Being public in the Dutch private life science sector

EXECUTIVE SUMMARY

The biotech science industry is a relatively new industry, since it started to develop in 1970. The global market leader, with difference, in biotech is the US biotech industry, which is measured in aspects such as available financial capital, entrepreneurship, social acceptance, total revenue, etc. After the leading position of the US biotech market comes to European biotech market. The entrepreneurial spirit, management performance and role of the small biotech firms are very well developed in the US biotech market. In turn these aspects are less developed in the European biotech market. Therefore in this thesis these aspects are analyzed in both the US biotech market and the European biotech market. In addition, the management performance aspect is analyzed in more detail. Biotech managers learn best through work experience as biotech managers and from other biotech managers that are more experienced. For small biotech firms to perform mutual research with large biotech firms allows the small biotech firms to learn from more experienced large biotech firms how to cope with future growth stages. In The Netherlands there exist a shortage of large life science firms. Also are the large life science firms in The Netherlands spread very diverse throughout different clusters. Therefore for small firms it is not just about cooperating with firms that are established in different clusters, but being actually present in the different clusters. By being present in different clusters, biotech firms are able to learn from more parties. In addition small biotech firms in The Netherlands should try to set up more research cooperations with other biotech firms, as there exist very few cooperations between private biotech firms. While in the UK and the US there exist many cooperations between private biotech firms. Furthermore for small biotech firms in The Netherlands, to improve their performance it is best to cooperate with firms from other EU-countries and non-EU counties. Therefore, the focus of research cooperation for small biotech firms in The Netherlands should be on large and medium sized biotech firms outside The Netherlands. In order to improve the performance of small biotech firms in The Netherlands, small biotech firms in The Netherlands should allow more experienced biotech parties like suppliers of capital or medium sized and large biotech companies, to advice or take part in the management board of small biotech firms.

Keywords: *biotech, small biotech firms, large biotech firms, alliances, biotech management, entrepreneurial spirit, management performance, non-Dutch biotech alliances, third party influence*

FOREWORD

‘’If you're playing baseball and thinking about managing, you're crazy. You'd be better off thinking about being an owner.” (Casey Stengel)

Biotechnology as an industry experienced growth during the last four decades and is therefore considered a relatively new industry. Nevertheless the industry has already become increasingly essential to many different areas of modern life, e.g. agro-food, bio(pharmacy), chemistry.

The objective of this thesis is to set the difference between more efficient and less efficient functioning biotech firms in The Netherlands, from a managerial perspective.

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CHAPTER 1: INTRODUCTION AND GENERAL PERSPECTIVE OF THE BIOTECH INDUSTRY

In this first chapter the industry that is to be researched, the biotech industry, will be introduced through a general analysis; which includes the history and development of the industry, followed by the current situation of the global biotech industry.

1.1. The history of the biotech industry

Although biotechnology finds its roots much earlier in time, in the form of the cross-breeding of animals and the development of hybrid plants, for this thesis the focus is on ‘modern biotechnology’, which began in 1973. This revolution started with the new innovation ‘DNA recombinant technique’. Recombinant DNA is a method of making proteins, such as human insulin and other therapies-in cultured cells under controlled manufacturing conditions. Stanley Cohen of Stanford and Herbert Boyer of University of California-San Francisco discovered the basic technique for recombinant DNA, which became the foundation for genetic engineering (Cohen et al., 1973). As a result from this innovation, new companies started, whereas some as early as 1975 and 1976 (Zucker and Darby, 1997a; Zucker and Darby, 1997b). Boyer spun-off from the university and started Genentech, which today is biotechnology's largest company by market capitalization. In 1980, with the objective to promote commercial development of new technologies, the US government started to encourage universities and other institutions by granting the patenting of innovations in micro-organisms. This new legislation falls under the Bay-Dohl Act, which in the US has encouraged universities to get ownership in their research and development. The seminal Bay-Dohl Act (1982) made it easier for US universities and federal laboratories to realize financial gains through the patenting of technologies that were developed with public funding. Driven by such policies, interaction between the public and the private sector intensified. The results from a study performed by US university technology managers indicated the advance of the market through this legislation. In addition US university licensees increased with 75% between 1991 and 1996. Furthermore in 1997 universities and research institutions received $611 million in licensing fees, up from $248 million in 1992 (Rauser, 1999).

