit.

5.2.3.Knowledge institutes

Knowledge institutes are very interesting organizations. According to the findings of this research they look very similar to large pharmaceutical companies, which is not what one would expect at first hand because the university research is so fundamental and not commercially driven. Both pharmaceutical companies and institutes focus on knowledge creation. They can do this because they have large incomes to pay for internal equipment, facilities and employees.

However, most of the financial sources of universities come from the government and not because of selling medical products. Therefore, the focus of knowledge creation of institutes lies on different areas which do not meet with the areas of pharmaceutical firms. Knowledge institutes can choose to research any topics even though the risk is high of not finding any useful results. This difference in financial source can also be seen in the motivation of the researchers. Intrinsic motivation is their main focus because they can follow their own interest and ambition. This is rewarding enough to stay motivated and no monetary awards are needed. Scientific awards are all the more efficient within these knowledge institutes.

But there is an uncomfortable relation between universities and companies. Pharmaceutical companies and universities look differently at the strengths of their collaborations. This difference was addressed in chapter 4.3.2. Where this difference exactly comes from was not found during the interviews although one might expect that it is because they both do not know what the other party knows. Universities might underestimate the knowledge base of the companies and the companies might underestimate the usefulness of the knowledge of the universities. The further the universities and companies are separated from each other the more they underestimate each other. This might explain why large pharmaceutical firms do not cooperate with knowledge institutes as much as the SMBEs.

During the analysis of the results it was found that each company has chosen for acquisition or creation or both. That means that all companies were aware of the importance of input of new knowledge into the company to increase their knowledge base. But when looking deeper into this input of knowledge it was found that companies could be separated into two strategies which both had their own characteristics (large pharma, SMBE and knowledge institutes). This division can be compared with the make or buy decision which needs to be made in many other industries as well (Walker and Weber 1984). Large pharmaceutical companies have money and thus make their own results while SMBEs need to buy their research results from outside the company. This is no true black-white division. Even large pharmaceutical firms sometimes buy certain research and also SMBEs do internal research. However, this typical difference can best be compared to the make-or-buy discussion and seems applicable for the pharmaceutical industry as well. Table 6 gives a summary of these three groups of pharmaceutical organizations is given in.

Table 6 Summary of characteristics of the different pharmaceutical organization groups.

	Large pharmaceutical companies	SMBEs	Knowledge institutes
Advantages	Competitive advantage	Quick, cheap and easy	Fundamental
Disadvantages	Time consuming, expensive and difficult	Low competitive advantage	Not always applicable
Knowledge processes	Creation, sharing and identify gaps	Acquisition	Creation
Knowledge network	Low with all companies	Universities and Leiden companies	
Motivation	Money, no patients	Patients, no money	Science, no money
Characteristics	Old, large Pharmaceutical with many resources	Young, small Biotechnology/Biopharmaceutical, within Biopartner with fewer resources	Large universities
Schumpeter	Mark II	Mark I	
Make or Buy	Make	Buy	Make
Financial source	Selling medicines	Grants, VC and selling services	Government/companies

5.3. The knowledge reactor model

Earlier in this paper a bathtub model was suggested (Dierickx and Cool 1989). In this model the knowledge base of a company was represented by water inside a bathtub. The knowledge base could be expanded with knowledge processes which allowed increasing the output of applicable ideas. But when output is continued with a higher speed than knowledge is being put into the bathtub you run the risk of drying up. During the findings of this thesis it was found that all companies were somewhat aware of the function of this model. One cannot increase innovation performance (knowledge application) when there is no knowledge base left. Thus input through knowledge acquisition or knowledge creation is essential if a company wants to have a high innovation performance. That is why all companies chose either of these processes. However, as discussed in chapter 5.2, different

kinds of organizations prefer different kinds of knowledge inputs, thus changing the simplicity of the bathtub model.

Additionally it was found that knowledge input does not automatically result in successful output of products in the pharmaceutical industry. To speed up certain processes knowledge sharing and knowledge distribution were used. But as chapter 5.1 described, different phases of pharmaceutical innovation require different methods for speeding up the knowledge transfer. This can also be added to the bathtub model. It is because of this that a new knowledge model is proposed representing the difficulties in knowledge processes for the pharmaceutical industry.

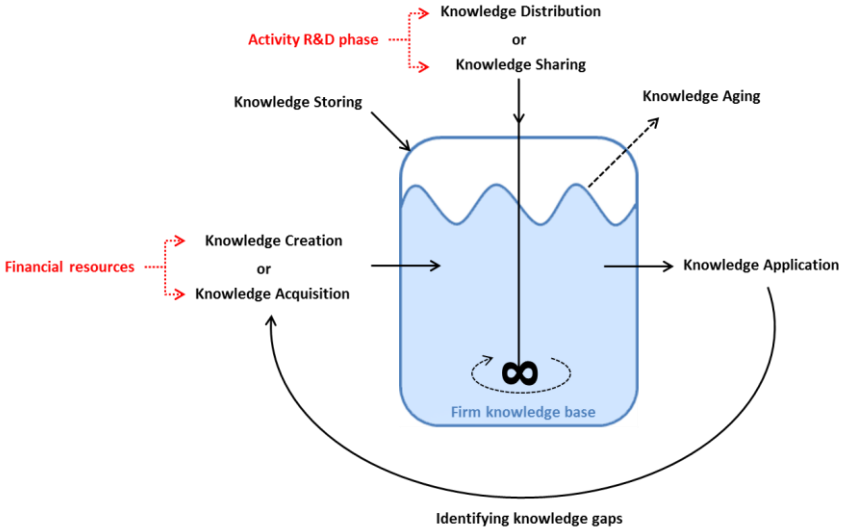

Figure 22 The *knowledge reactor model* representing the knowledge processes and the difficulties for the pharmaceutical industry. The black arrows represent the flows of knowledge because of knowledge processes. The red arrows are influential factors for the knowledge processes.

The newly proposed model is called the '*knowledge reactor model'* which is given in Figure 22. All the seven knowledge processes measured in this thesis are represented as a certain flow. The content of the reactor is the knowledge base of a firm, just as in the bathtub model. It is needed to create output which is innovation of the firm. But whenever too much knowledge is drained from the reactor it becomes empty and the output of knowledge is stopped. Knowledge can also leave the reactor through aging. Some knowledge becomes aged or forgotten whenever it becomes unused for a while. But by using a good knowledge storage system (KMS) you can decrease the amount of knowledge aging or escaping the firm's knowledge base. This is represented in the model by vaporization/leakage of the content through the reactor wall. To prevent the reactor from drying out companies can focus on knowledge creation or knowledge acquisition. Each type of organization has a different preference for this due to their financial resources. But whenever there is too much input and not enough output you run the risk of overflowing your reactor with knowledge. More knowledge will become forgotten or aged when there is no sufficient KMS present allowing the company to handle the increased knowledge base. Whenever companies find that the output is not satisfactory they can use the process of identifying knowledge gaps to increase the input. In the pharmaceutical industry there is a preference of using knowledge acquisition because of the speed, ease and costs that are bound to this knowledge process. There still remains one problem with the newly acquired or newly created knowledge which was not solved in the bathtub model. Mostly, just a few employees receive the knowledge from internal or external sources. It needs to diffuse through the firm to make it part of the firm's knowledge base. Knowledge distribution and knowledge sharing help in this diffusion process which is represented by a stirrer in the model. It will not allow increasing the output of knowledge application but it will increase the speed of the diffusion through the company. Dependent on the phase in which a pharmaceutical firm is active it uses a different kind of knowledge transfer process.

If we look closely at this model we can understand why increasing the innovation performance of a pharmaceutical industry is so complex. Just focusing on one simple knowledge process will not result in a steady situation. This has to be done by carefully balancing all the processes keeping in mind the different approaches for different organizations in different R&D phases. This also shows that every pharmaceutical company needs to be active in all knowledge processes in order to create a

minimal innovation output. This was also found during the interviews. The interesting part of this model is that the creation/acquisition ratio is influenced by financial resources and that the distribution/sharing ratio is influenced by R&D phase. The other three knowledge processes are not yet understood to say what determines this activity.

5.4. Other findings

Some other conclusions could be drawn from the results of this thesis. A first interesting finding was the actual benefits the scientific cluster of the LBSP has. The LBSP is found to be beneficial for contacts between companies in the park. During the interviews managers mentioned that they were attracted to this park because of the lack of contacts with LSH companies they had in the former location. It would be expected that because of the internet companies can reach out to each other as easily as passing by. However, the geographical location does seem to play a certain role of lowering the bar for approaching another company. It definitely decreases the transportation costs which is beneficial for any company who is in need of services. Another interesting result is that most of these connections were quite informal. Employees switch companies very often within the LBSP and thus a large network has been created surpassing the company boundaries on an informal basis. But a disappointing fact is that most of these informal connections only resulted in knowledge transfer about non research related topics. The topics addressed at these informal conversations were more about handling the regulatory organizations or how much to pay for employees. But true open innovation with collaborations on discovery and development of drugs on certain areas were not mentioned by the managers during the interviews. Much can be improved to increase open innovation in the LBSP.

Another interesting finding is the difficulties with the Leiden TTO. There is a unique opportunity within Leiden of companies meeting universities. However, it is found that the knowledge institutes would like to see more interaction with the pharmaceutical companies and think they could be more of service for start-up companies. It was mentioned by the manager of company 15 that LURIS might be able to provide certain services beneficial for the science park. It was already found that other initiatives are being organized to reach the similar result. The manager of company 16 spoke of a platform where researchers can pitch their findings and rich pharmaceutical companies can spend small grants to stimulate these researchers to continue finding results for a short period. LU is now thinking of setting up a similar platform. The grants can then be used to pay graduate students to work for a short period for creating more results for the invention. Whenever the results keep on being successful it can then be licensed to the interested company. This formula, which has been proven successful, allows companies to have more reliable results of the new techniques and allows universities to attract money for continuing research on the area of the technology.

A more general result of this thesis is that the emphasis of innovation in the pharmaceutical industry lies more on tacit knowledge than on explicit knowledge. Dunne and Dougherty draw the same conclusion from their research and said that this was due to the multidisciplinarity of this industry (Dunne and Dougherty 2011). However, the underlying result was that distribution is needed in a later phase of the R&D process. Not so many companies have developed their products into this phase yet and that is why less focus on explicit knowledge is measured. It is true that the pharmaceutical industry is a multidisciplinary field but not likely to be the reason why tacit knowledge is more often used by pharmaceutical companies. It would also seem as if knowledge storage is not considered so important in the pharmaceutical industry. It might be that this would be a point where the pharmaceutical industry really would need to improve, to see whether they can create better KMS. It can also be that most of the companies not need to focus on it because they already have a good storage system. When looking at the knowledge reactor model storage is proposed important for knowledge losses. This might not appear to be a problem in the pharmaceutical industry and that is why it was not discovered often during this research.

IP strategy was mentioned in the literature to be an issue for small biotechnology companies. They have less employees and thus less time to focus on patenting important techniques and inventions. But in order to protect the drug pipeline and to attract VCs IP is very important. During this research no problems with IP strategy were discovered. Many companies were combining the patenting strategy with publishing in scientific journals. Also the choice of knowledge creation or knowledge acquisitions did not seem to focus of the IP strategy. Before we mentioned that knowledge institutes are using science as a motivator and no monetary awards. Similar results are found for public

and private companies. Privately owned pharmaceutical companies are using science more as a motivator and do not have the financial resources to pay their researchers in special awards. Publically owned companies have stocks on the market and sometimes a larger spending rate. This allows them to give monetary awards like stock options.

A final remark should be made about the categorization of the companies. In the introduction it was attempted to create a distinction between certain pharmaceutical companies. Already then it was found that a clear distinction is difficult because lately two industries (biotechnology and pharmaceutical) have been merging. The same difficulty is found when the managers are asked to explain their definition of pharmaceutical, biopharmaceutical and biotechnology companies. All were able to clearly distinguish the pharmaceutical companies because these are the large old companies with a large product portfolio. However, the distinction between biopharmaceutical and red biotechnology firms was so thin that it can be concluded that there should be no distinction between these companies.

6. Conclusion

The pharmaceutical is reducing in innovation performance indicated by the reduced amount of medicines which are being approved for market introduction. There are still many untreatable diseases thus the output for new medicines is still wanted. Managers therefore have to look deeper in their organizations to see what is increasing and what is decreasing their innovation output. In this thesis it was tried to find an answer to the main question as to understand the innovation process of this industry:

"*What are the internal critical success factors for innovation management in the pharmaceutical industry?"*

During this explorative research interviews with managers of pharmaceutical companies were used to collect data. The topics at interest during these interviews were knowledge processes, knowledge network, motivation, company characteristics and innovation performance. It was expected that mostly knowledge would play a role in the innovation process which is eventually confirmed.

By looking at the knowledge processes, the knowledge network, the employee motivation and the company characteristics a distinguish between two R&D phases, and three types of pharmaceutical organizations involved in R&D were found. The two R&D phases, learning phase and confirming phase, correlate with the activity in certain clinical trials. In the *learning phase* a company is focused on a personalized KM strategy where knowledge sharing and knowledge application is more important and patients can be used as a motivator. When companies continue to move products in their drug pipeline explicit knowledge becomes more important and so knowledge distribution becomes an important knowledge process focus point. Also the personalized KM changes into a codified KM during the so called *confirmation phase*. This last phase exists because pharmaceutical products are forced to walk through these long clinical trials.

