



KTH Industrial Engineering
and Management

Drug **R&D** Management

Practitioners' Challenges
and Knowledge Needs

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Abstract

R&D productivity in the pharmaceutical business has gradually decreased during the last decades. While companies are spending more on R&D, fewer drugs are reaching the market. It is said that the cost of bringing a successful drug to the market is now \$1 billion, which includes all failure drugs. At the same time, governmental regulations for drugs development have become tighter. Companies are therefore desperately trying to find new ways to develop more innovative drugs more effectively. There is a growing need for more knowledge about Drug R&D Management in the industry, which is the reason for KTH Industrial Economics and Management initiating a research program in this field.

The present study is a feasibility study of this research endeavor. It outlines the scope of the field and explores areas for further study. Anchored in interviews with key industrial actors, the aim is to identify which organizational challenges practitioners are presently facing for successful drug R&D management.

Four themes of challenges within the business have been identified. These are:

- *Specialization within the R&D Process* – There is a trend that different actors specialize within the innovation process of developing new drugs. The concept is to source activities to organizations that have the best capabilities. What are the consequences of this business model? What is the core competence of different actors?
- *Balancing Freedom and Control in R&D Operations* – R&D by definition, comprises activities with unknown outcomes. Work in projects most probably takes trajectories that were not originally thought of. Typically the most suitable individuals for performing such activities are scientists with a deep specialization within the field of research. How are freedom and control of work balanced within R&D? What type of control is most suitable? How can scientists be managed?
- *Resource Allocation and Project Portfolio Management* – Projects in a project portfolio are dependent on each other and on their environment. The ecology in which a project lives will determine how it is evaluated and financed, and how risk-willing its owners are. There is a need of knowledge to describe how different project environments are organized.
- *Organizing for Knowledge Exchange* – Knowledge in biosciences is growing exponentially. Managing knowledge is therefore crucial, but how to do it successfully is the question. Working in big collaborative networks requires companies to manage knowledge outside the boundaries of the firm. There is also a need to bring in knowledge from other industries.

The themes can encompass different theoretical disciplines - from a strategic point of view to a cognitive aspect of innovation. This study argues for a comparative multiple case study approach focusing on the preconditions and business logics of different R&D organizations. The cases should look into the different organizational domains of Bio-tech firms and Big Pharma multinationals, comparing the two business logics and strategies. Innovation in the context of single firms in the pharmaceutical industry can thus be explored and give rise to knowledge through examples of practical problem solving and methodology in drug R&D management.

Abstract¹

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1. INTRODUCTION

During the last several decades, the R&D productivity of the pharmaceutical industry has declined dramatically (Hopkins et al. 2007; Garnier 2008). Pharmaceutical companies are spending more on their research activities, but fewer products are reaching the market. Commercial drug R&D has the characteristics of being highly regulated during the development phase, having close ties with universities and government-funded research institutes (McKelvey 1996), being very costly (DiMasi, Hansen and Grabowski 2003), and having binary success (Pisano 2006). These characteristics differ significantly for different types of products and diseases, enabling companies to have a range of R&D strategies. Work is often performed in networks with collaborating organizations that take different roles in the innovation process (Pisano 2006). R&D projects can therefore take different shapes during their lifetime. Although R&D is organized differently, the aim is still the same: to develop pharmaceuticals that are needed on the health care market.

It is said that costs for bringing a successful drug to the market have now risen to \$1 billion, when all failure drugs are included (DiMasi et al. 2003). Therefore, companies are trying to find both new innovative drugs (product innovation) and new ways to develop drugs (process innovation). Development projects are becoming bigger, with more collaborative actors in the innovation process and more researchers that need to be coordinated among even more technological disciplines and specialist areas (Powell, Koput and SmithDoerr 1996; Mendez 2003). Projects are becoming more complex. At the same time, regulations for what drugs can be approved for the market have become stricter (Garnier 2008). There is strong pressure on companies to increase their efficiency in R&D, make better project choices, improve the resource allocation between projects, and compress the activities in order to increase the productivity of ongoing research projects. The traditionally well performing industry is now on the lookout for knowledge on how to organize their R&D (Garnier 2008).

This study thus aims to answer the question of what specific challenges different actors in the pharmaceutical industry are faced with. Anchored in interviews with key industrial actors, the aim is to identify the most significant organizational challenges for successful R&D management in pharmaceutical companies. This is a feasibility study with the ambition to result in a number of research questions for future studies.

1.1. Design of the study

In order to identify the most significant organizational challenges for successful drug R&D management, this study consists of interviews with key industrial actors. The aim is to identify the key managerial issues for practitioners in the contemporary pharmaceutical industry, with special focus on management of R&D. This means identifying the concerns felt by the actors of the industry about practical work

As the research is exploratory, a qualitative research method is preferable. Interviews with single individuals make it easy to quickly get a sense of what topics are important for them. By using an exploratory method that permits the interview to enter a trajectory that is not given beforehand, the interviewee can comprehensively deal with the topic she or he feels is important. In addition, the interviews were complemented with background information from other sources like newspaper articles, conferences, and studies of the industry.

The interviews were structured as follows: each interview started with an introduction, where the aim of the study was discussed. The interviewee was then given time to narrate about his or her professional background and current role. Later, the conversation moved to the topic of the interview. Most of the times, there were no schedules for the interviews. The questions were asked from a perspective of general individual experience and seldom specific to the company where the respondents worked. The questions were chosen spontaneously as attendant questions to the topic or in relation to earlier interviews when the topic was meant to be changed. The topics of the later interviews were thus more deeply discussed, because by this time more knowledge had been accumulated from earlier interviews.

In order to explain the purpose and method of the study, a short information sheet was sent out to individuals who were desirable as participants in the study. This sheet contained the purpose of the study along with a primary idea for a theme to study. The theme that was described led the interviewees into a discussion of that specific theme even though the study was mostly exploratory, aimed at finding new themes.

1.2. Interviews with 23 Executives

The interview study consists of interviews with 23 current or former middle management, CEOs, functional managers, investment managers, consultants, board members, or inventors from R&D organizations at pharmaceutical companies, venture capital firms, or what is commonly referred to as biotechnology firms¹. The individuals were chosen from their experience in the business and they most often talked in a general fashion about the questions asked. Most of them have more than 20 years of experience in the industry from different organizations. The organization types they represent are the most important actors in the innovation process of pharmaceutical research.

Most of the interviews were recorded, but, in accordance with the wishes of the interviewees, at five interviews only notes were taken.

The individuals were chosen with the aim of covering the most significant players in the Swedish pharmaceutical industry. However, in order to add a glimpse from the international scene, interviews with a director of drug delivery at Abbott Soliqs in Germany and two executives at AstraZeneca in Great Britain were also included.

The list of the interviewees is presented in appendix 1. Most of the interviewees have an educational background in natural sciences such as medicine, biology, chemistry or engineering. Also, most of them hold a PhD. They are representative of the employees of the industry, which constitutes a fairly homogenous group with respect to background and education.

1.3. Analyzing the Interviews

The aim of this study is to identify the most significant challenges that practitioners in the pharmaceutical industry face when they manage R&D. The findings constitute the opinions and views of the interviewees. The main focus of the analysis lies in cate-

1. Biotechnology firm (or Biotech firm) is sometimes a misleading concept. There is no homogenous group of biotechnology firms. What seem to be common characteristics of what is regarded as a biotechnology firm is that it is commercialized from university research in applied medicine or biotechnology, it is financed by venture capital, it is small in size, and it has no products on the market. These companies are used to commercialize academic research that can result in both new drugs and new products that enable process innovation when researching new drugs.

gorizing the material from the unstructured interviews, i.e., choosing what statements are significant, interpreting what interviewees are saying and why, and comparing the quotations with each other.