The patenting of innovations in the life science market resulted in the move from the ´common model´ toward the ´privatization model´. In the common model all research is public and innovations are freely incorporated in “downstream” products for diagnosing and treating disease. In the ´privatization model´ the government functions are transferred to the private sector, e.g. ownership, financial support. According to Heller, both the ´privatization´ and the ´commons´ model have promises and risks. What favors the privatization model is that patents and other forms of intellectual property protection for innovations create incentives to undertake risky research projects and could result in a more equitable distribution of profits across all stages of R&D. This argument is also the downside of the privatization model, where privatization can cause an astray, in case too many patents exist and in turn block future research (Heller, et al., 1998). The possibility of patenting created an explosive growth of companies in the biotechnology. One year after the first patent was granted in the U.S., eighty new companies were found in the U.S. biotechnological sector. As a result from the explosive growth of US life science companies discussed above, there are currently in California two areas of global importance: one at San Diego-La Jolla, south of Los Angeles, and the other at Bay- Area, near San Francisco. These areas are defined as clusters. A cluster is defined as an interconnection of enterprises and institutions in a precise sector of knowledge, with the establishments close to each other and interconnected through all kinds of networks, starting with those concerning clients and suppliers. In both biotechnology clusters, it does not take more than 10 minutes to move from one company to the other (Sassen, 2004). These clusters have for example the objective to lower the average time to set up a licensing contract between a university and a biotechnology company, which took in 2004 about ten months. These ten months is considered too long, and the cluster association gathers all the stakeholders to discuss the relevant matters and conclude rapidly (Mamou, 2004).

In addition, several large American chemical companies invested for hundred millions of dollars in the biotechnological industry’s R&D. Continuously the biotechnology advanced with rapid pace; as a result biotechnology has brought forward more than 200 new therapies and vaccines, of which products to treat cancer, diabetes, HIV/AIDS and autoimmune disorders. Biotechnology is furthermore responsible for hundreds of medical diagnostic tests that keep the blood supply safe from the AIDS virus and detect other conditions early enough to be successfully treated. Also home pregnancy tests are biotechnology diagnostic products.

1.2. Defining the biotech industry

The word 'biotechnology' was introduced in 1919 by a Hungarian engineer, named Karl Ereky, to refer to methods and techniques that allow the production of substances from raw materials with the aid of living organisms. many studies set their own definition of biotechnology. This in turn creates difficulties, while analyzing the biotechnological industry. There is however one definition generally accepted, which will also be the definition that is used in this report. This standard definition of biotechnology had been set during the Convention on Biological Diversity (1992):

'Any technological application that uses biological systems, living organisms or derivatives thereof, to make or modify products and processes for specific use'.

This definition was agreed by 168 member nations, and also accepted by the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO) (Sasson, 2004). Biotechnologies are a collection of techniques or processes using living organisms or their units to develop added-value products and services.

Biotechnology is a very broad concept and covers many different areas and as mentioned in the introduction, the industry has already become increasingly essential to many different areas of modern life, of which a broad range of bio-industries have risen after the commercializing and industrialization of biotechnology. Biotechnology has applications in four major industrial areas, specified in the table below; (medical) health care, crop production and agriculture, (industrial) non-food uses of crops and other products (e.g. biodegradable plastics, vegetable oil, biofuels), and environmental uses Biotechnology and bio-industry are becoming an integral part of the knowledge-based economy, because they are closely associated with the progress in life sciences, and the applied sciences and technologies linked to them. These four sectors are closely associated with the economic impact of human-induced change to biological systems (Graff and Newcomb, 2003).

Table 1: The four major industrial areas of biotechnology

AgBio/Agro-Food	Veterinary healthcare, biopesticides, plant agriculture, food technology, biocleaning, bioremediation, water treatment, waste recycling, white biotech, green biotech.
Human healthcare	Biomaterials, drug delivery, drug discovery, gene therapy or healthcare cell therapy, genomics, vaccines, red biotech.
Environment / Biodiagnostics	Environmental diagnostics, industrial diagnostics, healthcare diagnostics, bio-chemicals, equipment, instrument, and miscellaneous.
Service concerns / General biotechnology	Bioprocessing. chemicals, contract research, contract manufacturing; bioinformatics, functional genomics, high throughput screening.