The organizations can be split into large pharmaceutical firms, SMBEs and knowledge institutes which seem to coincide with the *make-or-buy* struggle found in other industries. It is the amount and the source of financial resources which creates the difference between these companies. As a consequence, companies behave differently in areas like the focus on knowledge creation or knowledge acquisitions, the strengths of cooperation with universities and companies and the patient/money/science motivation. However, the fact that both SMBEs and large pharmaceutical companies are still developing many new drugs means that both the innovation theories of Schumpeter are confirmed within this industry and that increase of innovation performance should come from both company categories.

This exploring research now has increased the understanding of innovation management of the pharmaceutical industry enabling to answer the main question of this thesis:

"*What are the internal critical success factors for innovation management in the pharmaceutical industry?"*

It was predicted that knowledge would lay at the heart of innovation management in the pharmaceutical industry and thus influence innovation performance. The knowledge reactor model proposed in Figure 22 confirms this and directly points out the critical factors for the pharmaceutical industry. Companies are forced to choose an approach of focus between knowledge acquisition and knowledge creation due to their financial resources. As a consequence they need different motivational drives for their employees and have a different knowledge network. Another critical factor is the diffusion of knowledge inside a firm. The results show that the phase of R&D determines the most suited knowledge process for knowledge diffusion. Again, knowledge sharing and knowledge distribution have their own preferable combinations with certain motivational drives and connections to universities. These are internal critical factors found during this research but there are probably many still to be found. But because the innovation performance cannot yet be measured accurately nothing can be said on how to increase the drug output of the pharmaceutical industry. Thus this thesis does not contain a solution for the problem addressed in the introduction. This thesis sets a good foundation from which further research can be performed to see how these critical factors interact with innovation performance to see how the problem of reduced drug output can be solved.

7. Final remarks

7.1. Implications

7.1.1. Scientific implications

This thesis provides a better insight into the innovation management of the pharmaceutical industry which has its implications for the scientific community and for the managers of pharmaceutical firms. It has been mentioned by many that knowledge management and absorptive capacity are very important for this industry. This thesis connected these two branches of innovation management by breaking up knowledge management into seven different knowledge processes. Absorptive capacity is focused on acquiring external knowledge and then internalizing it into the company with knowledge sharing, storing and distribution. The fact that the knowledge network was found important for all sorts of companies confirms the importance of knowledge acquisition but also the model of KM proposed in chapter 2.2.2.

Some important trends were found during this explorative research into innovation management in this specific sector. The R&D process of the pharmaceutical industry can be combined into two phases (learning and confirming phase) which seem unique for this industry. Only in this industry a project takes so much time and requires so much expensive research until first revenues can be earned. Over time a company walks through these phases while products go through different clinical trials. Eventually the focus changes from tacit knowledge sharing to explicit knowledge distribution. This change of focus seems to be similar to the change of personalized an codified KM (Hansen, Nohria et al. 1999). These findings were confirmed by the factor analysis, which need to be interpreted carefully due to the low reliability.

Also two different innovation strategies were found in this sector which makes a distinction in focusing on external knowledge acquisition or internal knowledge creation. This make or buy decision has been found in many other industries and is now confirmed in this industry as well. It was made possible connect these findings with the Schumpeter I and II theories which now allow us to use other findings about these theories as well.

Additionally the knowledge reactor model was proposed which fits the results of this thesis. This model explains the choices pharmaceutical companies can and have to make and where the bottlenecks lie within their innovation management. It might be that this model can also be applied to other industries meaning that the same distinction is applicable between large and small companies and to see whether companies walk through the similar two R&D steps of learning and confirming. Scientists active in the innovation management area can look at the knowledge reactor model and try to expand it by looking at other internal critical factors like formalization and creativity.

7.1.2. This research also showed that the R&D in the pharmaceutical industry is led by four major motivations; patient motivation, money motivation, scientific motivation and intrinsic motivation. It is interesting to see what drives pharmaceutical researchers. Motivational theories can then be compared to this finding. Managerial implications

This research also contains implications for the managers of pharmaceutical companies. The results give a guiding map for companies to show what factors are important during what stage of discovery and development. It can help executives and entrepreneurs to write or adjust their business plans when working in the pharmaceutical market. For example, managers now know that over time they should shift the focus of tacit knowledge to explicit knowledge and have to be prepared for this transition by creating a good knowledge management system.

Another important aspect is the difference in organization for this sector. If a company is a SMBE without any products on the market it must focus on knowledge acquisition and protection of this knowledge. Universities can provide in cheap research. Patient groups can be used for extra motivation of employees by choosing ambassadors and having presentations of patients in the company to point out the importance of their work. It is wise for these companies to settle in an environment where many other companies in the area of research are located because then knowledge collaborations are easily made. Also, the costs of transportation for certain products and specialized

services can then be reduced. Incubator facilities, like the Biopartner building, are an excellent example of these kinds of companies.

However, large pharmaceutical companies need to look for different aspects. Their focus on diseases is so large that patient motivation will be of no use. Instead, intrinsic motivation, financial and scientific rewards should be used to keep performance at a high level. Knowledge creation is a better focus point for these companies because they have the resources for it. Eventually the results will show a large competitive advantage which is good for the continuation of the business. However, large pharmaceutical companies should be aware of scientific development and stay in contact with universities as no to miss any radical innovations. Some strengths were summed up and weaknesses of the different kind of organizations which can help managers be prepared for these occurrences.

7.2. Reflection

We have seen the results and the conclusion which were found during this explorative research. It can be said that this research has had some successes but also some weak points.

First of all we were able to see and learn many things about the pharmaceutical industry. The fifteen companies which were interviewed were very diverse and each manager allowed having a deeper look into the managerial aspects of innovation in a pharmaceutical company. Each conversation was very open and therefore the managers were able to answer very detailed and argue why they answered certain questions on knowledge processes, knowledge network and motivation. It is because of the depth of these interviews that so many findings were wound.

However before the research was started the focus was already narrowed down to a certain extend. It might be that the approached of each interview was without any prepared focus points that the managers would have come up with many different potential critical factors. But this would have required much more time during the interviews and many more interviews which were simply not possible for this thesis. Even though some directions were chosen upfront it is still believed that the topics discussed during the interviews are actually of great importance because of the confirming interviews.

A disappointing fact during this explorative research was the low response rate on the questionnaire. The questionnaire was designed to verify findings during the interviews but also to measure formalization and a creative team climate. A low response rate is to be expected during research. However it was expected that the response of employees to be low and not the response of different kinds of companies to be low.

Finally, a lot of time and effort was put into reading existing scientific literature on innovation management and innovation performance in the pharmaceutical industry. However, not so many successful and useful results were found during this study. First, the focus of this thesis was put on creating hypotheses and then testing these hypotheses during the research. However, as it turned out there was not so much known about the pharmaceutical industry and all research results were very scattered without any overlap. If it was possible to do it all again less time would have been spent on examining the literature and creating hypotheses and more time would have been spent on retrieving responses on the questionnaire.

7.3. Recommendations further research

Although this explorative research has increased understanding there is still much to be learned about innovation management in the pharmaceutical industry. The data was gathered from fifteen companies within the Leiden Bio Science Park which resulted in the knowledge reactor model. However this model would need to be tested on a large scale with many pharmaceutical companies. From the findings of this thesis it can be predicted that all companies in the pharmaceutical industry will focus on either knowledge creation and/or knowledge acquisition because the input of new knowledge is one of the most important things for the continuation of innovation. Additionally it can be expect that the creation/acquisition ratio is influenced by the amount of financial resources a company has. It can also be expected that the two knowledge transfer processes (distribution and sharing) will always be an important focus point for companies dependent on the activity in certain clinical trials. Early clinical activity is more focused on knowledge sharing while further clinical activities is using knowledge distribution more.

One would expect that companies which focus on knowledge acquisition would have a stronger knowledge network. This was not found during this research but not a good measuring tool was used for measuring the strength of the knowledge network. It would be recommended to see if knowledge SMBEs have a better knowledge network or that actually all pharmaceutical companies need to have a large knowledge network. When using a better measurement tool one can perhaps better understand why the TTO is not considered useful within Leiden.

The knowledge networks differed per company during this thesis. From these results it can therefore be predicted that in large scale research SMBEs will be found to have better contacts with organizations. It would be interesting to look into the exact reason behind this to see whether money, origin of the company or the approachability of the SMBEs are the main reason. Additionally it can be predicted that SMBEs will be using more local companies and large pharmaceutical companies will look further away from their settlements.

During the interviews three major extrinsic motivations were found for the pharmaceutical companies. The industry is special because customers are patients which rely very much on the output of the companies. Research employees can be made aware of the customer dependence more than in other industries. It would be interesting to see how the intrinsic and extrinsic motivations are used in other industries compared to the pharmaceutical industry to see if patient/customer motivation really is unique and has a significant input for this industry. From the results of this thesis it can be foreseen that in large scale research will show that large pharmaceutical companies will use patients as a motivator less than SMBES. Large pharmaceutical companies will be more focused on monetary awards and SMBEs are not financially able to do this.

One important aspect which would be of interest in further research is looking into innovation performance. The factor analysis showed some interesting results but must be confirmed with a larger data set. Then relationships between the individual knowledge processes and innovation performance can be analyzed. To see if both Schumpeter I and II theories work for the pharmaceutical industry it would be worthwhile to measure if the differences, like knowledge creation or acquisition and monetary awards or patient motivation, would have significant influence on innovation performance.

It would be interesting to see how all these predictions would hold with companies from other industries as well. Although the confirming phase would seem rather unique for the pharmaceutical industry because of the long clinical trials, it might be that in other industries such a long confirming phase is also required. Additionally, separation between small and large companies can be found in any industry with perhaps the same knowledge process focus points, similar knowledge networks and using the same motivational drives for their research employees.

Because of the low response rate on the survey nothing could be said about formalization and creative team climate. It is recommended to look into these aspects to see if the strategies and the phases would differ on these kinds of aspects. The questionnaire of 0 could be used. Similar steps could be undertaken as was done in 0.

8. Acknowledgements

I would like to thank the people of the Leiden Bio Science Park foundation for allowing me to do my research within the LBSP and Nettie Buitelaar in particular. They provided me with many important connections within the pharmaceutical companies. It is because of them that I had a high response rate on the exploiting interviews and thus was able to gather these high quality data. They allowed me to work within their office where I was able to work undisturbed on my thesis and to discuss any topics or difficulties with them as well. Also my thanks go out to Dr. R.M. Verburg for his time and effort put into guiding my graduation research, especially for the times he had to travel to Leiden for meeting me. Additionally, I would like to pay my gratitude to all the managers with whom I had the pleasure of asking questions to for my research. The interviews were very informative and approachable which made collaboration run smoothly. They all put some time available for me to gather data for my master thesis and I am very grateful for this. Finally, I would like to thank Jiska Kentrop, Martin Das, Cedric Furr and Ferry Koolen for their time and effort into supporting and helping me with the writing of this thesis.

Appendix A: Definition of Small and Medium sized Enterprises

Many governments acknowledge the importance of Small and Middle Sized Enterprises (SMEs). Most of the enterprises over the world are SMEs, as can be seen in Table 7. The Netherlands counted 629,063 SMEs overshadowing 1,637 large firms in 2012 (EU 2012). This means that in the Netherlands over 99% of the firms registered are from the category SME in 2012.This is to be expected considering that many enterprises like bars, restaurants and shops belong to the SME group. Larger firms account for more income and employment. Therefore society benefits greater form large enterprises as from SMEs. However, in 2012 65.4% of employment and 63.2% of the added value came from the SMEs proving that the SMEs have a critical influence on the Dutch economy (EU 2012).

Table 7 Data suggesting the importance of SMEs for national or regional economy. Data might be outdated due to the sources used, however still emphasize the importance of SMEs.

Country	SMEs contribute…	Reference
Australia	96% employment	(Desouza and Awazu 2006)
Britain	99% of firms, 50% jobs	(Gray 2006)
China (Jilin region)	99.5% of firms, 47% of economy, 70% employment	(Dong 2010)
China	99% of firms, 60% total output industry, 75% urban employment	(Dong 2012)
European Union	66% employment	(Dong 2012)
	99.8% of firms, 60% GDP	(Turner, Ledwith et al. 2012)
Germany	90% pharmaceutical firms	(Eppinger and Vladova 2013)
India	8.7% GDP, 45% manufacturing output, 40% merchandise[1]	(Nagayya and Tirumala Rao 2013)
Ireland	25% turnover, 14% economy	(Turner, Ledwith et al. 2010, Turner, Ledwith et al. 2012)
New Zealand	35% economic output	(Desouza and Awazu 2006)
The Netherlands	99.7% enterprises, 65.4% employees, 63.2% added value	(EU 2012)
Turkey	99.5% firms in the industry, 64% employment, 36% added value	(Bozbura 2007)
United Kingdom	95% businesses, 65% workforce, 25% GDP	(Desouza and Awazu 2006)
United States	60% employment	(Dong 2012)

To support these small sized firms government therefore has to stimulate and invest into these firms to increase employment, which is a topic of great interest considering the financial crisis going on in Europe (Nagayya and Tirumala Rao 2013). To remain fair in subsidizing systems a clear definition of a micro, small, medium and large sized enterprise is needed. It is for this reason that the EU has made a user guide for participating countries which defines the different sized enterprises. In Table 8 these guidelines are summarized. The size of the enterprise is dependent on three variables; *employees*, *turnover* and *balance sheet total*. The employee boundary is a hard ceiling meaning that in case a company passes the amount found in the table it automatically alters in enterprise size. The turnover and balance sheet total are soft boundaries. In case only one of the two ceilings is crossed the enterprise will not alter of enterprise size. However, in case both of these ceilings are crossed the enterprise will go up in enterprise size regardless of the amount of employees. The Netherlands uses the same definition of SME because it is part of the EU and thus works with European funding.