The open-ended interviews led into a variety of different narratives and explanations of challenge in managing drug R&D. The interviewees' narratives had different trajectories. Some interviews came to focus on the history of the organization that the interviewees represented (or have worked at) and what challenges it has faced, i.e., how the organization had survived different challenging periods. At other times, the whole pharmaceutical industry's challenges were discussed with the help of examples of single projects or companies. The material was significant or relevant in different ways for the purpose of this study. While some interviewees contributed pinpointing quotations, others contributed long narratives of what is important. The latter is not easily channeled through this study.

The analysis of the interview material was structured as follows: first, all of the recordings were transcribed. The whole material, consisting of the transcribed interviews and notes, was examined to construct an overall picture. Second, all interesting quotations from the transcribed interviews were selected. There is of course a personal preference for what is regarded as interesting and could fit into the scope of this study; many subjects were purposely dismissed. The quotations were grouped together by relating similar quotation topics to each other. In this way, the specific challenges could be validated as being applicable to more than one person. A web of interconnected quotations was formed and themes emerged where a group of quotations was demarcated from the rest of the web. Third, the themes were divided into sections that constitute different aspects of the theme. These sections are presented as the subtitles of each theme in the next chapter. Finally, the results were validated by discussing them at a focus group with participants from the study and additional practitioners from the industry. Also, the report manuscript was sent out to all interviewees so that they could comment on the material.

2. FINDINGS – FOUR THEMES OF CHALLENGES AND NEEDS FOR KNOWLEDGE

From the interviews, four themes of perceived challenges emerged. The first theme deals with what an R&D organization should do and its capabilities with regards to structure and organizational contingencies. The title of the theme is *Specialization within the R&D Process*, with the emphasis on specialization. The interviewees point to a trend towards finding the core competence of a firm and specializing in that particular competence. Focusing on its core capabilities, a firm needs to outsource certain functions and collaborate with firms specializing in other functions. Consequently, collaborating successfully is a related challenge that the managers express.

The second theme deals with the challenge of *Balancing Freedom and Control in R&D Operations*. It moves from what a firm should “do”, to how it should be “done”. The R (research) part of R&D in the pharmaceutical industry is often referred to as the discovery phase. This work is therefore explorative in character and outcomes of activities are not known from the beginning. On the one hand, the interviewees argue that scientists should be given freedom to explore new ideas for products. The control of what is done should be decentralized to specific research units. On the other hand, the interviewees argue that R&D is part of a profit-driven company with a need of corporate control. In order for an organization to eliminate inertia, extensive hierarchies, management concepts for work process, and centralized organizational control should all be aligned. These are all reality in today's R&D organizations and they deprive the scientists of power. The duality between giving freedom to the scientists and controlling their work is the challenge discussed in the second theme.

The third theme is *Resource Allocation and Project Portfolio Management*. It deals with challenges that an organization faces when working in a multi-project based organization. How the projects should be organized and how resources should be distributed among the projects are issues that managers need to consider. Big multi-project organizations are concerned with having a well balanced risk in their project portfolio and are constantly forecasting the probability of project success. The same applies to venture capital firms that have a similar role to that of a project office in a multi-project organization. How a project portfolio is organized is another challenge identified within this theme.

The third theme covers the challenges of *Organizing for Knowledge Exchange*. An R&D organization's task is to create new knowledge and convert it into products ready for the marketplace. Managing knowledge is, therefore, a key challenge. As stated earlier, there is a trend towards organizing R&D through collaboration. As theme 1 deals with what collaboration should be about, theme 4 discusses the challenge of successful collaboration.

Each theme is divided into sections presented through quotations from the interviews. In this way, the voice of the managers is channeled through the text. The core of their struggles, challenges, and needs for knowledge can thereby be discussed.

2.1. Theme 1 – Specialization within the R&D Process

In theme 1, the interviews revolve around what a specific organization should do and why; what a firm's R&D strategy is, in other words. The respondents point to different settings in which R&D is organized. The conversation often came to rest on a discussion of the difference between organizing R&D in a “Big Pharma” company (e.g. AstraZeneca) and in a biotech company. The respondents elaborated on how different organizatio-

nal setups are better for performing certain activities while others are worse. The challenge of theme 1 is thus which R&D activities an organization should focus on and why.

The theme is structured into three sections. The first deals with the challenge of how organizations position themselves with respect to the structure of the industry. The following section explores organizational size, which seems to be viewed as a key contingency factor. The frequently used multi-organizational, network-based, way of organizing R&D requires organizations to collaborate with each other. These specific challenges are explored in the final section.

2.1.1. Positioning Oneself in the Value Chain of R&D

There is a conception among the interviewees that different actors in the industry are differently suited to performing different activities in the R&D process. The common underlying ideal conceptual model looks like this: ideas for new drugs, namely to find new biological mechanisms or targets to address, should come from an academic environment. These ideas should be commercialized by starting a Biotech company to explore this mechanism more closely and find a molecule that can become a candidate drug. The late and expensive parts of the development should be done by pharmaceutical companies that are supposed to “buy out” the project from the Biotech firm. The different actors should shape their strategy so that they fit into the R&D process and can specialize in their role:

“Academia should work with industry to a much larger extent. They take an idea a bit further and maybe the biotech companies develop it even more and the pharmaceutical industry’s role will be to do what costs the most money, the development process, that is. When you have to make patient studies, work with regulatory affairs, manufacture, and bring the drug to the market that costs money. That is the role of the big pharmaceutical companies. You will see many different models, of course; this is not the only one.”

(Director, Pharmaceutical Company)

As indicated in the quote, the phases are not entirely defined. At least, it is not defined in the early phases when the hand-over from academia to the biotech company should take place. The respondent also believes that there ought to be a shift in the R&D process so that projects should stay in academia even longer than today. This means that the projects should be financed by academic funding even longer.

This view of how the different actors should position themselves manifests a notion of the organizations as being isolated from each other: that some organizations are specialized in their role without interacting with the other actors. However, this is not entirely the case:

“It’s often said that it is first an academic project and then it becomes a commercial project, but in reality it is exactly the same group of people working in the project if you look over a three year period. You will not see that after one year, because it takes some time for people to change environment. The project was bought by one person, but that person recruited the people from academia that were working with the project in the first place.”

(Director, Industry Association)

So even though projects change organization, the set-up of people might be the same.

Consequently, conceptually the value chain with work in phases isolated from each other is problematic. When creating an infrastructure for the R&D process, one needs to consider mobility of people and influence of ideas, culture, climate, and other factors between the different phases of projects. In order to do that, more knowledge is needed on how this takes place.

2.1.2. Strategy and Size

In drug R&D there are two main types of organization that perform R&D activities: the big pharmaceutical company with a large portfolio of R&D projects and the small company with typically one single dominant project. The big pharmaceutical company most often has products on the market that finance the R&D while the small companies' R&D is typically financed by venture capital. There is much debate about the optimal size for innovating new drugs and what strategy is suitable in relation to organizational size. On the one hand, size can be used for generating economies-of-scale. On the other hand, large size usually leads to rigid structure that might hinder innovation.

Some common diseases are researched by many companies. A successfully innovated product addressing such a disease can potentially be very profitable since the market for common diseases is large. However, because of the size, there are already products on the market. Therefore, new products have to show and ensure better performance than existing ones and the focus on side effects will thus be stronger. For the drug to be approved, the company needs to show policy makers that the risk of side effects is very small. To ensure this, large clinical trials involving a great number of patients have to be organized:

"When it comes to diseases that have some endpoints that will give cardiovascular effects, not only will the patient lose weight but there will be a smaller risk of cardiovascular diseases, then there needs to be bigger patient material. It takes about 10 000 – 30 000 patients and big follow ups even after you have received an approved product. There are big costs and big risks involved. The development risk of investing, the scientific risk of testing non-typical mechanisms, and the commercial risk that comes up because there is big competition in these areas are all risks that have to be acknowledged. It is not possible for a small company to spread the risk by having many parallel projects at the same time. This is not a suitable strategy."