Table 8 EU guidelines for SME (EC 2003).

Size Enterprise	Head count	Turnover	Balance sheet total
Micro	<10	≤€2 million	≤€2 million
Small	<50	≤€10 million	≤€10 million
Medium	<250	≤€50 million	≤€43 million
Large	From 250 and over	>€50 million	>€43 million

The EU definition of SMEs is just one point of view. In the scientific literature many definitions and categorizations of SMEs are to be found. Almost all scientists focus solely on employees count and not on turnover or balance sheet numbers. This is probably a consequence of the

[1] Facts are of Small and Medium Sized Manufacturing Enterprises in India

difficulty of acquiring turnover and balance sheet numbers, especially when most of these SMEs are privately owned. Some results of SME literature categorization can be found in Table 9. As can be seen the ceiling of 250 is mostly used separating SMEs from large enterprises. There is less consistency on the sub categorization of the SMEs although the EC definition seems to be the most commonly used (Table 8). It is for this reason that in this thesis the EC definition will be used in categorizing micro, small and medium enterprises with the employee ceilings of 9, 49 and 249 respectively. Also, these EC guidelines are used by the Dutch government, which is the area of interest for this thesis. Turnover and balance sheet numbers will not be used for size indication because these numbers are difficult to acquire. Additionally many SMBEs do not even sell any medicines on the market because their products are still in the clinical trials. This means that they do not have normal turnover numbers.

Table 9 Categorization of enterprise sizes commonly found in literature.

Employees count for groups	**Reference**
EC definition; Micro is <10, Small is <50, Medium is <250, the rest is Large	(Bozbura 2007, Radzevičiene 2009, Carr 2010, Turner, Ledwith et al. 2010, Turner, Ledwith et al. 2012, Teirlinck and Spithoven 2013)
SMEs are smaller than 500 employees	(Freel and Robson 2004, Narula 2004, Wolf, Kaudela-Baum et al. 2012)
SMEs are smaller than 250 employees	(Egbu, Hari et al. 2005, Hutchinson and Quintas 2008)
SMEs are smaller than 100 employees	(Desouza and Awazu 2006)
SMEs are between 10-499 employees	(Håkonsson, Burton et al. 2012)
SMEs are between 5-250 employees	(Spiegel and Marxt 2012)
SMEs are between 20-250 employees	(Guzmán, Serna et al. 2012)
SMEs are between 25-250 employees	(Keizer, Dijkstra et al. 2002)
SMEs are between 2-100 employees	(Bagnoli and Vedovato 2012)
SMEs are between 21-99 employees	(Terziovski 2010)
Small is 10-49 employees and Medium is 100-499 employees	(Van de Vrande, De Jong et al. 2009)
Categorized into 20-49 employees, 50-99 employees and 100-200 employees	(Holm and Poulfelt 2003)

Appendix B: What is the Leiden Bio Science Park

The area of research is the Leiden Bio Science Park (LBSP), located in the Netherlands. Therefore some background information will be given about the population region for it might influence some outcomes of research. First the Dutch pharmaceutical industry is shortly described. Afterwards the Dutch cluster market is briefly looked into. Finally, the LBSP firms and park activities are mentioned finishing the environment description of the investigated population.

B.1 Dutch pharmaceutical industry

The Dutch government has been focusing their economic policy on the so called 'top sectors' (in Dutch: 'Topsectoren') (Dutch National Government 2012). In these top sectors it is tried to stimulate growth by cooperating with universities, companies and local government. One of these nine top sectors is the Life Sciences and Health (LSH) area, which corresponds to the Dutch pharmaceutical and biotech industry. The goal of the national government for this LSH top sector is to be in the top three of fastest growing countries for pharmaceuticals in Europe in 2025. Another wanted result would be that 10% of the revenues from this industry would be reinvested in new R&D for Dutch LSH firms. This will create jobs for Dutch employees and also positively influence the Dutch economy. Currently the LSH only provides 3% of the Dutch revenues which they want to increase (Dutch National Government 2012). In Figure 23 one can see that in 2011 66% of the Dutch LSH firms were engaged in R&D activities.

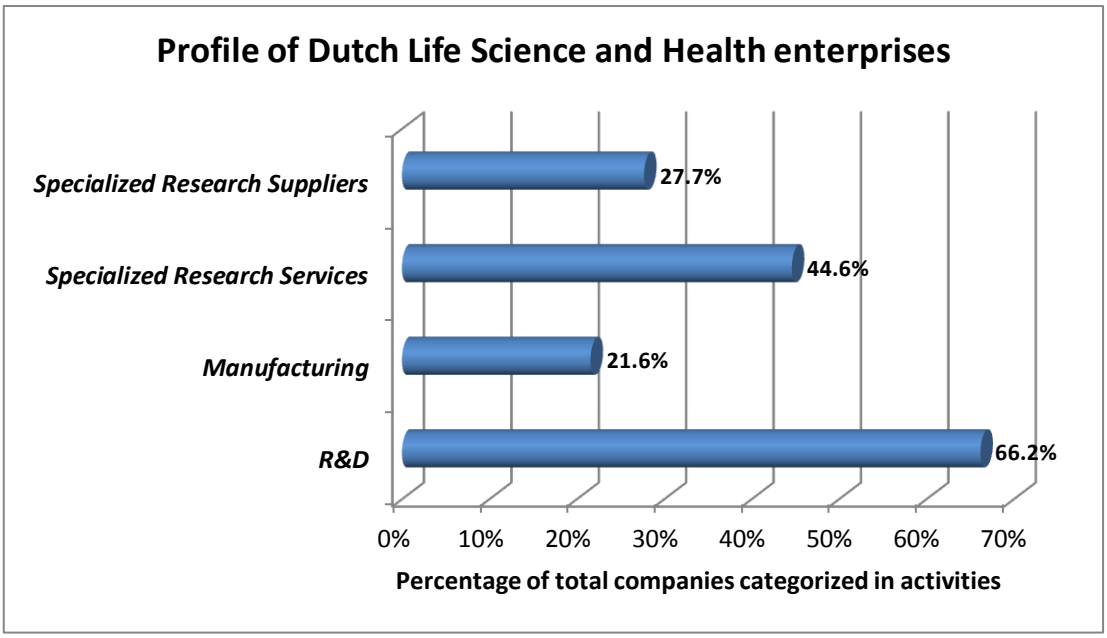

Figure 23 Dutch Life Science and Health enterprises categorized into different activities performed at the firm in the year 2011. (The Decision Group 2013)

The Decision Group has been investigating the Dutch LSH industry since 2008. During these years they found a growth in both LSH firms and employee count (see Figure 24), especially for the micro sized enterprises. However, the large firms have decreased their employees in the Netherlands. MSD is a good example of these recent developments. In 2010 almost 2200 employees were fired in the R&D department of MSD in Oss (NOS 2010). Fortunately this amount was reduced to 500 after negotiations. In the case of Solvay the outcome was less fortunate. Abbott, the owner of Solvay, cut off 3000 jobs. Many of these fired personnel seized the opportunity to start new companies which explain the rise of SMEs and SME employees (Raaphorst 2012). This was anticipated by many professionals whom have been surveyed by The Decision Group. Almost 60% of the respondents expected positive effects when large firms would disappear from the LSH clusters. They anticipated a growth in number of companies and a stimulation of innovation (The Decision Group 2012).

Another research, performed by NautaDutilh, looked into the biotechnology sector of the Netherlands (Kerkhof 2012). They found that most of the Dutch biotech companies (65%) have the strategic goal to develop medical products up to phase I or II and from that point joining in an alliance

with a large pharmaceutical company. An early take over by large pharmaceutical firms was the strategic goal of 17% of the biotech companies and only a small amount considered a strategy of IPO. This means that many small biopharmaceutical companies are looking for an eventual buy out or association with large pharmaceutical firms.

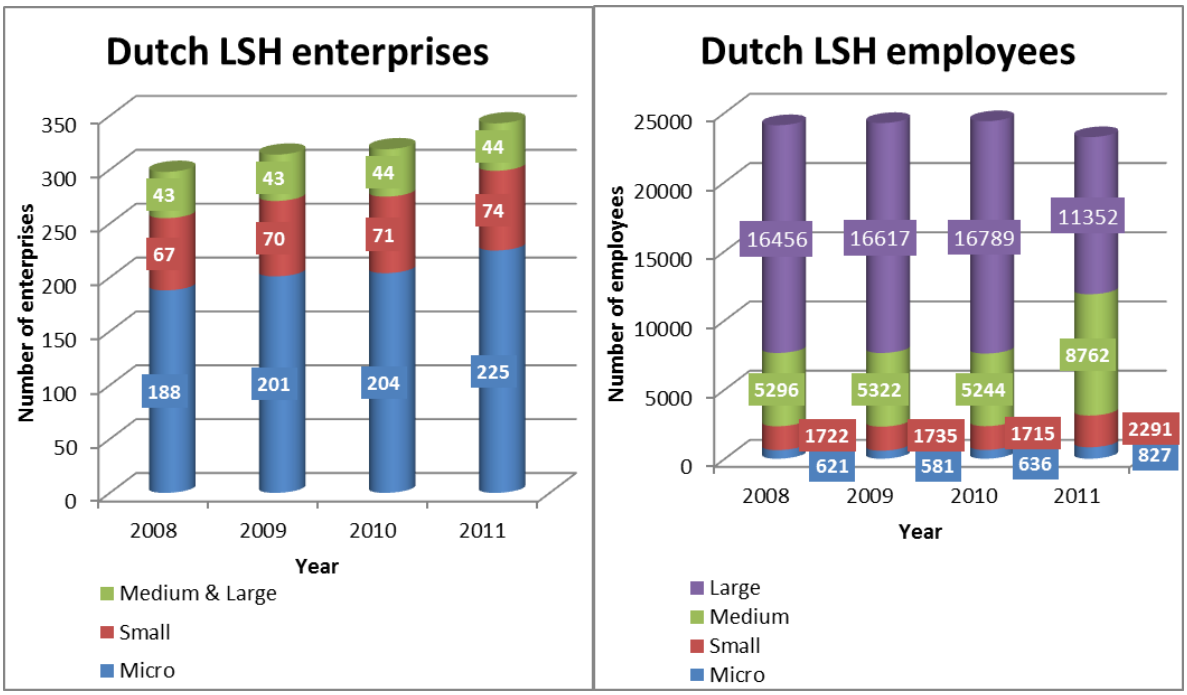

Figure 24 Results from The Decision Group outlook 2013 in the Dutch Life Sciences and Health sector. Left reflects the amount of firms present in the Netherlands. Right represents the total amount of employees working in the Dutch LSH grouped into the firm's sizes (The Decision Group 2011, The Decision Group 2012, The Decision Group 2013).

B.2 Dutch clusters

The Netherlands counts eight LSH clusters (Topteam Life Sciences & Health 2011) of which only five contained a campus site. Most of the LSH clusters campuses are focused on technology like the High-tech campuses in Eindhoven and Enschede. The Medical Delta cluster, however, is one of the largest LSH clusters of the Netherlands. It contains many important biopharmaceutical firms (LBSP, Technopolis Delft, Biotech campus Delft, RDM campus). This means that LBSP is in a very active region with a large pharmaceutical network. This would be beneficial considering open innovation, venturing and spin-offs. These external factors all contribute to highly innovative region. More information on these Dutch LSH cluster can be found in Figure 25.

In 2009 Buck consultants started a research into the Dutch campuses which was commissioned by the Dutch Ministry of Economic Affairs (Buck Consultants International on behalf of Dutch Ministry of Economic Affairs 2009, Buck Consultants International on behalf of Dutch Ministry of Economic Affairs 2012). This resulted in a list of campuses which could be categorized into *starting*, *growing* and *adult* campuses in the Netherlands. In 2009 there were only four campuses labelled with the adult status, among which the LBSP. But LBSP could be considered as the largest life science park of the Netherlands. This was confirmed in their follow up research in 2012 where they measured 122 firms and over 5400 employees in the park ranking it the number three campus of the Netherlands. These researchers also concluded that LBSP was also one of the most important campuses of the Netherlands, together with the High Tech Campus (Eindhoven), Kennispark Twente (Enschede), FoodValley (Wageningen), Chemelot (Sittard-Geleen) and Science park Watergraafsmeer (Amsterdam) judged by their open innovation and specific innovation policy.

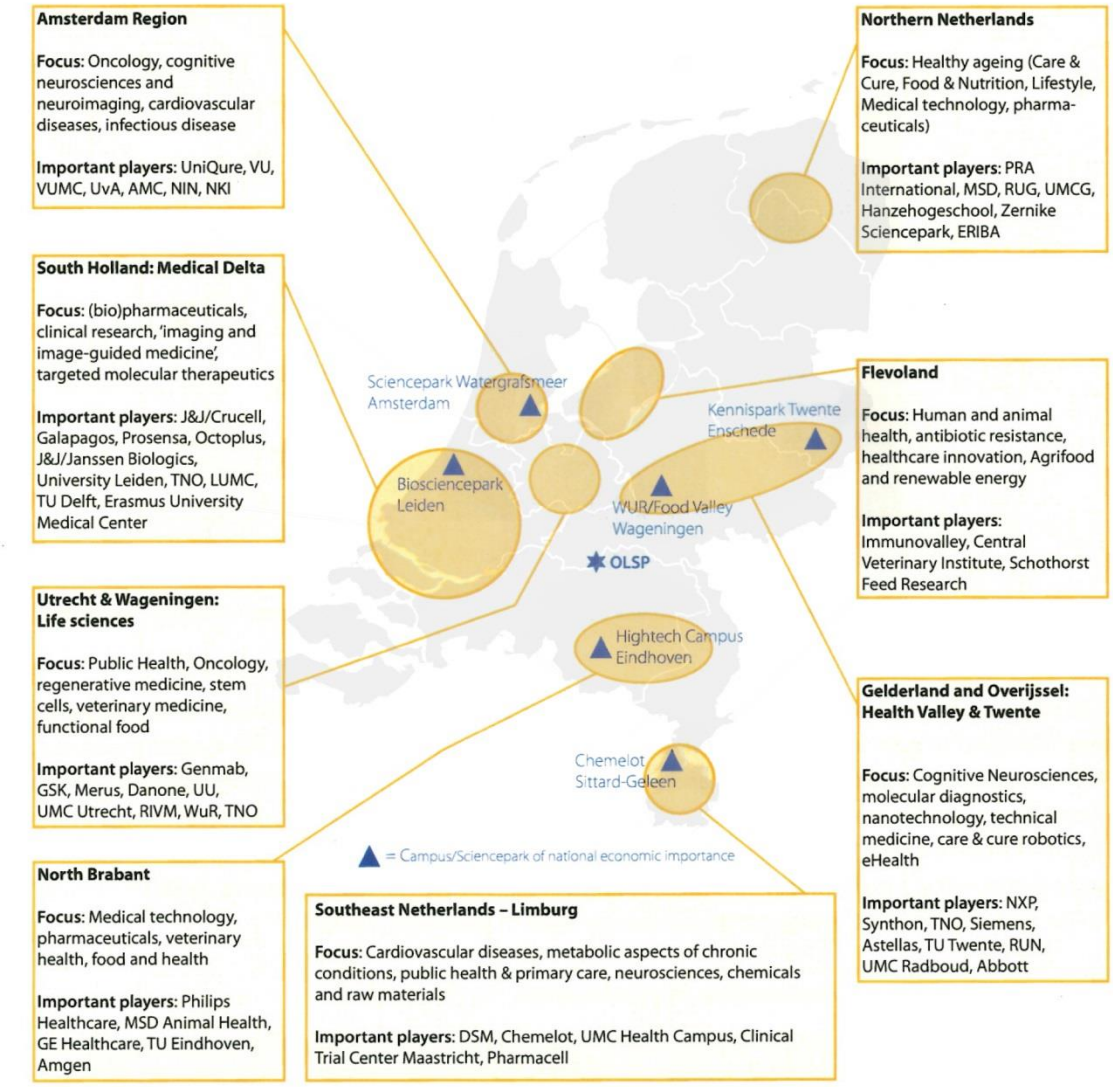

Figure 25 Life science and biotechnology firms clustered in the Netherlands (Raaphorst 2012). LBSP is part of the Medical Delta.

B.3 LBSP outline

The start of Leiden Bio Science Park has been dated on the 4th of April 1984. It was at this moment that the Academisch Bedrijven Centrum was founded, which was the first incubator situated in Leiden. Already the LUMC and Centecor (which later became Janssen Biologics) were located in this area. From this point many new firms were settling in the growing life science cluster. In 1985 already three companies were present in the park. By now 181 firms and institutes are joined in the LBSP in an area of 110 ha. The LBSP even keeps on growing, considering that in 2012 eighteen enterprises have joined the LBSP (Leiden Bio Science Park foundation 2012). Rabobank has looked into the life science deals made in Europe between 2008 and 2011 (Raaphorst 2012). From these top 15 deals, ranging from €132 million to €2,500 million, ten deals originated from Dutch companies and eight of those deals were from companies located in the LBSP. This underlines the importance and the size of this cluster. In 2009 the LBSP was even awarded as the best business park of the Netherlands.

The park is being guided by an organization called Leiden Bio Science Park foundation (LBSPf). This organization is focused on five aspects of the science park in which they try to develop the cluster to a greater potential. These five tasks are; developing LBSP into a complete cluster, creating a favorable environment for LSH companies in R&D, facilitate companies and institutes with infrastructure and house holding, provide with a healthy education and labor market and finally to let all parties collaborate on national and international markets. LBSPf tries to achieve these goals by having close contacts with all the major enterprises of the park. In this way many initiatives have

already started like the monthly science café meetings (for employees), CEO breakfast, a park shuttle bus and the plan of building a Bio Simulation Factory. LBSPf is also actively involved in acquisition of new companies in the science park. One of the most recent successes is the 2012 building of Astellas European Headquarter in Leiden.

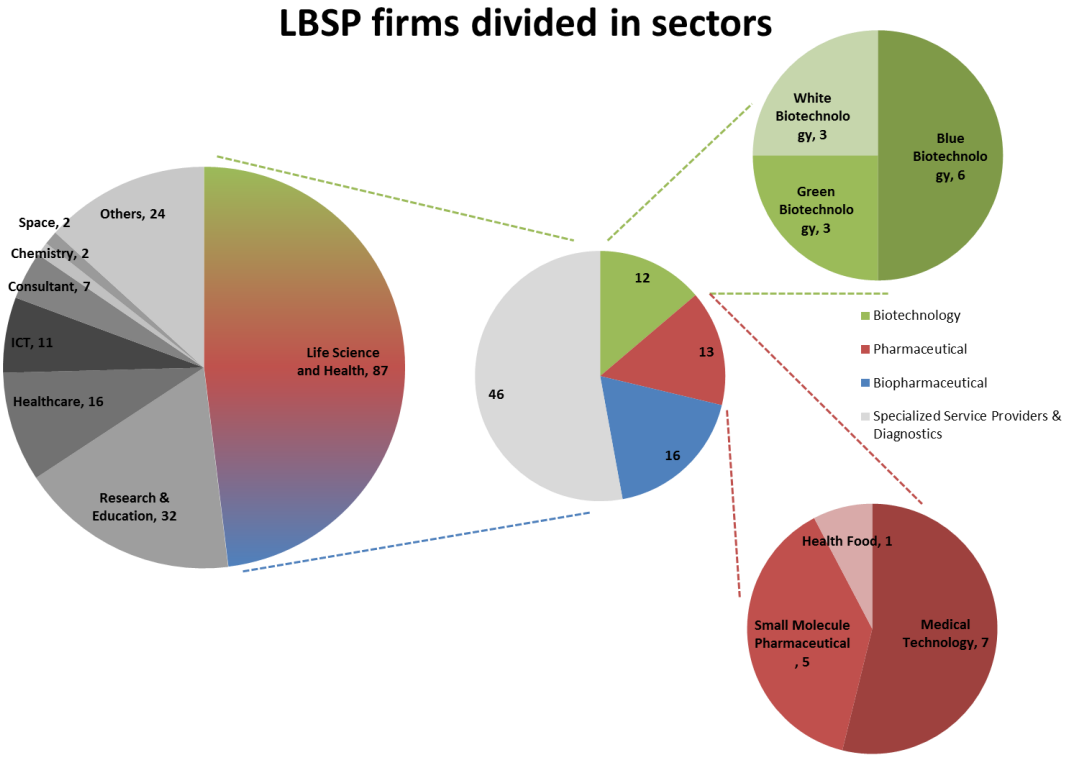

Figure 26 An oversight of all the 181 firms/institutes present in the Leiden Bio Science Park. All are first divided into industry sectors (left) than into Life Science and Health Industries (middle) and finally into the specific areas mentioned in appendix A (LBSPf 2013).

In Figure 26 all the organizations of the LBSP are categorized into different sectors. As expected, most of them are active in the Life Science and Health industry (48%). The second largest industry, represented in the LBSP, is that of research and education (18%). Also some other firms are located in the LBSP because of the clustering of technology and beneficial infrastructure (a train running every five minutes, a shuttle bus for the park, a car sharing program, start-up facilities)

In chapter 1.1 a division was made between pharmaceutical and biotechnology industry. The biopharmaceutical industry (red biotechnology) was an overlapping region. Therefore throughout this thesis a separation of three industries will be made; biotechnology, pharmaceutical and biopharmaceutical companies (Figure 26). Most of the LSH companies located in the LBSP are SSPs for the (bio)pharmaceutical companies. The second largest group is that containing biopharmaceutical firms (or red biotechonology) counting 20 companies. Rabobank also looked into the largest innovative biopharmaceutical firms (Raaphorst 2012). From the top 15 largest Dutch biopharmaceutical firms nine are located in the LBSP (ISA Pharmaceuticals, Galapagos, Octoplus, HAL Allergy, Prosensa, Pharming, Profibrix, to-BBB and DCPrime). This list was ordered by comparing the activity of their drug pipelines. This means that the LBSP biopharmaceutical group makes an ideal representation of the Dutch pharmaceutical industry both successful and less successful. The target group for this master thesis should contain only firms whom actually are involved in R&D. Therefore companies which have R&D facilities in their departments of Leiden need to be used. This reduces the biopharmaceutical group to 14 enterprises (see Table 10).

LBSP also contains a few classic pharmaceutical companies which are involved in discovery and development of small chemical medicines. However, only three of these companies perform R&D activities in Leiden.

The LBSP does not only remain successful because of their company developments but also because of the educational institutes which create a supply of knowledge and spin-off companies. Within the LBSP the science faculty of the Leiden University is located in which many research institutes are present. One of those institutes is the Leiden Academic Centre for Drug Research (LACDR) which cooperates with many pharmaceutical firms. Another institute of the Leiden University is also partly focused on medical biology. The Leiden Institute of Chemistry (LIC) also has similar areas which have overlap with the interest of discovery in the pharmaceutical industry. Finally, the LBSP contains a University Medical Centre (LUMC) which has had many partnerships within the park throughout the years. One other interesting development worth mentioning is the planning of building a Bio Simulation Factory. This is to train employees in the practical side of Good Manufacturing Practices (GMP). For a relatively small fee companies can train their new employees. Not all of these research and educational institutes truly contribute to the discovery and development of NCEs or NBEs. From the 27 institutes of Leiden only four will be used as target group for this master thesis. These are the LUMC, the LACDR, the LIC and the TNO research institute. Finally LBSP contains a target group of 21 organizations which can be approached for further research. The list of the target group can be found in Table 10.

Table 10 The company or institution names of the eventual target group for this master thesis. All companies are engaged in discovery and development of NCEs within the LBSP.

Areas of industry
Biopharmaceutical enterprises (14)
Pharmaceutical enterprises (3)
Research and Educational Institutions (4)

Appendix C: Summaries of the first two interviews

Two interviews were held with (former) CEO's of pharmaceutical companies. To protect the identity of the managers and the companies we will refer to expert X and expert Y.

Expert X now works within a small company. It is located in one of the incubator facilities of the LBSP called Biopartner, which allows expert X to speak to many other companies. This location within the Biopartner facility allows his company to have many informal knowledge network relations on an informal basis. This knowledge acquisition seems to work very easily with informal interactions like social drinks and hallway conversations. He even mentions that some people have joined in a cooking club or golf club with cross company relations.

Expert Y explained that their company uses a platform technology which can be used on many existing medicines. They are thus focused on acquiring knowledge from outside the company and try to directly connect this information with output of new products made by their platform technology. This interesting connection between knowledge acquisition and platform technology was also referred to in the theoretical framework (Dadfar, Dahlgaard et al. 2013). Although many of their products actually come from outside the company, the not-invented-here syndrome was of no issue, assured expert Y. Another form of knowledge acquisition mentioned by expert Y, which he described as a success factor, was the diversity of their employees. They have hired many differently specialized scientists whom have their own area of expertise. In this way the company was able to cover many aspects of research understanding more of this complicated industry.

Universities were mentioned in both interviews as an important actor within the innovation cycle. Universities are creative and thus can increase the knowledge acquisition process. However, the universities lack the commercial insight for true innovation, according to expert X. Thus having connections with knowledge institutes can help but is not the only vital input of knowledge. Internal knowledge creation or outsourcing commercial research is essential to create competitive advantage. It was also mentioned that collaboration with these universities can sometimes be difficult because of different rules applied by each TTOs.

The role of formalization was also mentioned during the interviews. Both expert X and Y concluded that informal meetings and communications seemed to be beneficial for the company. One of the companies even refused to hold formal meetings because they believed that every rule put on the researchers would compromise creativity. When formal meetings are held conversation outcomes would be written down and stored which could make any employee vulnerable. This would all decrease knowledge sharing activities, according to expert X

Motivation of employees is hard to manage. But that doesn't mean it is unmanageable within pharmaceutical companies. During the exploring interviews it was found that payments do influence employees in research. When researchers share in commercial successes of the company, employees will try to increase this profit. So from experience payment structure would influence applying knowledge activities. Also managers can influence intrinsic motivation by screening for this motivation in new employees. Expert Y explained that during interviews for new job positions they can look for intrinsically motivated people and thus indirectly manage intrinsic motivation within the company.

Finally it was asked how expert X and Y would try to assess innovation performance within the company. Both agreed to the fact that innovation is hard to be measured, especially in young pharmaceutical companies. One suggested that the product pipeline and the grants appointed to the company would be a good indicator. Products in the pipeline suggest that successful innovation has proceeded. The more clinical trials have started in a shorter amount of time, the higher the innovation performance. Also the acquisition of grants is related to innovation performance. Expert Y explained that these two, sponsors and pipeline products, reinforce each other. Sponsors for these kinds of drugs will only invest when they see performance of products. And when more money has been acquired more research can be to prove the performance of the new drug. Another suggested measure was the profitability of the company. However this is difficult to apply for all companies considering that many companies do not have any sales yet because their drugs have not been approved for the market.