(Director, Pharmaceutical Company)

Consequently, some models for drug development are not suitable for small companies, simply because there need to be economies-of-scale in order to balance the big risks. Small companies can therefore not research drugs that cure diseases like diabetes. Instead, they need to focus on less risky diseases where the market is not as large, or position themselves in an early research phase and sell their ideas to Big Pharma companies that can perform the clinical studies.

With size comes structure. With structure come hierarchies and control. In the eyes of the respondents, size will therefore hinder innovation and affect what R&D activities a big company should have in-house. Early research that requires more flexibility for the scientists is not considered to fit into the model:

"I believe that this model is a bit obsolete for the pharmaceutical industry where the early basic research should be performed by the pharmaceutical companies. It does not fit into the model where you have a research factory that measures productivity. It does not fit for innovation, defined as new inventions. The industry model is to take what evolves in research groups or in research work outside the industry and industrialize it."

(Director, Pharmaceutical Company)

Because of the size of the company and the control it needs in its operations, big companies are said to need a model that enables them to work downstream in the R&D process. Instead, early research should be directed to small companies and projects should be bought in. One respondent even says: "If I was the CEO in a Big Pharma company I would close down all of the R&D operations" (Investment Manager, Venture Capital). Yet Big Pharma companies still continue to have early research in their organization.

Being a big company does not mean that there has to be a rigid structure and strong control mechanisms per se, but it seems to be the view of most of the respondents. One respondent proposes two alternatives for strategy change to address this problem for the Big Pharma companies:

"There are two ways to solve it. Either you provide space for these scientists that are like madcaps that cannot function in furnished rooms. These are the people that discover new stuff. They might be placed in a lab environment somewhere outside, but they are still hired by the company to perform research. The alternative is to get the scientific knowledge from elsewhere."

(Former director, Pharmaceutical Company)

By providing space for the madcaps, the respondent means not controlling the behavior of the scientist as much as is done now. He proposes that in order for the big company to perform early research, the scientist has to be placed outside the organization and given a great deal of autonomy. The respondent continues by explaining that the environment of a big company is not suitable for the explorative scientist:

"It is a question if basic research to find new mechanisms and such fit into the corporate world. At Pharmacia we had small groups of three-four individuals that worked on finding something new. They could stand in one corner and work, but they did not fit into the organization when the structure became bigger and very strict. They disappeared, all of them. Today I think that it is wrong not to give these people space."

(Former director, Pharmaceutical Company)

Not only does the size create an environment that is not suitable for basic research, but it also makes scientists flee the workplace.

The Biotech companies are associated with being start-up firms and they face the opposite problem of the Big Pharma companies: being too small.

"It would be good if one was able to merge these firms into a holding company to have a firm with 6-7 projects within the same area. It would be better if one merged the overheads and shared some of the experience and competence. It will be less risky then. Individuals can more easily talk to colleagues. One risks getting the same effects as in the big cooperation, so it should not be too big. You can maybe have a company that has 25 employees. It should not get any bigger."

(CEO, Biotech Company)

Thus, size of an organization seems to be an important aspect of how R&D is or should be managed. Depending on the size, the organization will be able to manage risk and research environment differently. The question is whether research can be successfully performed in a big pharmaceutical company. Respondents propose licensing of projects in late stages for big companies and that is what the next section will be about.

2.1.3. Sourcing and Collaboration

“Collaborate or die” were the concluding words of the conference Pharma 2020 arranged by PriceWaterhouseCooper and BioSweden in 2009. Focusing the organization on core capabilities requires more collaboration. There is strong emphasis on cooperation in the sector. Concepts like strategic alliances, open innovation, in-licensing, merger and acquisition, contract research organizations (CRO), and virtual companies are all frequently used by the interviewees. New problems with interorganizational collaboration arise like trust issues, transaction costs, business models for selling work, leadership, etc. The business model of hiving off companies from universities and the trend of specialization has grown significantly. Consequently, so has the interest in knowledge about cooperation.

“It is tradition that the pharmaceutical business does everything by itself. More and more routines are outsourced in the development process, some companies license out manufacturing, and more companies buy candidates for the later clinical phases.”

(Director, Pharmaceutical Company)

When companies are outsourcing more and more, the question is what is the core competence of the firm? Many of the interviewees believe that development and especially clinical studies is the core competence of pharmaceutical companies in terms of R&D. By building competitiveness with economies-of-scale in the development organization, the process needs to be fed from behind with research projects. However, there are downsides to this strategy:

“A project which I used to work in aimed to develop a drug against glaucoma. In the late clinical studies, it was discovered that there was a nasty side effect for blue eyed patients who used the medicine. They developed nasty green spots on the eyeballs. The project was close to being terminated, but we decided to examine what had gone wrong. It turned out that the side effects were not dangerous at all. The process was reversible, meaning that when the patients stopped using the medicine the spots disappeared. We managed to remove the obstacles and solve the problem. This would probably not have been possible if we had bought the project from somebody else. We would not have had the expertise in-house and would probably have terminated the project.”

(Former director, Pharmaceutical Company)

What the quote indicates is that there are new challenges when buying projects. When working with a project in-house, the scientists become experts on the drug and can better solve problems that arise. Also, an organization has stronger confidence in drugs developed in-house than when bought in, which can be referred to as the “not-developed-here syndrome” as one of the respondents expressed it.

Another important aspect that the interviewees point to is the need to have professional scientists who can select successful projects and understand the science behind them. Therefore, the purchase function becomes increasingly important. In order to make a good job of purchasing projects, the scientific professionals have to stay up to date within their field of expertise, which is an organizational challenge in itself.

2.2. Theme 2 – Balancing Freedom and Control in R&D Operations

In academia, the scientists have a great degree of individual freedom to explore what they believe is interesting, but in pharmaceutical companies the work of the researchers must be aligned with the goals of the company to a higher degree². Balancing freedom and control is one of the challenges that pharmaceutical firms face when organizing R&D.

This theme moves from *what should we do* to *how should we do it*. It deals with different aspects of how the interviewees reason in terms of organizing for freedom and structure in R&D. It moves from a strategic point of view to an operational. In the first section, we will explore the structural part of freedom and control. How is structure manifested in the R&D organization and in what ways are control mechanisms used? Typically an R&D organization in the pharmaceutical industry consists of 40 or 50% PhDs. The following section will therefore explore what challenges R&D managers face concerning leadership of PhDs. The last section of the theme deals with the structure and control problem that is associated with a matrix organizational structure. Who should be in control: the functional organization or the projects, vertical or horizontal control?

2.2.1. Organizing Structure for Control in an R&D Organization

Drug R&D projects are specific in the sense that they are high risk, which means that they seldom result in something purposeful. There is a high probability that projects are terminated before they result in a successful product, which makes all the work done in the project more or less meaningless. It is no wonder that company executives want to check that the right activities are carried out within the project. At the same time, research requires a degree of freedom for the scientists to work on what they think is right and interesting.

The most common concept of structuring R&D operations in the pharmaceutical industry is perhaps the *lean sigma model*. The concept has several purposes, of which eliminating unnecessary activities in the innovation process is one. The interviewees point to different ways that pharmaceutical companies have used lean sigma to successfully make operations more efficient, from making logistics more efficient to broader aspects of managing work in R&D.

Another common management concept used in drug R&D is the stage-gate model. The innovation process is divided into activities, the stages, which are followed by an evaluation, the gates. With the stage-gate model, evaluation of R&D projects is homogenized and conducted in a structured way.