Appendix D: Methods and results of questionnaire

D.1 Methods questionnaires

After the interviews the managers were asked to send a questionnaire to one average research team. The reason for these questionnaires was to collect more quantitative data which could be used for confirming certain findings of the interviews and to create scales for further research on this area. The variable measured in the questionnaires can be divided into dependent, independent and control variables. Each will be discussed below. All questions can also be found in Table 11. The questionnaire was estimated to take up between 10 and 15 minutes because it would increase the response.

D.1.1 Dependent variable

As a dependent variable *innovation performance* was chosen. Innovation management is focused on increasing the innovation performance of the company. The nine items mentioned in chapter 3.2.5 were used as dependent variables. The answers given by the managers were answers for the company as a whole. This means that the answers were also applicable for researchers within the company.

D.1.2 Independent variables

There were four variables measured during the interviews; knowledge processes, knowledge network, formalization and creative team climate. The *knowledge processes* were measured similar in the questionnaire as during the interviews. Researchers were asked to name the three knowledge processes their company is most focused on. These seven knowledge processes were also measured on a new created five-point Likert scale ("Strongly disagree", "Disagree", "Neither agree nor disagree", "Agree", "Strongly Agree" and "Not Applicable"). For each knowledge process four statements had to be answered. Most of these questions came from scientific literature (Alavi and Leidner 2001, Song, Van Der Bij et al. 2005, Song, Van Der Bij et al. 2006, Rhodes, Hung et al. 2008, Jiménez-Jiménez and Sanz-Valle 2011, Alegre, Sengupta et al. 2013) and some were specially made for this thesis. All these items and their origin can be found in 0. Not all items could be used directly because of different definition of certain knowledge processes. Some items were adjusted to fit the questionnaire style.

The *knowledge network* was measured by asking to value the intensity of relationships with universities (in/out LBSP), LSH companies (in/out LBSP) and other companies (in/out LBSP) similar as questioned during the interviews. Answers were gathered using a five-point Likert scale where the options were "Very weak", "Weak", "Average", "Strong" and "Very strong". The researchers were also allowed to fill in "Not applicable" when no knowledge relationships existed with a certain group of organizations.

Formalization was also measured with a four items scale from scientific literature (Cardinal 2001) with one additional item created for this research. This last question was added because the scale was too much focused on formalization in the research labs and not also outside it. The questions could be answered by using a five point Likert scale with the answers "Strongly disagree", "Disagree", "Neither agree nor disagree", "Agree" and "Strongly Agree". In case the question would not be fitted for the conditions of the researcher they were also able to answer "Not applicable".

Finally the last independent variable was measured called *creative team climate*. This was measure with a scale made by Gilson et al. (Gilson, Mathieu et al. 2005). The same five-point Likert scale was used as that of formalization.

D.1.3 Control variables

In most cases research needs to be performed in ceteris paribus conditions. We have chosen the LBSP location to keep as many conditions constant for all the companies. However, some aspect differed for the organizations which were measured as control variables. Two of these control variable results were already gathered for the company during the interviews, namely the *age* of the company and the *size* of the company. The size was grouped according to the definition given in 0. This definition states that the amount of employees defines the size of the company. For this reason we looked at the employee count of the company in total, working in Leiden in total, working on R&D and working on R&D in Leiden (see Table 11).

During the questionnaire only two other variables had to be measured. One is the *amount of years the researchers was employed* by the company. With this information it can be seen if the person is well enough integrated into the company to answer these kinds of questions. The second control variable is the *job description*.

Table 11 Variables which were measured during this thesis. Most of the results of these variables were gathered during the questionnaire. Innovation performance, size and age were measurement gathered during exploiting interviews.

Dependent variables	
Innovation performance	Drugs in pipeline since 2010 (Preclinical, Phase I, II, III and approved on market)
	External finance since 2010
	Patents filed in 2010
	Scientific articles published since 2010
	Amount of R&D spend in 2012
Independent variables	
Knowledge processes focus	Choose top three processes (adjusted from Weggeman)
	4 items for each knowledge process measured (5-p Likert) (Alavi and Leidner 2001, Song, Van Der Bij et al. 2005, Song, Van Der Bij et al. 2006, Rhodes, Hung et al. 2008, Jiménez-Jiménez and Sanz-Valle 2011, Alegre, Sengupta et al. 2013)
Knowledge network	Intensity of relationships (5-p Likert)
Formalization	5 items scale for formalization (5-p Likert) (Cardinal 2001)
Creative team environment	3 items scale of creative team environment (5-p Likert) (Gilson, Mathieu et al. 2005)
Control variables	
Size	Employee count
	Employee count R&D
	Employee count in Leiden
	Employee count R&D in Leiden
Age	Age of the company
Years employed	Amount of years employed at the company
Job description	Job description

D.2 Results questionnaire

There were twenty responses from six companies on the questionnaire. However, one response was without any answers and thus had to be removed from the dataset before analysis. The nineteen responses contained answers to different newly created scales. Therefore, first correlations between the underlying items were analyzed to see whether the items actually measured a similar underlying factor. Thus for all knowledge processes (*application*, *acquisition*, *creation*, *distribution*, *sharing*, *storing* and *finding gaps*), *creative team climate* and *formalization* scales were checked for reliability with the Cronbach's alfa value. These values were calculated by using SPSS. These are given in Table 12. A good Conbach's alfa would be around 0.7-0.8. Unfortunately only four out of the nine scales reached these requirements. However, because the amount of data was low we cannot actually say many things about this reliability value.

The items of the scales were reduced to one scale by using principle component analysis forcing it down to one factor, even though the reliability was too low to see whether the factors would be formulated in the same direction. These results are also given in Table 12. All were positively correlated after applying reverse coding to the item 2 of the knowledge application scale meaning that all items were defined in the correct direction. No further correlation analysis between these scales and innovation performance could be performed because of the small group size.

	Scale factor	Cronbach alfa
Application		0.496
App1	0.462	
App2	0.419	
App3	0.41	
App4	-0.02	
Acquisition		0.607
Acq1	0.415	
Acq2	0.434	
Acq3	0.321	
Acq4	0.221	
Creation		0.607
Cre1	0.465	
Cre2	0.333	
Cre3	0.367	
Cre4	0.269	
Distribution		0.761
Dis1	0.322	
Dis2	0.362	
Dis3	0.291	
Dis4	0.286	
Sharing		0.588
Sha1	0.376	
Sha2	0.401	
Sha3	0.329	
Sha4	0.371	
Storing		0.672
Sto1	0.335	
Sto2	0.361	
Sto3	0.379	
Sto4	0.33	
Finding gaps		0.811
Gap1	0.278	
Gap2	0.353	
Gap3	0.243	
Gap4	0.351	
Creative team climate		0.713
Team1	0.42	
Team2	0.366	
Team3	0.451	
Formalization		0.871
Form1	0.258	
Form2	0.225	
Form3	0.257	
Form4	0.222	
Form5	0.255	
	Scale factor	**Cronbach alfa**

Table 12 Correlations and Cronbach's alfa values for the scales measured during exploiting questionnaires.

Appendix EScales used for questionnaire

E.1 Introduction

Dear Sir/Madam,

Currently I'm graduating for my master's degree in Management of Technology at the TU Delft. In this thesis I am focused on the pharmaceutical industry. This industry is special in many ways; it has high costs for innovation and product development, high risks in product failure and long project cycles before market introduction can start. But the pharmaceutical industry is also very important for society and therefore the continuation of innovation is needed. That is why my research is focused on innovation performance within this particular industry.

This questionnaire is designed to study different aspects perceived by research employees. With your help I will be able to gain insight into innovation processes within pharmaceutical companies. Therefore I'd like to ask you to respond to the questions honestly. Your response will be kept strictly confidential and used for scientific purposes only. Answering these questions will take up 10-15 minutes.

Thank you very much for your time and cooperation.

Vincent Das
Intern at Leiden Bio Science Park foundation
vincent.das@leidenbiosciencepark.nl

E.2 Control variables

- **Since what years have you been employed at your current company?**
  - Since the year <*number*>
- **Which of the following best describes your R&D job role?**
  - Scientist (junior/senior)
  - Researcher (junior/senior)
  - Research technician (junior/senior)
  - Other <…>
  - Research manager
  - QA manager
  - IT staff

E.3 Knowledge processes

Knowledge is used in many activities within a pharmaceutical company. For this reason I would like to know more about the most important knowledge processes within your company. The 7 knowledge processes, altered from scientific literature, are defined as:

Knowledge application = using knowledge to create new products, processes or services.
Knowledge acquisition = generating knowledge from outside the company (like conferences, consulting and external training).
Knowledge creation = generating knowledge from inside the company (like experimentation, brainstorming and systematic problem solving).
Knowledge distribution = employees impersonally sharing knowledge inside the company (like intranet, shared drive and sending memo's).
Knowledge sharing = employees personally sharing knowledge inside the company (like discussions, formal meetings and coffee brake conversations).
Knowledge storing = writing down knowledge in papers, journals or documents (like repositories, lab journals protocols).
Finding knowledge gaps = localizing unknown areas within the scope of company.

- **From the above mentioned 7 knowledge processes, which 3 are most important for your company? (check 3)**
  - Knowledge application
  - Knowledge acquisition
  - Knowledge creation
  - Knowledge distribution
  - Knowledge sharing
  - Knowledge storing
  - Finding knowledge gaps

- **How much do you (dis)agree with the following statements?**
  <1 Strongly disagree, 2 Disagree, 3 Neither agree nor disagree, 4 Agree, 5 Disagree 6 Not applicable>
  Applying
  - We rapidly respond to technological changes in our industry by applying what we know. (Song, Van Der Bij et al. 2005)
  - Even if we develop a great technology, we probably would not be able to take advantages of it in a timely fashion. (reversed) (Song, Van Der Bij et al. 2005)

- We periodically review our product development efforts to ensure that we have applied the knowledge we have created. (Song, Van Der Bij et al. 2005)
- As soon as we create new knowledge, we try to find applications for it. (Song, Van Der Bij et al. 2005)

Acquiring

- The employees attend fairs, exhibitions and external trainings regularly. (Jiménez-Jiménez and Sanz-Valle 2011)
- We periodically create knowledge through cooperation with industry associations. (Alegre, Sengupta et al. 2013)
- We periodically create knowledge through cooperation with R&D institutions such as universities and technological institutes. (Alegre, Sengupta et al. 2013)
- We periodically do technology acquisitions (patents, equipment, consultants etc.). (Alegre, Sengupta et al. 2013)

Creating

- We do a lot of in-house knowledge generation (experiments, brainstorming). (Song, Van Der Bij et al. 2006)
- We have a high degree of academic qualified employees in the R&D function. (Alegre, Sengupta et al. 2013)
- We position ourselves on the technological front line. (Alegre, Sengupta et al. 2013)
- We have a suitable human resources devoted to the R&D function. (Alegre, Sengupta et al. 2013)

Distributing

- Employees are willing to share their experience and knowledge digitally. (Rhodes, Hung et al. 2008)
- Employees use e-mail or other digital channels to share their knowledge with others. (Rhodes, Hung et al. 2008)
- Knowledge is categorized in the database for use by all company employees. (Rhodes, Hung et al. 2008)
- There are individuals responsible for collecting, assembling and distributing internally employees' suggestions. (Jiménez-Jiménez and Sanz-Valle 2011)

Sharing

- Employees are willing to share their experience and knowledge in person. (Rhodes, Hung et al. 2008)
- The company transfers employee experiences to other employees through informal meetings (coffee break, lunch, elevator or hallway conversations). (Rhodes, Hung et al. 2008)
- The company transfers effective knowledge to employees through internal training, courses and presentations. (Rhodes, Hung et al. 2008)
- There are individuals within the organization who take part in several teams or divisions and who also act as links between them. (Jiménez-Jiménez and Sanz-Valle 2011)

Storing

- We have qualified gathering and information processing systems. (Alavi and Leidner 2001)
- We have a control and revision systems for innovation projects. (Alegre, Sengupta et al. 2013)
- We have feedback systems allowing knowledge created in finished innovation projects to be used in new projects. (Alegre, Sengupta et al. 2013)
- Databases are always kept up-to-date within our company. (Jiménez-Jiménez and Sanz-Valle 2011)

Finding knowledge gaps

- There are individuals within the organization who look into what is known and what is needed. (new)
- There are individuals within the organization who look into the database to look into knowledge gaps. (new)
- Employees are aware of what is known within the company and what not. (new)
- Employees regularly look into databases to prevent double work. (new)

E.4 Knowledge network

- **How would you describe the knowledge transfer between your company and the following organizations?**
  <1 Very weak, 2 Weak, 3 Average, 4 Strong, 5 Very strong>
  - Local universities in Leiden
  - Local life science companies in Leiden
  - Local non-life science companies in Leiden
  - Universities outside Leiden
  - Life science companies outside Leiden
  - Non-life science companies outside Leiden

E.5 Company Culture

- **How much do you (dis)agree with the following statements?**

<1 Strongly disagree, 2 Disagree, 3 Neither agree nor disagree, 4 Agree, 5 Disagree 6 Not applicable>

Creative team environment

- Team members welcome change. (Gilson, Mathieu et al. 2005)
- Team members encourage each other to try new things, even though they might not work. (Gilson, Mathieu et al. 2005)
- Team members are willing to try creative solutions to solve difficult problems. (Gilson, Mathieu et al. 2005)

Formalization

- Many written rules about laboratory procedures exist. (Cardinal 2001)
- We have rules and procedures stating how to perform normal daily activities. (Cardinal 2001)
- There are standard procedures for individual tasks. (Cardinal 2001)
- There is strict enforcement of written rules and procedures. (Cardinal 2001)
- We have many formal meetings and formal discussions. (new)

E.6 Leiden Bio Science Park

The Leiden Bio Science Park is a unique area in the Netherlands where many life science companies are situated closely to each other. Many things happen on the park between companies which stimulates open innovations.