Although there are many significant differences between structured ways of organizing – like process thinking, lean sigma, or stage-gate – there are also important similarities. These are ways for managers to control what is being done in a structured way in order to homogenize management. This has been the emphasis during the interviews

2. Most of the respondents expressed this in one way or another.

rather than how the single models work. Why the idea of management concepts is a controversial one could be explained by the following quotation:

"We are in a pretty early phase where we start to apply a more mechanical and industrial thinking in R&D. I am not sure that it will become generally accepted. We are testing different ways of measuring. It is not that many years that we have been doing this. If you look at how many management generations we have been doing this, it is maybe two."

(Investment Manager, Venture Capital)

The new models for managing drug R&D are quite new and have not been really evaluated yet. Management models within R&D still need time to mature and it is possible that the "mechanical" methods will disappear. The challenge is to combine structure and freedom:

"If we were only going to create freedom, dynamism, liberty, and keep people away from structure it still wouldn't be productive... We have to bridge structure and freedom. The question for us is: How can we be purposeful, innovative and efficient so that the outcomes are as high as possible? Innovation for me is about outcomes."

(Director, Pharmaceutical Company)

Creating a structure that provides scientists with freedom to work in the same direction is a major challenge, which is exemplified by the quotation: "the challenge for the pharmaceutical company is to organize R&D so that all activities are aligned in the same direction" (Former director, Pharmaceutical Company). By stating "aligned in the same direction", the respondent means that the organization needs to work towards common goals, values, and visions. How this structure can be formed and what it is comprised of, is a dilemma. In the next quotation, the respondent believes that there are several aspects that need to be in order:

"You have to think in a very holistic way, yet an integrated way, about the organization. Behavior, symbols, culture, climate, measurements of performance, leadership styles have all got to be pulling in the same direction to make it possible to have a innovative and efficient organization. That is the challenge we face to get the momentum model right."

(Director, Pharmaceutical Company)

By working with all of the parts she lists, the respondent believes that it is possible to make the individuals in the organization work in the same direction. These are all integrated in complex ways and the parts influence each other. For example, to one respondent the culture aspect is comprised of systems, behavior, and symbols:

"We think about culture as being a factor of three different things: the behavior of people in that they feel they need to exhibit, the systems that are in place that drive people to behave in a certain way and the symbols they see around them. These three parts will affect the way that people think they are expected to behave in AstraZeneca R&D organization."

(Director, Pharmaceutical Company)

The managers face the challenge of creating a corporate culture so that people behave in a way that is aligned with the objectives of the company. Such a culture can be managed by shaping the system, symbol, and behavior in the right way.

Respondents that are now working in a big R&D organization emphasize how “mechanical” ways to organize are important to achieve efficiency and cost effectiveness in operations. At the same time, respondents that have been working in big organizations and are now working in smaller ones stress how structures used to control what scientists should do, and monitor what they are doing, are not the proper way for organizing. One example:

“It is not possible to order good research. If you think that, you do not understand what research is. The big discoveries were not made on knowledge that was known from the beginning, they just occurred. You cannot find a new mechanism for treatment of some disease when you are assigned that task.”
(Former director, Pharmaceutical Company)

The respondent stresses the importance of letting scientists deciding what to do themselves and without the influence of managers. Homogenizing for discovery projects takes away the possibility of discoveries simply occurring.

Whether structured ways of working should be used or not when organizing R&D is something that will probably always be controversial. However, the consequences of using concepts is definitely something that needs to be explored.

2.2.2. Leadership of PhDs in a Commercial Environment

The R&D organization of a pharmaceutical company, big or small, typically consists of mostly academic scientists, PhDs. These scientists come from an academic environment where their task is to make new scientific findings which allow us to better understand biology. The type of explorative research that is conducted to create more knowledge about biology is often referred to as basic research. There are many similarities between working as a researcher in a pharmaceutical company and in academia, but also important differences. The respondents point to the fact that scientists working in a commercial environment use many similar methods and laboratory equipment to those used in academia, but basic research is conducted differently.

The interviewees say that the main difference between research conducted in the two different environments is the purpose of the knowledge created. While research in academia has the objective of creating more knowledge about biology and publishing the results in a peer-reviewed journal, the research in pharmaceutical companies has the purpose of creating knowledge that can be used to successfully develop drugs. Organizing research with these two determinations should be and is done differently, according to the interviewees.

To one interviewee, researchers in the commercial environment should focus the task on what makes the biggest profit for the pharmaceutical company where they are employed. This can be challenging for the researcher who goes from one environment to the other:

“Many companies have become more American and then you have terrible hierarchal structures where everyone is afraid to take a decision before the boss at the top approves it. Scientist are a bit like artists, they need to work with a

high degree of liberty and think big. These structures are quite rigid. There is not much space. They do not fit into the hierarchical model. It does not suit for the madcaps to do what they want. It was a big shock for me when I joined Kabi after working at the university."

(Former director, Pharmaceutical Company)

To the respondent, the hierarchy of the firm deprives scientists of their freedom to decide what to do. Scientists work within given frames. The challenge is whether to organize the company so that the scientists will have liberty to make their own choices, quickly teach the scientists to work in the system, or not to have the scientists in a company at all.

There is another aspect of the challenge of having an organization with many researchers from academia. The respondents say that a commercial environment not only differs from an academic environment in what activities are carried out, but also how they are carried out. In academia, researchers earn their PhDs by working individually and proving to their peers that they themselves have the talent to make discoveries that no one else has made before, in the opinion of one respondent. This individualism is not as important in the commercial setting:

"What surprised me when I started working in the industry was that after a meeting we made decisions on what the group should do and made collective deadlines. This took a while for me to get used to, since in academia after project meetings everyone went to work on their own tasks."

(Former Director, Pharmaceutical Company)

The former director argues that there are different ways to work in the two different environments in terms of team work versus individual efforts. Because there is a mobility of people between the academic and commercial settings, the two environments influence each other. Adjusting from an environment with one culture of work to another takes time as the quotation above points out. Another example:

"The environment that we saw had similarities with what an academic sort of institution environment has. It's more individual and less collaborative. It makes people want to make sure that their ideas are right before they open their mouths because they don't want to get shot down. What is normal to most people is what would be the sanctuary challenge, what you could call peer-review if you were understating."

(Director, Pharmaceutical Company)

In the opinion expressed, the academic competitive environment is not viable in a profit-seeking company. Still, ideas need to be challenged in some sense, which can be done through the academic peer-review or in another model that is more commercially applicable. Finding a model for choosing the right ideas to work on becomes a key issue.

People management is important for several reasons. Here are two aspects discussed: the need for creation of academic freedom for the scientists and interconnection between the academic and the commercial environment. Companies have different HR strategies in their R&D organizations, which is something that needs to be explored further.

2.2.3. Vertical or Horizontal Control?

As stated earlier, there seems to be an ongoing change in the R&D process. Actors are repositioning themselves in the value chain. Thus, they are becoming more bureaucratic and specialized. Innovation is becoming like a relay where one firm takes an innovation to a certain point and hands it over to the next actor that will take it a bit farther, and so on. The same notion of organizing the industry as a whole can also be seen in the organization of the big companies, where the companies create departments, each specialized in one particular function. The same way that the different actors in the industry drive the project to a certain point is used by the different departments in the Big Pharma organization. The quotation explains how this works and also shows criticism towards organizing in this way:

"Today the big pharmaceutical companies work a bit like in silos. You have the research silo, the development silo, and the marketing silo. You often have a pretty bad handover when you go from one step to the other... I felt it at Pharmacia. We did many projects that were very good and then in a way threw them over a wall and did not know what happened to them. There was someone else who picked up the project and continued it. You were never asked to help. You did not know what happened with the product."

(Former director, Pharmaceutical Company)

The interviewee points out the challenge with working in an innovation process where work is divided into departments. In order to make such an organization successful, the handovers need to function well. The best way for managing knowledge in a project is thus to keep the people in the project all the way, according to the quotation, i.e. not bureaucratize work in the project to different departments.

It has not always been this way. According to several respondents, the two old Swedish pharmaceutical companies AstraZeneca and Pharmacia were organized with specific project teams working all the way from research into new products to marketing them. This way to organize has certain advantages:

"Research was tied to marketing. You followed your product from A to Z. You made small companies in the big, where you had everything. It created a whole other commitment to the project. You had the scientists with you all the way to the end so that they could help you market the products and so on."

(Former director, Pharmaceutical Company)

Thus, organizing R&D with a focus on projects creates not only better knowledge within the project, it also stimulates the commitment of the scientists.

Working in such a matrix organization with functional departments specialized in different parts of the innovation process creates the challenge of who is responsible and accountable for work done in the projects:

"The challenge of working in a matrix organization is deciding who is responsible and accountable for work done. The functional department and the project face different challenges in the work."

(Former director, Pharmaceutical Company)

Since the R&D project goes through several steps, where different department are accountable for the activities, there is a mutual responsibility for the work done. According

to the quotation, there is a discrepancy between what is important for the project team and for the functional team. While it is important for the functional organization to use the best technology for the purpose and allocate the right resources between the projects, it is important for the project to manage what activities should be done with limited resources, to prioritize between activities, in other words.

Single project companies do not have this challenge since they have not built a functional organization. It is the project team that decides what activities to do and they do them themselves or outsource them to a CRO. The lack of responsibility from a specialized functional organization can thus cause a quality problem. In one respondent's opinion, single project companies do not use as good scientific methods in the innovation process as the bigger matrix organization does. There is no functional organization for innovating the drug R&D process to perform the specific task better each time. There are, for example, often animal and cell models in preclinical development used in single project companies that are inferior to those in matrix organizations, according to the respondent.

So what is the best way to organize a matrix organization and balance responsibility between the specialized line organization and the fast-working project team with knowledge about the specific project?

2.3. Theme 3 – Resource Allocation and Project Portfolio Management

What is the basis for which projects are given resources, how many projects are given resources, and how much do they receive? These are the basic challenges of theme 3. It is manifested in two ways by the respondents. The first section explores the way that R&D projects are evaluated, and, more specifically, the social aspect of evaluation. The second section of the theme deals with how risk is managed in the R&D organization. Risk management can explain why projects in certain environments receive resources while they are shelved in other environments.

2.3.1. Evaluating R&D Projects

Evaluating what projects are viable and can become successful is a key task in any R&D organization. When evaluating an R&D project, practitioners take into account their expectation of the performance of the project and balance it against the cost it takes to develop it into a finished product. Typically, projects are evaluated several times during their lifetime. Apart from the technological evaluation that goes on throughout the whole innovation process, there is an economic evaluation as well. While a small venture capital financed company will be evaluated by the financiers when additional investments have to be made, a project in an R&D organization with an extensive project portfolio is evaluated by different scientific and finance committees.

According to the respondents the typical way to organize for evaluation of drug R&D projects is referred to as a gatekeeping or stage-gate model. In order to pass through the innovation process there are gates that only admit projects that meet certain criteria. These gates are guarded by gatekeepers that make the decision whether the R&D project will receive further resources to continue work and how much. The challenge is to decide how many gates to have and what should be the criteria for a project to pass through. One would think that because the decisions are based on technological viability that they are black or white, but a clear and objective interpretation of test results of drug performance does not exist in many cases. The interviewees relate many examples

(Losec, Seloken, the drug described above against glaucoma, etc.) of projects that were condemned and almost permanently terminated and later shown to be successful. The technological aspects of project evaluation have partly been covered in section 2.2 and we will leave it by just saying that technological variables cannot always make clear what projects are going to be successful; therefore there are other evaluation criteria at play.

A common variable to use when deciding a project's success rate is to calculate its market value. This means deciding the probability of the project reaching the market and how big the profits would be if it reached the market. Thus, executives would know if the project should be continued or not. These calculations are not entirely reliable: one can conclude this from the next quotation, which illustrates a company needing SEK 130 million in order to continue their R&D project.

"[How do you know that you are worth 130 million for future investments?] It is incredibly difficult to say. There are different ways to calculate it. Sometimes you can calculate how much money has been spent in the company already and how much money it takes to reach a certain level. We are at least worth that, because that is already put into the company. Another way is to start out from the last valuation and then calculate how big the market is. Say that we could take 20% of a market of \$20 million each year... We are not stock listed so it is not the market value that determines the value. It is difficult. It is the current owner that decides and they can say whatever they want. If they do not get a buyer then it is probably not worth it. [It sounds a bit like a gut feeling] Exactly, but we can make certain models anyway."

(CEO, Biotech Company)

It is interesting that models are used for valuation of a project even though they fail to reflect an objective value. Since there has to be an elimination of projects that are not successful in order to allocate resources to those that can become successful, valuation needs to be done. Valuation is used to give the project a figure that allows it to be compared to other projects and be translated into money when talking to investors, as the next quotation suggests.

"Valuation of R&D projects is not really scientifically done. There is a lot of internal business politics involved. If a project is valued at SEK 50 or 100 million, this can be due to a small change in just a few parameters. Still we use project valuation because we do not have a better tool. What else can we do?"

(Investment Manager, Venture Capital)

The respondent states that there is a need for valuation of projects even though it is very difficult to do it objectively. Valuation becomes an internal and external rating system for evaluating projects. As there are no clear ways to show why a project is worth "SEK 50 or 100 million" there are social ingredients present when deciding what value a project is assigned. There is a need for knowledge about how to use valuation when working with a project portfolio and allocating resources.

"There is always a war between projects. They fight about the flow of money. The one that will show the highest probability of leading to success will get more money than the others."

(Director, Pharmaceutical Company)

In a multi-project company there are seldom enough resources for executing a whole project portfolio; therefore, projects are internal competitors with each other for resources. What the respondent describes is a kind of Darwinistic system where the best fitted project gets the most resources. What defines a well fitted project is not only the technological viability but also the project team's ability to market the project internally:

"Many of our projects were put into cold storage just because we were not good enough at marketing them. The Americans in the company said: 'There are no problems. The project will be finished within two to three years'. We, on the other hand, said that: 'We have these problems and we have to solve them and it will take some time'. We are very much engineers in Sweden, who focus on the problems and therefore did not get as much funding for our projects. As we look back, the projects that we got resources for went as we thought they would. We had the problems that we said we would have and it turned out that way. Nothing became of the American projects, as I recall."

(Former director, Pharmaceutical Company)

Depending on the perception of the projects' performance, the resources will be allocated accordingly. If a project is marketed in a better way it will thus receive more resources, as the quotation above exemplifies. The respondent gives a similar example of a project leader at AstraZeneca who was very trusted by senior management and therefore received extensive resources, enabling that project leaders' projects to move faster.

Even though there are social aspects at stake, some interviewees point out that it is impossible to claim that a project is viable when its experiments show otherwise. "The scientific fact is stronger than any social criterion", they say. So neither the social aspects nor the scientific aspects can be discredited. How the two aspects interplay and in what way they influence project survival is a challenge for a further research topic.

2.3.2. Managing Risk in an R&D Organization

Bringing a drug to the market costs over \$1 billion and takes between 10 to 20 years (DiMasi et al. 2003). Along the innovation process, many great candidates are deselected because they do not perform well enough. Either they show an effect that could damage the human body or they have limited therapeutical performance. The probability of succeeding in a drug R&D project is extremely low. At the same time, projects cost more in later phases of the innovation process:

"The later you are in that process the more expensive it gets. If we have agreed on this it must be the ultimate goal to select the safest candidate for development as early as possible. In other words, you want to kick out the risky ones early in the process."