- **How often have you attended the monthly Life Science Café meetings in 'De Stal'?**
  - Never
  - 1-2 times
  - 3-5 times
  - 6-10 times
  - Over 10 times
- **If you ever have attended these meetings, what was your main motivation?**
  - The opportunity to learn from presentations
  - The opportunity to speak to other companies informally
  - Because co-workers were going
  - Because of the free drinks
  - Not applicable
  - Other reason

What do you miss in the Leiden Bio Science Park considering innovation and knowledge processes? If there is anything you would like to share or add which you could not mention before comment in here.
<open box>

E.7 Closing remarks

Thank you for putting your time and effort into answering this questionnaire. Your collaboration for my graduation project is very much appreciated.

Vincent Das
Intern at Leiden Bio Science Park foundation
vincent.das@leidenbiosciencepark.nl

Appendix F Coding of the interviewed companies

	Preclinical	Phase I	Phase II	Phase III	Selling	Size	Sort of company	Category of company	IP strategy	Age	Location	International
Company 1	Yes	No	No	No	No	Micro	Private	Biotechnology	Publishing	Young	Elsewhere	No
Company 2		Yes	No		Yes	Large	Public	Biopharmaceutical		Old	Elsewhere	Yes
Company 3	Yes	Yes	Yes	No	No	Medium	Public	Biotechnology	Publishing	Young	Biopartner	No
Company 4	Yes	Yes	No	Yes	Yes	Large	Private	Biopharmaceutical	Publishing	Old	Elsewhere	Yes
Company 5	Yes	Yes	No	No	No	Small	Public	Biotechnology	Both	Young	Biopartner	Yes
Company 6	Yes	No	Yes	No	No	Small	Private	Biotechnology	Patenting	Young	Biopartner	No
Company 7		Yes	Yes	Yes	Yes	Large	Public	Pharmaceutical	Patenting	Old	Elsewhere	Yes
Company 9	Yes	Yes	Yes	No	No	Large	Public	Pharmaceutical		Young	Elsewhere	Yes
Company 10		No	No	Yes	No	Large	Public	Biotechnology	Publishing	Young	Elsewhere	Yes
Company 11	Yes	Yes	No	No	No	Micro	Private	Biopharmaceutical	Patenting	Young	Biopartner	No
Company 12	No	No	No	No	No	Medium	Public	Pharmaceutical	Patenting	Old	Elsewhere	Yes
Company 13	No	No	No	No	No	Large	Institute	Biopharmaceutical	Publishing	Old	Elsewhere	No
Company 14	No	No	No	No	Yes	Small	Public	Biopharmaceutical	Both	Old	Elsewhere	No
Company 15	No	No	No	No	No	Large	Institute	Pharmaceutical	Publishing	Old	Elsewhere	No
Company 16	No	No	No	No	No	Large	Institute		Publishing	Old	Elsewhere	No

Table with all the coded variables found for the companies interviewed for this thesis. The order of companies was the order in which the meetings were held and are therefore randomized. During the interview of company 8 it was found that it did not fit the profile of interest and thus the data was not used. The clinical phases were coded whenever a company had a certain drug in that phase. The size was determined on behalf of the employee count (see appendix B). The category of company was asked to the manager during the interview. IP strategy was chosen by comparing the amount of patents filed and scientific publications sent to journals. Age was split into young (under 15) and old companies 15 and older). Sort of company, location and internationalization were found on the company websites.

Appendix G : Spearman correlation matrix of the codes used for the companies

Correlations

			Product in preclinical phase	Product in clinical phase 1	Product in clinical phase 2	Product in clinical phase 3	Selling company	Size category of the company	Institute or company	Private or public company	Category of company	IP strategy	Older or younger as 15	Situated in Biopartner	International company
Spearman's rho	Product in preclinical phase	Correlation Coefficient	1.000	.714**	.598*	.378	-.076	-.411	-.683*	-.478	.570	.128	-.845**	-.598*	-.239
		Sig. (2-tailed)	.	.009	.040	.226	.815	.185	.014	.193	.067	.708	.001	.040	.454
		N	12	12	12	12	12	12	12	9	11	11	12	12	12
	Product in clinical phase 1	Correlation Coefficient	.714**	1.000	.258	.411	.251	.000	-.452	.069	-.087	.211	-.289	-.411	-.417
		Sig. (2-tailed)	.009	.	.373	.145	.386	1.000	.104	.840	.776	.490	.317	.145	.138
		N	12	14	14	14	14	14	14	11	13	13	14	14	14
	Product in clinical phase 2	Correlation Coefficient	.598*	.258	1.000	.189	-.026	-.139	-.389	-.069	.134	.148	-.447	-.189	.043
		Sig. (2-tailed)	.040	.373	.	.519	.930	.635	.169	.840	.662	.630	.109	.519	.884
		N	12	14	14	14	14	14	14	11	13	13	14	14	14
	Product in clinical phase 3	Correlation Coefficient	.378	.411	.189	1.000	.440	.401	-.330	.179	-.142	-.222	.000	.050	-.411
		Sig. (2-tailed)	.226	.145	.519	.	.115	.155	.249	.599	.644	.466	1.000	.865	.145
		N	12	14	14	14	14	14	14	11	13	13	14	14	14
	Selling company	Correlation Coefficient	-.076	.251	-.026	.440	1.000	.248	-.302	.125	-.270	.162	.564*	.364	-.342
		Sig. (2-tailed)	.815	.386	.930	.115	.	.374	.275	.699	.350	.597	.029	.183	.211
		N	12	14	14	14	15	15	15	12	14	13	15	15	15
	Size category of the company	Correlation Coefficient	-.411	.000	-.139	.401	.248	1.000	.442	.483	-.477	-.441	.523*	.609*	-.405
		Sig. (2-tailed)	.185	1.000	.635	.155	.374	.	.099	.111	.084	.132	.045	.016	.134
		N	12	14	14	14	15	15	15	12	14	13	15	15	15
	Institute or company	Correlation Coefficient	-.683*	-.452	-.389	-.330	-.302	.442	1.000	.	-.295	-.486	.468	.302	.468
		Sig. (2-tailed)	.014	.104	.169	.249	.275	.099	.	.	.306	.092	.079	.275	.079
		N	12	14	14	14	15	15	15	12	14	13	15	15	15
	Private or public company	Correlation Coefficient	-.478	.069	-.069	.179	.125	.483	.	1.000	-.273	.000	.239	.250	-.478
		Sig. (2-tailed)	.193	.840	.840	.599	.699	.111	.	.	.391	1.000	.454	.433	.116
		N	9	11	11	11	12	12	12	12	12	10	12	12	12
	Category of company	Correlation Coefficient	.570	-.087	.134	.142	-.270	-.477	-.295	-.273	1.000	-.289	-.639*	-.540*	.263
		Sig. (2-tailed)	.067	.776	.662	.644	.350	.084	.306	.391	.	.363	.014	.046	.364
		N	11	13	13	13	14	14	14	12	14	12	14	14	14
	IP strategy	Correlation Coefficient	.128	.211	.148	-.222	.162	-.441	-.486	.000	-.289	1.000	-.068	-.370	-.211
		Sig. (2-tailed)	.708	.490	.630	.466	.597	.132	.092	1.000	.363	.	.824	.214	.490
		N	11	13	13	13	13	13	13	10	12	13	13	13	13
	Older or younger as 15	Correlation Coefficient	-.845**	-.289	-.447	.000	.564*	.523*	.468	.239	-.639*	-.068	1.000	.645*	-.071
		Sig. (2-tailed)	.001	.317	.109	1.000	.029	.045	.079	.454	.014	.824	.	.009	.800
		N	12	14	14	14	15	15	15	12	14	13	15	15	15
	Situated in Biopartner	Correlation Coefficient	-.598*	-.411	-.189	.050	.364	.609*	.302	.250	-.540*	-.370	.645**	1.000	-.262
		Sig. (2-tailed)	.040	.145	.519	.865	.183	.016	.275	.433	.046	.214	.009	.	.346
		N	12	14	14	14	15	15	15	12	14	13	15	15	15
	International company	Correlation Coefficient	-.239	-.417	.043	-.411	-.342	-.405	.468	-.478	.263	-.211	-.071	-.262	1.000
		Sig. (2-tailed)	.454	.138	.884	.145	.211	.134	.079	.116	.364	.490	.800	.346	.
		N	12	14	14	14	15	15	15	12	14	13	15	15	15

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Appendix H : Interview with the Leiden University Technology Transfer Office LURIS

The Leiden University has a Technology Transfer Office since 2005-2006. Because this TTO has a legal team which is specialized in contracts for financing, it has been combined with raising funds for the research of the university. That is why the TTO of Leiden is called the Leiden University Research and Innovation Services (LURIS). The organization is divided into three teams, each with a different responsibility in the technology transfer cycle (see Figure 27).

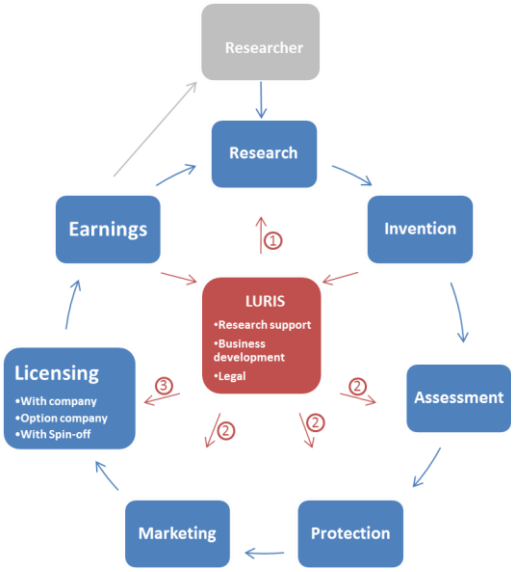

Figure 27 Technology transfer cycle according to LURIS. The three departments of LURIS have their own specific role within the cycle. 1 = Research support, 2 = Business development and 3 = Legal

The technology transfer cycle starts with the research being performed at the Leiden University (LU) or the Leiden University Medical Centre (LUMC). Because the institutes are funding the research and paying for the researcher's salary, the institutes have ownership over every invention that comes out of the research. The research support team helps attract funds to certain research projects and supports some of the research goals of the LU. Eventually some research can be turned into an invention. If this is the case, then LURIS will ask the researcher to file an *Invention Disclosure Form*. From this point the business development team will analyze the invention and create a marketing and protection strategy. Companies are actively involved in these inventions which can have three positive outcomes; companies want an option, which means that they want the UL to look further into the invention and later on the company can buy the license, companies can license if they find the invention a success or it can become a spin-off company for which interested entrepreneurs are looked for. In the final case LURIS will make a license agreement with the spin-off company because this company will no longer be an entity of the LU or the LUMC. This agreement is put into a contract by the legal team who will negotiate about the terms and the prices. Eventually a small amount of the earnings will go to LURIS for financing. Another amount will go to the research group where the invention came from. Finally, 1/3 of the earnings go to the researcher(s) responsible for the invention as an incentive. LURIS will never go for a sale of an invention to prevent technologies being shielded by large companies.

Not all inventions will go to the market through LURIS. LURIS is an organization with only 21 employees. These employees are not focused on all the faculties of the LU, because that would not be enough. LURIS therefore is solely focused on the exact sciences in which the life sciences are the most important focus point. This choice was made because the LU/LUMC is located within the LBSP. Some of the inventions do not go to the market via LURIS because of this lack of employees. Inventions are sold/spread by direct personal contacts with the scientist(s).

LURIS plays an important role in the innovation process of companies. They support technology transfer of inventions from the researchers of the LU. They can also build bridges between those inventions and potentially interested companies. The relationships with these companies are conserved by own initiative but some companies also seek them out because of their interesting portfolio. LURIS would like to have more interaction with companies in the LBSP but it seems that most of the companies have grown so much that they are not interested in young technologies anymore. The benefit of the inventions from LU/LUMC is that they are highly innovative but bear a large risk because much marketization needs to be done. That is why large companies find it safer to expand by buying small biotechnology companies which have made more progress with innovations. This would mean that LURIS should start focusing more on spin-off companies. However, because spin-off companies need to license technologies, LURIS cannot help writing their business plan because it would be a conflict of interest. The university itself also does not support spin-off companies in any way except some ad hoc training.