(Director, Pharmaceutical Company)

An important challenge in drug R&D today is how to terminate projects before they become too expensive. R&D projects are so expensive that a high safety level is needed to allow them to pass through late stages in the R&D process. If a project shows bad results in an experiment there is a big risk that this project will soon be kicked out of the R&D process.

"You can never foresee what will happen /.../ Everything can look so damn good and when we test on the patients nothing happens. Something happens in the body that makes the drug disappear. It was not what we had in mind when we developed the drug or it has a side effect that we could not dream about. It is extremely difficult. [It seems a bit paranoid to terminate the project as soon as there is the smallest side effect.] That's the way it is."

(Director, Pharmaceutical Company)

It is easy to terminate projects that show failure in performance and there is, of course, a problem in terminating projects too early. It is dangerous to continue with a project too long, but at the same time one cannot give up too easily. Take, for example, the drug for glaucoma that was discussed in section 2.1.3. There were forces that wanted to terminate that project because the drug showed a nasty side effect, but luckily the scientists were allowed to continue and find a way to solve the problem. Depending on how risk is managed in the organization, the project will be terminated or continued.

The interviewees reason quite differently about risk. Take the next two examples. The first quotation is from an optimistic venture capitalist arguing that it is important to find and invest in good projects. The second quote is from an executive expressing the pessimism that exists in some pharmaceutical companies.

"When we are stressed about whether we have invested in the right company, our boss tells us: 'Investing in a bad idea is not so dangerous; not investing in a good idea can ruin a whole fund.'"

(Investment Manager, Venture Capital)

"The industry is conscious that it shelves projects that could probably result in successful products, but they are afraid. The insecurity is so big before every decision every year."

(Director, Pharmaceutical Company)

Risk is managed differently in organizations. There seems to be a polarization between how venture capital firms and their portfolio companies manage risk and how the big multi-project R&D giants manage risk:

"Naturally we are more willing to take risks in a small company like this than a big company that maybe has many products on the market and get really scared. They might be terminated too early."

(CEO, Biotech Company)

Two interesting aspects to consider are: What is the proper way to do it and when do organizations allow projects with high risk to continue to run? In a small firm, the options are to continue or to terminate the whole operation.

Ideally, we would know beforehand what projects will not be successful and continue with the ones that will. This is of course impossible, but there are methods that can be used to give more information about how the drug will react in the human body. This is what the next quotation is saying:

"The holy grail in the pharmaceutical industry is to go from an accuracy of 1 out of 20 to 1 out of 10 when it comes to the expensive part of drugs R&D: the clinical studies. A way to do it, lowering the development risk, is to buy good

ideas and innovate the development process, that is making smarter studies that give better answers, that is. To take away the 9 or 19 projects that do not yield anything because they cost so much [...] It is the industry's biggest challenge: to innovate and at the same time be industrial."

(Director, Pharmaceutical Company)

The challenge is how to organize for this.

2.4. Theme 4 – Organizing for Knowledge Exchange

The key to an R&D organization is to have the right knowledge at the right time. Since medicine is one of the most researched areas in academia, collaboration with industry to bring in knowledge from elsewhere becomes a key issue. A pharmaceutical firm's collaboration can be organized through close contact with academic institutions or with other firms in research alliances. Many of the interviews conducted in this study have been located at a university campus area where the firm's lab and headquarters are situated. Collaboration helps the firm progress in its product development. The first part of this theme will therefore focus on just that: managing knowledge in collaborative networks.

But bringing in the knowledge needed is not only achieved by collaborating within the pharmaceutical business. The interviewees talk about how it is important to bring in knowledge from other industries, not primarily for the product development, but for process innovation and business development. Using technologies from other industries may well help improve certain parts of the R&D process. This is becoming a topic for discussion since the pharmaceutical industry has been regarded as a closed community and is now opening up with the purpose of searching for ways to solve productivity decline.

2.4.1. Managing Knowledge in Collaborative Network

As earlier stated, there is a trend towards outsourcing functions in the innovation process of drug R&D. The pharmaceutical industry has gone from consisting of companies that have most functions in-house to an industry with more actors specialized in different parts of the innovation process. Different actors take different roles in the innovation process and a single firm's innovation capability³ is dependent on the actors it collaborates with.

Both large multi-project and small single-project pharmaceutical companies are collaborating more. The one-project company inevitably has to collaborate, because it is very costly to build the entire infrastructure when there is only one project that needs it:

The principle is not to build too much infrastructure before one knows the product will be commercially viable. The needs are exactly the same for a Big Pharma company as they are for a small company. The same things need to be done, but you cannot have big regulatory or clinical departments in a small company. If you are making small molecules, you may not have the chemical part in the firm either. When you build these small companies, you have to look at the core competence and what it is that is really necessary to drive this further. Then you work almost exclusively with a core of the targets you work with and buy services from contract companies.

(Investment Manager, Venture Capital)

3. Innovation capability is a concept used by the interviewees for describing how well an organization is able to perform in terms of innovation.

The respondent describes how he believes a small company should be managed; with a core of developing drugs for the treatment of the targets that have been discovered. This can go to the extreme and small one-project firms sometimes consist of the project management team and outsource all the work to contract companies. This is what the interviewees refer to as “virtual” pharmaceutical companies; an organization exists, but most work is done outside it. In a sense, all small one-project companies are virtual since they outsource most of their research to other actors. Some quotations indicate that a small research-intensive pharmaceutical firm is automatically a virtual company.

On one hand, organizing R&D projects in a pharmaceutical company with much collaboration enables each actor to become more specialized in their particular function. On the other hand, knowledge is produced in separate organizations requiring knowledge management systems to work in inter-firm contexts. All organizations in an innovation system might face problems knowing about all the innovation activities performed by the individual actors:

I think Pfizer has a good business model, because they have a huge network of cooperation. Maybe too large. They're losing sight. It is a key driver to innovation that you open up basically the source of information coming in.

(Director, Pharmaceutical Company)

The respondent points out two challenges of engaging in too big collaborative networks. Firstly, it is difficult to keep track of everything that is done. It seems that it is difficult to integrate information systems over company boundaries. Being in a node in a research network requires organization to know what other partners are doing as well. Secondly, a collaborating organization has to share valuable information about its research. Working with R&D is somewhat of an arms race. R&D projects hold much valuable information and knowledge that needs to be protected so that it does not land in the hands of competitors. Pharmaceutical companies have been rather protectionist; typically there are confidential disclosure agreements (CDA) that regulate secrecy within a project. The respondent argues that the pharmaceutical companies need to liberalize the innovation process, enabling new kinds of collaboration. How can this be done and how business models should look to stimulate knowledge management in collaborations is a challenge for the future.

2.4.2. Bringing in Innovations from Other Industries

The pharmaceutical industry has been described as having been very closed. This has had impacts on how long it has taken for some new technologies to come into the pharmaceutical industry:

One key aspect, which I strongly believe in, is that the pharmaceutical industry is probably no longer a very closed community. It was very hard to get inside and even more so with new technologies. Consider how long it took for other technologies to move into the pharmaceutical industry. I haven't seen a study on this, but my gut feeling is that it took far longer than in any other industry.

(Director, Pharmaceutical Company)

The respondent argues that it has taken longer for the different technologies to establish themselves in the pharmaceutical industry compared to other industries. It is not

only product innovations that have fallen behind, also modern management concepts used in other businesses have only recently been introduced into the pharmaceutical industry:

The problem made us adopt a philosophy of looking at other industries to see how they work with efficiency, monitoring, etc. The pharmaceutical industry was completely eccentric earlier. Then we started adapting. We are still in a pretty early phase where we are trying to apply more mechanical and industrial thinking.