Appendix I : Factor analysis

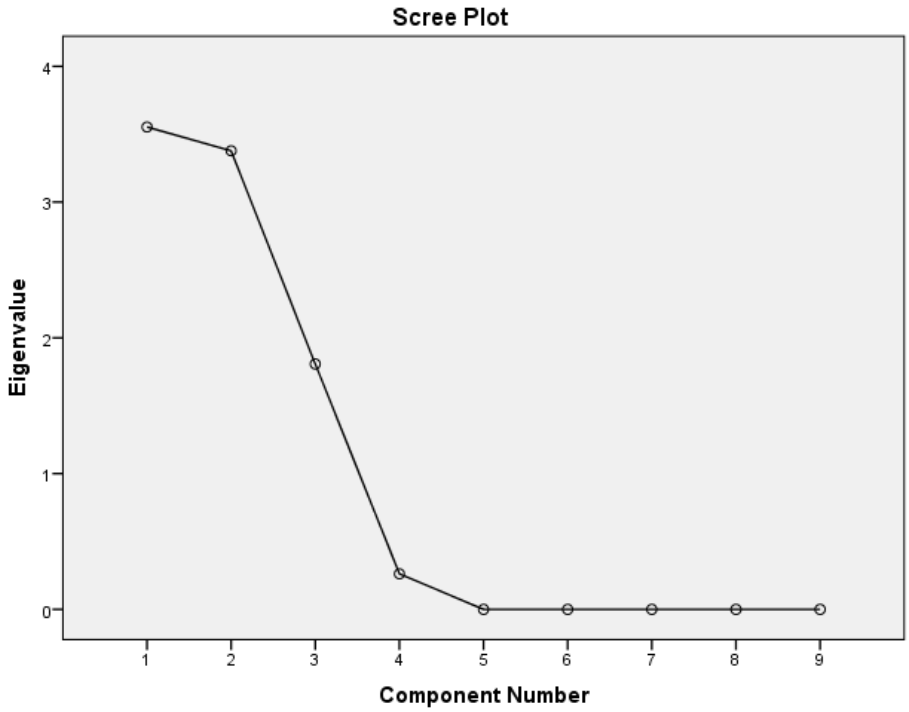

Figure 28 A Scree-plot of the eigenvalues for the nine innovation performance items. Data of these nine innovation performance items was gathered during the interviews or found in annual reports. Point of inflexion was given at component number 4.

Literature list

Scientific literature

Abou-Gharbia, M. and W. E. Childers (2013). "Discovery of innovative therapeutics: Today's realities and tomorrow's vision. 1. Criticisms faced by the pharmaceutical industry." Journal of Medicinal Chemistry **56**(14): 5659-5672.

Alavi, M. and D. E. Leidner (2001). "Review: Knowledge management and knowledge management systems: Conceptual foundations and research issues." MIS quarterly: 107-136.

Alegre, J., K. Sengupta and R. Lapiedra (2013). "Knowledge management and innovation performance in a high-tech SMEs industry." International Small Business Journal **31**(4): 454-470.

Amar, A. D. and J. A. Juneja (2008). "A descriptive model of innovation and creativity in organizations: a synthesis of research and practice." Knowledge Management Research & Practice **6**(4): 298-311.

Andriessen, J. (2006). "Managing knowledge processes." Managing Technoloy and Innovation: RM Verburg, RJ Ortt & WM Dicke (Eds). Routledge, London: 263-285.

Arechavala-Vargas, R., R. Rico-Huerta and F. Leonel-De-Cervantes (2012). Cooperation in regional innovation networks among small and medium enterprises: Case study of a veterinary pharmaceutical company in Jalisco, Mexico, Vancouver, BC.

Argote, L., B. McEvily and R. Reagans (2003). "Managing knowledge in organizations: An integrative framework and review of emerging themes." Management Science **49**(4): 571-582.

Artz, K. W., P. M. Norman, D. E. Hatfield and L. B. Cardinal (2010). "A longitudinal study of the impact of R&D, patents, and product innovation on firm performance." Journal of Product Innovation Management **27**(5): 725-740.

Bagnoli, C. and M. Vedovato (2012). "The impact of knowledge management and strategy configuration coherence on SME performance." Journal of Management and Governance: 1-33.

Bandura, A. (1994). Self-efficacy, Wiley Online Library.

Barden, C. J. and D. F. Weaver (2010). "The rise of micropharma." Drug Discovery Today **15**(3-4): 84-87.

Biedenbach, T. (2011). "The power of combinative capabilities: Facilitating the outcome of frequent innovation in pharmaceutical R&D projects." Project Management Journal **42**(2): 63-80.

Bozbura, F. T. (2007). "Knowledge management practices in Turkish SMEs." Journal of Enterprise Information Management **20**(2): 209-221.

Braganza, A., C. Edwards and R. Lambert (1999). "A taxonomy of knowledge projects to underpin organizational innovation and competitiveness." Knowledge and Process Management **6**(2): 83-90.

Cardinal, L. B. (2001). "Technological Innovation in the Pharmaceutical Industry: The Use of Organizational Control in Managing Research and Development." Organization Science **12**(1): 19-36.

Cardinal, L. B. and D. E. Hatfield (2000). "Internal knowledge generation: The research laboratory and innovative productivity in the pharmaceutical industry." Journal of Engineering and Technology Management - JET-M **17**(3-4): 247-271.

Carlile, P. R. (2004). "Transferring, translating, and transforming: An integrative framework for managing knowledge across boundaries." Organization Science **15**(5): 555-568.

Carr, M. (2010). "The small- and medium-sized enterprises office (SME office) at the European medicines agency." Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz **53**(1): 20-23.

Cattell, R. B. (1966). "The scree test for the number of factors." Multivariate behavioral research **1**(2): 245-276.

Chen, C.-J. and J.-W. Huang (2009). "Strategic human resource practices and innovation performance—The mediating role of knowledge management capacity." Journal of Business Research **62**(1): 104-114.

Chesbrough, H. W. (2003). Open innovation: The new imperative for creating and profiting from technology, Harvard Business Press.

Cockburn, I. M. (2004). "The changing structure of the pharmaceutical industry." Health Affairs **23**(1): 10-22.

Cockburn, I. M. and R. M. Henderson (2001). "Scale and scope in drug development: Unpacking the advantages of size in pharmaceutical research." Journal of Health Economics **20**(6): 1033-1057.

Cohen, S. N., A. C. Chang, H. W. Boyer and R. B. Helling (1973). "Construction of biologically functional bacterial plasmids in vitro." Proceedings of the National Academy of Sciences **70**(11): 3240-3244.

Cohen, W. M. and D. A. Levinthal (1989). "Innovation and learning: the two faces of R & D." The economic journal **99**(397): 569-596.

Cohen, W. M. and D. A. Levinthal (1990). "Absorptive Capacity: A New Perspective on Learning and Innovation." Administrative Science Quarterly **35**(1): 128-152.

Cooke, P. (2002). "Regional innovation systems: General findings and some new evidence from biotechnology clusters." Journal of Technology Transfer **27**(1): 133-145.

Dadfar, H., J. J. Dahlgaard, S. Brege and A. Alamirhoor (2013). "Linkage between organisational innovation capability, product platform development and performance: The case of pharmaceutical small and medium enterprises in Iran." Total Quality Management and Business Excellence **24**(7-8): 819-834.

Deeds, D. L. and D. M. Decarolis (1999). "The impact of stocks and flows of organizational knowledge on firm performance: an empirical investigation of the biotechnology industry." Strategic management journal.

Desouza, K. C. and Y. Awazu (2006). "Knowledge management at SMEs: Five peculiarities." Journal of Knowledge Management **10**(1): 32-43.

Dhawan, S. K., S. Roy and S. Kumar (2002). "Organizational energy: An empirical study in Indian R & D laboratories." R and D Management **32**(5): 397-408.
Dierickx, I. and K. Cool (1989). "Asset stock accumulation and sustainability of competitive advantage." Management science **35**(12): 1504-1511.
DiMasi, J. A., R. W. Hansen and H. G. Grabowski (2003). "The price of innovation: New estimates of drug development costs." Journal of Health Economics **22**(2): 151-185.
Dong, B. (2010). Research on the independent innovation and motivation mechanism of SMEs in China, Wuhan.
Dong, B. (2012). Innovation drivers analysis of the medium and small-sized enterprises in Jilin Province. Kuala Lumpur. **403-408:** 5172-5176.
Dosi, G. (1982). "Technological paradigms and technological trajectories: a suggested interpretation of the determinants and directions of technical change." Research policy **11**(3): 147-162.
Dunne, D. and D. Dougherty (2011). The absorptive capacity for complex, science-based innovation: The case of bio-pharmaceuticals, San Jose, CA.
Dyer, J. H. and K. Nobeoka (2000). "Creating and managing a high-performance knowledge-sharing network: The Toyota case." Strategic Management Journal **21**(3): 345-367.
Easterby-Smith, M., M. Graça, E. Antonacopoulou and J. Ferdinand (2008). "Absorptive capacity: A process perspective." Management Learning **39**(5): 483-501.
Egbu, C. O., S. Hari and S. H. Renukappa (2005). "Knowledge management for sustainable competitiveness in small and medium surveying practices." Structural Survey **23**(1): 7-21.
Eppinger, E. and G. Vladova (2013). "Intellectual property management practices at small and medium-sized enterprises." International Journal of Technology Management **61**(1): 64-81.
FIELD, A. (2005). "Discovering statistics using SPSS."
Freel, M. S. and P. J. A. Robson (2004). "Small firm innovation, growth and performance: Evidence from Scotland and Northern England." International Small Business Journal **22**(6): 561-575.
Gagné, M. and E. L. Deci (2005). "Self-determination theory and work motivation." Journal of Organizational behavior **26**(4): 331-362.
Gassmann, O. and G. Reepmeyer (2005). "Organizing Pharmaceutical Innovation: From Science-based Knowledge Creators to Drug-oriented Knowledge Brokers." Creativity and Innovation Management **14**(3): 233-245.
Gebhardt, C. (2013). "The making of plasma medicine. Strategy driven clusters and the emerging roles of cluster management and government supervision." Journal of Technology Transfer **38**(4): 401-414.
Gilson, L. L., J. E. Mathieu, C. E. Shalley and T. M. Ruddy (2005). "Creativity and standardization: complementary or conflicting drivers of team effectiveness?" Academy of Management Journal **48**(3): 521-531.
Gold, A. H., A. Malhotra and A. H. Segars (2001). "Knowledge management: An organizational capabilities perspective." Journal of Management Information Systems **18**(1): 185-214.
Gray, C. (2006). "Absorptive capacity, knowledge management and innovation in entrepreneurial small firms." International Journal of Entrepreneurial Behaviour and Research **12**(6): 345-360.
Guzmán, G. M., M. C. M. Serna and D. G. P. de Lema (2012). The relationship between knowledge management and innovation level in Mexican SMEs: Empirical evidence, Cartagena.
Hackman, J. R. and E. E. Lawler (1971). "Employee reactions to job characteristics." Journal of applied psychology **55**(3): 259.
Hackman, J. R. and G. R. Oldham (1976). "Motivation through the design of work: Test of a theory." Organizational behavior and human performance **16**(2): 250-279.
Håkonsson, D. D., R. M. Burton, B. Obel and J. T. Lauridsen (2012). "Strategy Implementation Requires the Right Executive Style: Evidence from Danish SMEs." Long Range Planning **45**(2-3): 182-208.
Hansen, M. T., N. Nohria and T. Tierney (1999). "What's your strategy for managing knowledge?" Harvard business review **77**(2): 106-116, 187.
Hatzichronoglou, T. (1997). Revision of the High-Technology Sector and Product Classification.
Hendriks, P. (1999). "Why share knowledge? The influence of ICT on the motivation for knowledge sharing." Knowledge and process management **6**(2): 91-100.
Hertzberg, R. P. and A. J. Pope (2000). "High-throughput screening: new technology for the 21st century." Current opinion in chemical biology **4**(4): 445-451.
Hewitt-Dundas, N. (2006). "Resource and capability constraints to innovation in small and large plants." Small Business Economics **26**(3): 257-277.
Hitt, M. A., R. E. Hoskisson, R. A. Johnson and D. D. Moesel (1996). "The market for corporate control and firm innovation." Academy of Management Journal **39**(5): 1084-1119.
Holm, M. J. and F. Poulfelt (2003). The Anatomy of Knowledge Management in Small and Medium-Sized Enterprises! Paper presented at the LOK Research Conference.
Howells, J., D. Gagliardi and K. Malik (2008). "The growth and management of R&D outsourcing: Evidence from UK pharmaceuticals." R and D Management **38**(2): 205-219.
Huang, H. C., M. C. Lai and L. H. Lin (2011). "Developing strategic measurement and improvement for the biopharmaceutical firm: Using the BSC hierarchy." Expert Systems with Applications **38**(5): 4875-4881.
Huang, J.-W. and Y.-H. Li (2009). "The mediating effect of knowledge management on social interaction and innovation performance." International Journal of Manpower **30**(3): 285-301.
Huitt, W. (2004). "Maslow's hierarchy of needs." Educational psychology interactive.