(Investment Manager, Venture Capital)

The philosophy the interviewee talks about has been partly discussed in theme 2. He argues that the reason that the pharmaceutical industry is opening up is due to the decline in productivity of the research organizations. Because there is a need for change, companies are looking elsewhere for solutions to their challenges. How this can be done is the challenge. "Opening up" is quite an abstract concept; therefore one of the interviewees gives some examples of how this could be made possible:

You have to create an atmosphere that fosters exchange. All the rest will follow. That sounds very easy, probably too easy. Once you've established an atmosphere in an environment where exchange is important, people will not only look out at their colleagues in the same building, they will look out to the outside. They will even go to non-pharma. I think what is very helpful is a campus structure. It is a structure where you create freedom to do unusual things.

(Director, Pharmaceutical Company)

The main issue for opening up is to create an atmosphere of looking for knowledge outside the business, according to the interviewee. The respondent argues that physical meetings between people from the pharmaceutical industry and the outside world are needed. Another example is to learn from other industries:

One thing I like is the European innovation forum which is conducted almost every year. People from various industries come together. The one I was attending was in the end of last year. They had people there from Pharma, engineering, construction, insurances, the automotive industry. It was actually conducted in the BMW headquarters in Munich. So the exchange of ideas on how to innovate is not necessarily tailored or limited to one industry. Some basic principles of innovation work for every industry. I like the open innovation.

(Director, Pharmaceutical Company)

Although there are examples of initiatives for bringing innovations into the business, the obstacles of doing so still have to be overcome. The challenge of "opening up" to the outside world is the same as opening up to competitors: the need for secrecy is high. Even though "cross fertilization is paramount to the pharmaceutical industry, the industry is not prepared to take in new technologies" (Director, Pharmaceutical Company). There is certainly a historical aspect to the need for secrecy in the business. The challenge might be cultural.

3. DISCUSSION – PROPOSALS FOR FURTHER STUDIES

This study aims to find the most significant challenges when managing drug R&D. The study's four themes point to different types of knowledge that managers are in need of. This section discusses how further research topics might look and what issues transcend the themes. The first two sections discuss methodological points of view for further research topics in regards to the findings of this study, and the last section looks at possible theoretical focuses of topics in relation to the themes of identified challenges.

3.1. Descriptive Studies of Drug R&D Environments

Every industry has its own context for innovation. The industry's structure, institutions, history, products, dominant actors and individuals, rules, scientific base, and worker personality types are all aspects that make every setting unique when considering innovation. The same applies to pharmaceutical companies. How pharmaceutical companies organize their R&D depends on the context of their environment. If the respondents' narratives and examples of how R&D is managed could be contextualized, the understanding of drug R&D management would be much richer.

Too general studies often face the challenge of being applicable to the single case. Generic management models might be applicable to one organization but not to another. In order to create knowledge about drug R&D management, one must first study single cases of R&D organization in the pharmaceutical industry and describe their environment. Regardless of the theme, most of the quotations indicate there is a need of deeper analysis of the subtexts. Understanding how the practical organizational problems are solved in the single case can help in understanding issues to consider when managing R&D in other situations. Also, a comparative analysis of multiple cases may provide insights into the consequences of managing R&D.

A possible descriptive study of drug R&D environments could comprise a number of case studies on an organizational level, i.e., the R&D department. Each case would involve studying the individual and organizational actions and the environment of the organization at the same time. After finding what key environmental factors are most significant, the cases can be compared to each other. Practically speaking, each case should be carried out at the company's facility with follow-on weekly visits over several months.

3.2. Biotech and Big Pharma – Two Environments for Drug R&D Management

One issue appears in all of the four themes of the study: the comparison between the Biotech company and the Big Pharma company. The interviewees point to the fact that these are the two significant categories for Drug R&D Management. The archetypical Biotech and Big Pharma company will specialize in different parts of the R&D process, organize their collaboration differently, balance between freedom and control differently, have projects in different types of project portfolios, and manage external knowledge differently. Future studies should describe how the context in the two environments of the Biotech and Big Pharma company respectively, affect drug R&D Management.

If we understand Biotech or Big Pharma as concepts, neither represents a homogenous group of companies⁴. This homogeneity does not even apply at the product level in the case of Biotech firms, i.e. Biotech firms are developing products for different markets. Some develop drugs while others develop different biotechnological tools (like methods for analyzing data from the electron microscope, specific monoclonal antibodies, or biosensors for analyzing biomolecular interactions) used for improving the process of developing pharmaceuticals. One would believe that Biotech companies are based on biotechnology (maybe at some point in time they were), but this is no longer always the case. Some of the Biotech firms also have equal products to those that have traditionally been a part of a Big Pharma company's product portfolio, i.e., small molecules. There are, of course, some characteristics that the respondents associate with a Biotech firm: start-up, close ties to a university, small in size, financed by venture capital, etc., but the main function of the concepts of Biotech and Big Pharma is the identity they create for the respondents.

The interviewees identify Biotech companies as being innovative, but with quality in their projects that is not as high as that of Big Pharma companies. That Biotech companies are regarded as more innovative is explained by the fact that they are formed with the purpose of commercializing novel scientific ideas from universities. The novelty of the science makes the ideas innovative. The rather low quality of the projects is explained by the fact that Biotech firms do not invest in high performance laboratory machinery and in scouting for novel scientific experimental methods. They simply do not have the experience or the capabilities to use development methods of the highest quality. The Big Pharma companies, in contrast, are considered to be too big to have operations running without a high degree of bureaucracy. These do not have as close access to the universities' front line science. The strength of the Big Pharma approach to organizing lies in the possibility to innovate the R&D process by having a functional organization with experts in all fields.

It is difficult to generalize the industry into two categories. The categories should instead be regarded as archetypes for organizing drug R&D. The Biotech company represents the small company method of organizing, while the Big Pharma represents the big multinational method of organizing. The size will also play a role in how the organizations will be studied, as some theoretical problems only exist in one of the categories.

Apart from the size of the companies, there is also the historical aspect. While most of the Big Pharma companies have existed for more than a century, the Biotech companies are newly founded "by definition". Seen from an industry perspective, Biotech companies are regarded as having emerged as an organizational form in the pharmaceutical industry during the 70's and 80's. The growth of biotech companies, like Genentech, Amgen, or Biogen, has in many ways shaped the industry. Often interviewees refer to these companies as trend-setting for successful management within the industry. The historical context of the organizational domain thus has an effect on how the drug R&D is managed.

Biotech firms and Big Pharma represent two ways that drug R&D is managed in the industry. The organizing of firms within both categories should be linked to the environment it exists in. Analyzing both categories at the same time could give valuable descriptions of the organizations.

⁴ In this study the Big Pharma represent the three pharmaceutical firms that have historically had big influence on the Swedish pharmaceutical industry: the Swedish part of AstraZeneca and the part of Pfizer that came from Pharmacia (that does not exist any longer).

3.3. Possible Theoretical Topics of the Themes

Apart from the methodological aspect of what organizations should be studied and why, there are also the theoretical considerations to take into account. The next section explores possible theoretical areas for future studies when exploring the four themes more deeply.

The first theme of *Specialization within the R&D Process* might lead the researcher into the topic of strategic management and adjacent theoretical subjects. Working with this theme will involve looking at how the firm's competence and capabilities fit into the anatomy of the industry, which partly moves the study into an industrial economic perspective, positioning the research above the single firm. Delving into the history of how the different ways to organize drug R&D have evolved is also relevant to understanding why certain organizations do what they do.