Hung, R. Y.-Y., B. Y.-H. Lien, S.-C. Fang and G. N. McLean (2010). "Knowledge as a facilitator for enhancing innovation performance through total quality management." Total Quality Management **21**(4): 425-438.
Hung, Y. C., S. M. Huang, Q. P. Lin and M. L. Tsai (2005). "Critical factors in adopting a knowledge management system for the pharmaceutical industry." Industrial Management and Data Systems **105**(2): 164-183.
Hunter, J. (2011). "Challenges for pharmaceutical industry: New partnerships for sustainable human health." Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences **369**(1942): 1817-1825.
Hurmelinna-Laukkanen, P., H. Olander, K. Blomqvist and V. Panfilii (2012). "Orchestrating R&D networks: Absorptive capacity, network stability, and innovation appropriability." European Management Journal **30**(6): 552-563.
Hutchinson, V. and P. Quintas (2008). "Do SMEs do knowledge management?: Or simply manage what they know?" International Small Business Journal **26**(2): 131-154.
Hynes Iii, M. D. (2009). "Project and capacity management: An application to drug development." Computers and Chemical Engineering **33**(12): 1994-1998.
Jantunen, A. (2005). "Knowledge-processing capabilities and innovative performance: An empirical study." European Journal of Innovation Management **8**(3): 336-349.
Jiménez-Jiménez, D. and R. Sanz-Valle (2011). "Innovation, organizational learning, and performance." Journal of Business Research **64**(4): 408-417.
Kaiser, H. F. (1960). "The application of electronic computers to factor analysis." Educational and psychological measurement.
Karim, S. (2009). "Business unit reorganization and innovation in new product markets." Management Science **55**(7): 1237-1254.
Katz, R. and T. J. Allen (1982). "Investigating the Not Invented Here (NIH) syndrome: A look at the performance, tenure, and communication patterns of 50 R & D Project Groups." R&D Management **12**(1): 7-20.
Keizer, J. A., L. Dijkstra and J. I. M. Halman (2002). "Explaining innovative efforts of SMEs. An exploratory survey among SMEs in the mechanical and electrical engineering sector in The Netherlands." Technovation **22**(1): 1-13.
Köhler, G. and C. Milstein (1975). "Continuous cultures of fused cells secreting antibody of predefined specificity." Nature **256**(5517): 495-497.
Lane, P. J., B. R. Koka and S. Pathak (2006). "The reification of absorptive capacity: A critical review and rejuvenation of the construct." Academy of Management Review **31**(4): 833-863.
Latham, G. P. and E. A. Locke (1991). "Self-regulation through goal setting." Organizational behavior and human decision processes **50**(2): 212-247.
Lee, S. M. and S. Hong (2002). "An enterprise-wide knowledge management system infrastructure." Industrial Management and Data Systems **102**(1): 17-25.
Liao, S. H., W. C. Fei and C. C. Chen (2007). "Knowledge sharing, absorptive capacity, and innovation capability: An empirical study of Taiwan's knowledge-intensive industries." Journal of Information Science **33**(3): 340-359.
Lichtenthaler, U. and E. Lichtenthaler (2009). "A capability-based framework for open innovation: Complementing absorptive capacity." Journal of Management Studies **46**(8): 1315-1338.
Lin, H.-F. and G.-G. Lee (2005). "Impact of organizational learning and knowledge management factors on e-business adoption." Management Decision **43**(2): 171-188.
Lowman, M., P. Trott, A. Hoecht and Z. Sellam (2012). "Innovation risks of outsourcing in pharmaceutical new product development." Technovation **32**(2): 99-109.
Malerba, F. and L. Orsenigo (1995). "Schumpeterian patterns of innovation." Cambridge Journal of Economics **19**(1): 47-65.
McKelvey, M., H. Alm and M. Riccaboni (2003). "Does co-location matter for formal knowledge collaboration in the Swedish biotechnology–pharmaceutical sector?" Research Policy **32**(3): 483-501.
Nagayya, D. and P. Tirumala Rao (2013). "Small and medium enterprises in the era of globalisation." Journal of Rural Development **32**(1): 1-17.
Narula, R. (2004). "R&D collaboration by SMEs: New opportunities and limitations in the face of globalisation." Technovation **24**(2): 153-161.
Nemet, G. F. (2009). "Demand-pull, technology-push, and government-led incentives for non-incremental technical change." Research Policy **38**(5): 700-709.
Nesta, L. and P. P. Saviotti (2005). "COHERENCE OF THE KNOWLEDGE BASE AND THE FIRM'S INNOVATIVE PERFORMANCE: EVIDENCE FROM THE US PHARMACEUTICAL INDUSTRY*." The Journal of Industrial Economics **53**(1): 123-142.
Nonaka, I. (1995). The Knowledge-Creating Company: How Japanese Companies Create the Dynamics of Innovation: How Japanese Companies Create the Dynamics of Innovation, Oxford university press.
Ortt, J. (2009). "From Invention to Large-Scale Diffusion in Five High-Tech Industries." IAMOT.
Ortt, J., S. Tabatabaie, G. Alva, G. Balini and Y. Setiawan (2009). From invention to large-scale diffusion in five high-tech industries. The 18th International Conference for the International Association of Management of Technology, Orlando.

Oshri, I., S. L. Pan and S. Newell (2006). "Managing trade-offs and tensions between knowledge management initiatives and expertise development practices." Management Learning **37**(1): 63-82.
Quintana-García, C. and C. A. Benavides-Velasco (2004). "Cooperation, competition, and innovative capability: A panel data of European dedicated biotechnology firms." Technovation **24**(12): 927-938.
Radzevičiene, D. (2009). "Developing small and medium enterprises using knowledge management frameworks: A case study in Lithuania." Aslib Proceedings: New Information Perspectives **60**(6): 672-685.
Rai, A., J. Reichman, P. Uhlir and C. Crossman (2008). "Pathways across the valley of death: novel intellectual property strategies for accelerated drug discovery." Yale Journal of Health Policy, Law, and Ethics **8**(1).
Rhodes, J., R. Hung, P. Lok, B. Y.-H. Lien and C.-M. Wu (2008). "Factors influencing organizational knowledge transfer: implication for corporate performance." Journal of Knowledge Management **12**(3): 84-100.
Rocha, M. M., G. B. A. Lima, V. J. Lameira de Jesus and O. L. G. Quelhas (2012). "Innovation as a critical success factor: An exploratory study about the partnership among university with pharmaceutical industry in Brazil." Journal of Technology Management and Innovation **7**(3): 148-160.
Roper, S., J. Du and J. H. Love (2008). "Modelling the innovation value chain." Research Policy **37**(6-7): 961-977.
Ryan, R. M. and E. L. Deci (2000). "Intrinsic and Extrinsic Motivations: Classic Definitions and New Directions." Contemporary Educational Psychology **25**(1): 54-67.
Schmid, E. F. and D. A. Smith (2002). "Discovery, innovation and the cyclical nature of the pharmaceutical business." Drug Discovery Today **7**(10): 563-568.
Schmid, E. F. and D. A. Smith (2002). "Should scientific innovation be managed?" Drug Discovery Today **7**(18): 941-945.
Schumpeter, J. A. and R. Fels (1939). Business cycles, Cambridge Univ Press.
Song, M., H. Van Der Bij and M. Weggeman (2005). "Determinants of the level of knowledge application: A knowledge-based and information-processing perspective." Journal of Product Innovation Management **22**(5): 430-444.
Song, M., H. Van Der Bij and M. Weggeman (2006). "Factors for improving the level of knowledge generation in new product development." R and D Management **36**(2): 173-187.
Spiegel, M. and C. Marxt (2012). Innovation behavior of technology-based SME, Vancouver, BC.
Stein, M. I. (1975). Stimulating creativity, Academic Press New York.
Sternitzke, C. (2010). "Knowledge sources, patent protection, and commercialization of pharmaceutical innovations." Research Policy **39**(6): 810-821.
Stiglitz, J. E. and A. Jayadev (2010). "Medicine for tomorrow: Some alternative proposals to promote socially beneficial research and development in pharmaceuticals." Journal of Generic Medicines **7**(3): 217-226.
Sundgren, M., E. Dimenäs, J. E. Gustafsson and M. Selart (2005). "Drivers of organizational creativity: A path model of creative climate in pharmaceutical R&D." R and D Management **35**(4): 359-374.
Sundgren, M. and A. Styhre (2007). "Creativity and the fallacy of misplaced concreteness in new drug development: A Whiteheadian perspective." European Journal of Innovation Management **10**(2): 215-235.
Swan, J. and H. Scarbrough (2001). "Knowledge management: Concepts and controversies." Journal of Management Studies **38**(7): 913-921.
Teirlinck, P. and A. Spithoven (2013). "Research collaboration and R&D outsourcing: Different R&D personnel requirements in SMEs." Technovation **33**(4-5): 142-153.
Terziovski, M. (2010). "Research notes and commentaries innovation practice and its performance implications in small and medium enterprises (SMEs) in the manufacturing sector: A resource-based view." Strategic Management Journal **31**(8): 892-902.
Turner, R., A. Ledwith and J. Kelly (2010). "Project management in small to medium-sized enterprises: Matching processes to the nature of the firm." International Journal of Project Management **28**(8): 744-755.
Turner, R., A. Ledwith and J. Kelly (2012). "Project management in small to medium-sized enterprises: Tailoring the practices to the size of company." Management Decision **50**(5): 942-957.
Van de Vrande, V., J. P. De Jong, W. Vanhaverbeke and M. De Rochemont (2009). "Open innovation in SMEs: Trends, motives and management challenges." Technovation **29**(6): 423-437.
Verburg, R. M. and E. J. Andriessen (2011). "A typology of knowledge sharing networks in practice." Knowledge and Process Management **18**(1): 34-44.
Verburg, R. M. and J. Andriessen (2006). "The assessment of communities of practice." Knowledge and Process Management **13**(1): 13-25.
Walker, G. and D. Weber (1984). "A transaction cost approach to make-or-buy decisions." Administrative science quarterly: 373-391.
Wang, Y. L., Y. D. Wang and R. Y. Horng (2010). "Learning and innovation in small and medium enterprises." Industrial Management and Data Systems **110**(2): 175-192.
Weggeman, M. (1997). Kennismanagement: Inrichting en besturing van kennisintensieve organisaties, Scriptum Schiedam.
West, W. and P. Nightingale (2009). "Organizing for innovation: towards successful translational research." Trends in Biotechnology **27**(10): 558-561.
Wolf, P., S. Kaudela-Baum and J. O. Meissner (2012). "Exploring innovating cultures in small and medium-sized enterprises: Findings from Central Switzerland." International Small Business Journal **30**(3): 242-274.

Woodman, R. W., J. E. Sawyer and R. W. Griffin (1993). "Toward a theory of organizational creativity." Academy of management review **18**(2): 293-321.
Xia, T. (2013). "Absorptive capacity and openness of small biopharmaceutical firms–a European Union–United States comparison." R&D Management.
Xu, J., R. Houssin, E. Caillaud and M. Gardoni (2010). "Macro process of knowledge management for continuous innovation." Journal of Knowledge Management **14**(4): 573-591.
Yeoh, P. L. (1994). "Speed to Global Markets: An Empirical Prediction of New Product Success in the Ethical Pharmaceutical Industry." European Journal of Marketing **Vol. 28**(Issue 11): 29-49.
Zahra, S. A. and G. George (2002). "Absorptive capacity: A review, reconceptualization, and extension." Academy of Management Review **27**(2): 185-203.
Zhaohui, Z. and C. Xiaokang (2011). Does R&D investment promote firms' performance? Evidence from the pharmaceutical and biological products listed firms, Wuhan.

Non scientific literature

Biopartner Leiden. (2013). Retrieved 21-12-2013, 2013, from http://biopartnerleiden.nl/home.html.

Buck Consultants International on behalf of Dutch Ministry of Economic Affairs (2009). Fysieke investeringsopgaven voor campussen van Nationaal belang. The Hague.

Buck Consultants International on behalf of Dutch Ministry of Economic Affairs (2012). Actueel beeld campussen in Nederland. The Hague.

CDER. (2010, January 28th 2013). "Is it true FDA is approving fewer new drugs lately? ." Retrieved 16-09-2013, 2013, from http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM247465.pdf.

Center for Drug Evaluation and Research (2012). "2011 Novel new drugs."

Dagblad, A. (2013, 11-12-2013). "Farmareuzen sjoemelen met kankermedicijn." Retrieved 11-12-2013, 2013, from http://www.ad.nl/ad/nl/4560/Gezond/article/detail/3560268/2013/12/11/Farmareuzen-sjoemelen-met-kankermedicijn.dhtml.

Dutch National Government (2012). Samenvatting Innovatiecontract Topsector Life Sciences & Health.

EC (2003). The new SME defenition, European Commission.

EU (2012). Small Business Act Fact Sheet 2012, Netherlands, European Commission.

Hopewell, D. (2003). "Biotech vs. pharma: once different, now collaborative entities." Retrieved 22-06-2003, from http://www.bizjournals.com/sanjose/stories/2003/06/23/focus3.html?page=all.

ITA (2010). Pharmaceutical Industry Profile. Office of Health and Consumer Goods, Internation Trade Administration,.

Kerkhof, J. (2012). Life Sciences Outlook 2012, Dutch biotech companies: from start-up to exit, NautaDutilh.

Lawlor, M. (2013). "Difference between Pharmaceutical and Biotechnology." Retrieved 17-04-2013, from http://www.morganmckinley.ie/article/difference-between-pharmaceutical-and-biotechnology.

LBSPf. (2013). "Park database." Retrieved 27-9-2013, 2013, from http://www.leidenbiosciencepark.nl/about_leiden_bsp/park_directory/park_database_google_map.

North Carolina Biotechnology Centre. "Collaborative Funding Grant." Retrieved 13/12/2013, from http://www.ncbiotech.org/research-grants/research-funding/collaborative-funding.

NOS. (2010, 8-7-2010). "Massaontslag bij Organon in Oss." Retrieved 8-7-2010, 2010.

PhRMA (2013). PhRMA Profile 2013. Pharmaceutical Research and Manufacturers of America.

Raaphorst, F. (2012). Biopharmaceutical Industry; Sector Report 2012, Rabobank International Corporate Clients.

Raaphorst, F. (2013). Biopharmaceutical Industry; Sector Report 2013, Rabobank International Corporate Clients.

The Decision Group (2011). Dutch Life Sciences Outlook 2011.

The Decision Group (2012). Dutch Life Sciences Outlook 2012.

The Decision Group (2013). Dutch Life Sciences & Health Outlook 2013.

The Human Mortality Database. (2013). Retrieved 20-12-2013, from http://www.mortality.org/.

Topteam Life Sciences & Health (2011). Topsectorplan Life Sciences & Health; Voor een gezond en welvarend Nederland.