Balancing Freedom and Control in R&D Operations, the second theme, might go into a cognitive theoretical background of leadership and organizational control. Studying control and freedom in an R&D organization requires an investigation of how scientists react to certain methods of organizing. Control comes in many shapes (like input, output and behavior control, which are the most common) and each has certain consequences for the organization. It is important to investigate the benefits and pitfalls of organizing in a certain way. A suitable method for this research topic would be an ethnography, which could truly look into how researchers work within the balance of freedom and control.

The third theme, *Resource Allocation and Project Portfolio Management*, deals with issues of an R&D manager or project portfolio owner. This topic should not go into valuation methods, calculation of risk, or planning of the execution of a project portfolio. These research areas might have to go into statistics and other positivistic sciences. Looking at how social aspects influence resource allocation and project portfolio management can prompt the researcher to move into the field of multi-project management or research on project based organizations. A possible research method could be retelling and analyzing narratives about how ecologies of projects get their resources and why.

Organizing for Knowledge Exchange, of course, deals with the theory of knowledge management. Knowledge management deals with how organizations learn from their experience and accumulate knowledge. This would involve analyzing IT systems and company culture for knowledge exchange.

4. Conclusion

This study has showed four themes of the significant challenges within drug R&D management: Specialization within the R&D process, Balancing Freedom and Control, Resource Allocation and Project Portfolio Management, and Organizing for Knowledge Exchange. Each theme of challenges opens up to further research topics on the subject. This study argues that future research topics should describe the context of organizing R&D single companies within the pharmaceutical industry. It should also involve a comparison between different contexts, like the context of the Big Pharma firm and the Biotech firm.

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APPENDIX – LIST OF INTERVIEWEES AND THEIR BACKGROUNDS

Teodor Aastrup is CEO of a company called Attana that develops platforms for analysis of biomolecular interactions. He has a PhD from the Royal Institute of Technology and developed the initial technologies that Attana was based on during his research. He founded the company in 2002 and it has grown since. Although still small in size, Attana sells its products and services to several big pharmaceutical companies.

Mats Berggren is CEO of the industry-wide organization SwedenBio. SwedenBio represents 180 small and middle-sized life science firms in Sweden. The organization itself is a gathering place for leading executives from the Swedish life science industry and is a platform for information and knowledge about the industry. It is also the voice of the industry to policy makers in Sweden.

Nils Bohlin is a director at consultancy firm Arthur D. Little's practice in Stockholm where he leads the Nordic life science practice. Bohlin service as a consultant to pharmaceutical companies and biotech clusters when it comes to management within the industry.

Johan Brun is the medical director at Pfizer in Sweden. He is responsible for the clinical trials that Pfizer has in Sweden. This involves organizing the trials and having contact with doctors. Brun also works with policy makers in order to ensure that Sweden is, and will be in the future, a suitable place to carry out clinical trials. Brun has a educational background as a medical doctor.

Jörg Breitenbach is CEO of Abbott Soliqs, which is responsible for drug delivery at Abbott. Drug delivery is the part of the development process of making pharmaceuticals into products such as pills, injections, inhalers, etc. Breitenbach has a PhD in chemistry.

Saied Esmailzadeh is Sweden's youngest to become an associate professor. During his research Esmailzadeh found the strong glass suitable for different applications, which he commercialized by founding the company Diamorph, a kind of Venture Capital firm. He has thereafter formed the innovation incubator Serendipity Innovations that commercializes research from universities in Sweden.

Paul Ilott is the lean sigma master black belt of the global R&D function within AstraZeneca. He is a PhD in mechanical engineering with the focus on energy management. He started his professional career at 3M working with lean management and came to AstraZeneca 10 years ago. Ilott heads a cross R&D project with the purpose to improve innovation in AstraZeneca.

Craig Johnstone is has a PhD in synthetic organic Chemistry and started to work at AstraZeneca after completing his research 15 years ago. He has been director of chemistry for a cardio vascular group in the UK. He is also involved with the innovation group that Ilott heads.

Staffan Josephson is currently CEO at Heart-Lung Foundation in Sweden and serves as a business consultant for Investor Growth Capital along with several board assignments at small and medium sized biotech companies. He is a professor in organic chemistry and served as VP of research at Kabi and Pharmacia during the 80s and 90s.

Lennart Hansson is investment manager of the business area life science at the venture capital company Industrifonden. He is a PhD in genetics and has a professional back-

ground from many of the important actors on the Swedish life science market, with executive positions at KabiGen, Symbicom, AstraZeneca, and Karolinska Development.

Marianne Hansson is CEO at AtlasAntibody. AtlasAntibody is commercializing the founding from the big Human Protein Research project, which aims to characterize the whole human proteome. AtlasAntibody sells self developed antibodies directed to find specific proteins and look at protein expression profiles of different cancers in order to develop candidate drugs. These candidates are still in early discovery phases. Hansson is a researcher from the Royal Institute of Technology within Biotechnology.

Pia Keyser is research director at Creative Antibiotics a small biotechnology firm developing the next generation of antibiotics. Keyser is chief of research at Creative Antibiotics and also responsible for all research collaborations the company executes. Her educational background has resulted in a PhD in molecular biology.

Erik Kinnman is chief strategic officer and head of investor relations at Swedish Orphan Biovitrum, which is a pharmaceutical company that specializes on orphan drugs and employs around 300 people. Kinnman is MD, PhD and Associate Professor from Karolinska Institutet and holds an MBA. He has held many senior leadership positions at AstraZeneca among other and also worked within the finance sector.

Ingemar Lagerlöf is CEO of Linkmed a small Venture Capital firm investing in start-up companies within life science. He has worked within the pharmaceutical industry for more than 30 years with companies such as Santos (now Novartis), KabiVitrum, Pharmacia & Upjohn, and Fisons Pharmaceuticals.

Björn Nilsson has experience from a range of leadership position in different pharmaceutical companies like KabiGen, Genentech, Pharmacia & Upjohn, Amersham Pharmacia Biotech, Karo Bio, Biacore, and Biovitrum and is now president of the Royal Swedish Academy of Engineering Sciences (IVA). He is a PhD and associate professor in biochemistry from the Royal Institute of Technology.

Anna Nilsson Vindefjård is initially a researcher in entrepreneurship and commercialization at Karolinska Institute and Stanford University. She has focused her studies on how scientific findings in the life science sector have been commercialized. Today she is director of research and innovation politics at LIF the industry association for researching pharmaceutical companies and also researcher at Karolinska Institute.

Katarina Nordqvist is a PhD and associate professor from Karolinska Institute. She has worked as a director for a research group at AstraZeneca and headed the Swedish governmental agency for innovation systems VINNOVA's section for Biotechnology. Today she is head curator and head of public programs at the Nobel Museum.

Marek Poszepczynski is investment associate at Karolinska Development a venture capital company focusing on investment in early stage pharmaceutical ventures mainly on ventures from Karolinska Institutet. He has also worked as a business controller at Biovitrum.

Eugen Steiner is a partner at HealthCap one of the biggest (in investment size) Swedish venture capital firms focusing on investments in life science. Steiner is a medical doctor and researcher and has also worked as a physician. He is responsible for HealthCap's investments and is often appointed as CEO in the start-up companies that HealthCap invests in.

Mats Strömqvist is CEO of the biotech company OmnioHealer, which is a part of a project group of Pergamum working with dermatology and wound healing. The company's project is in late preclinical trials. Strömqvist has 20 years of experience from different pharmaceutical companies like AstraZeneca and Pharmacia.

Thomas Uhlin is CEO of Aprea a company working with a pharmaceutical developed towards cancer patients. The company's product is in phase II clinical trials. Uhlin has experience from among others Pharmacia, Orexo and Doxa. He holds a B.Sc. in biology from Uppsala University.