Source: Life Sciences Monitor, 2005; Critical I comparative study for EuropaBio (2006)

Biotechnology is highly significant because it is a very space intensive industry that requires a continuous physical presence in the urban core and face to face relationships with universities, hospitals, and governmental entities that remain present in the urban core. Therefore biotechnology is characterized by industrial filtering (Bingham et. Al, 1993) which refers to the tendency of establishments to locate in metropolitan areas when they are new, because proximity to the higher skilled, higher cost labour associated with metropolitan locations is relatively important; and because of the imperative of entrepreneurs retaining close ties with research centres and hospitals. These close ties exist moreover, as biotechnology deals with fundamental research into the application of new scientific knowledge which is highly tacit and codified knowledge, in turn making it very difficult to transfer the knowledge abroad.

The process of bringing a product to the market can take anywhere from 10 to 15 years (see appendix, figure vii) and the costs of bringing it to market can get as high as 800 million US dollars (Fair, 2005). In addition, the life science industry has become more science intensive and innovation-driven, which makes it hard to select the start-up with the most potential. This has resulted in relationships between small start-ups who do the

R&D during the first five until seven years and the large pharmaceutical firms that commercialize and manufacture the viable products (Bingham et. Al, 1993).

Biotechnology develops both process and product innovations (Life Sciences Monitor, 2005: EuropaBio, 2006); within the agricultural sector for example, consumers are able to eat the biotechnology product innovations such as papaya, soybeans and corn. Biopesticides and other agricultural products also are being used to improve the food supply and to reduce our dependence on conventional chemical pesticides. Besides product innovations, biotechnology consists also of process innovations; environmental biotechnology products create the possibility to clean up hazardous waste more efficiently by harnessing pollution-eating microbes without the use of caustic chemicals. Also industrial biotechnology applications have led to cleaner processes that produce less waste and use less energy and water in such industrial sectors as chemicals, pulp and paper, textiles, food, energy, and metals and minerals. Furthermore the biotech process of DNA fingerprinting has dramatically improved criminal investigation and forensic medicine, as well as afforded significant advances in anthropology and wildlife management. This historical progress of the biotechnology sector has led to the current situation where there are more than 400 biotech drug products and vaccines currently in clinical trials targeting. The above described wide range of biotechnologies, from the most simple to the very sophisticated ones, gives each country the possibility to select those biotechnologies which suit its needs best. Each country can distinguish itself by specializing in a certain area(s), e.g. developed countries that use in vitro micro propagation and plant-tissue cultures to become world leading exporters of flowers and commodities (Sasson, 2004). The potential of the bio-economy to spur economic growth and create wealth, through enhancing industrial productivity, is unprecedented (Sasson, 2004). Therefore high income and technologically-advanced countries have invested heavily in research and development (R&D) of the life sciences, biotechnology and bio-industry. In 2001, the worldwide bio-industry was estimated to have generated $34.8 billion in revenues and employed about 190,000 persons in publicly-traded firms. The growth of the biotech industry has been impressive, as in 1992, the bio-industry was estimated to have generated $8.1 billion and employed less than 100,000 persons. The regions that mainly benefited from the 'biotechnology revolution' and derived bio-industries are the industrialized and technologically-advanced countries, those regions that invested heavily in R&D and technological innovation of the biotech sector. These regions are the USA, Canada and Europe, which represent together for 97% of the global biotechnology revenues, 96% of persons employed in biotechnology ventures and 88% of the total biotechnology firms.

1.3. Three different types of companies in the biotech industry

The biotech industry can be divided into three different company groups: 'dedicated life science companies', 'diversified life science companies' and 'next life science companies' (SenterNovem, 2005). The main difference between these different biotechnological company types is their research and development commitment (see the table below).

Table 2: The three different company types of biotechnology

'Dedicated' life science companies	Under this umbrella fall companies that focus only on biotech R&D, which is their core business. The main functions of these types of companies are R&D and the application of biotechnology in processes, products and services. These companies.
'Diversified' life science companies	This group of companies have integrated biotechnology in their already existing R&D and product activities. Besides biotech, these type of companies focus also on other industries for R&D, e.g. Unilever, Akzo-Nobel.
'Next' life science companies	This group of companies does not perform R&D research in biotechnology, however they incorporate already developed biotechnological products of others in their with their business activities.

In general the dedicated biotech companies are relatively small in size, generally represented by start-ups and SME´s with less than ten full-time employees. Meanwhile the diversified biotech companies are generally represented by large companies with at least ten full-time employees (BioPartner Network, 2005). The dedicated biotech firms represent generally start-ups or relatively young biotech firms and as these companies become more experienced and increase in size they grow into diversified biotech companies. Furthermore, the dynamism of the biotech industry is represented by the entry (start-ups) and exit (mergers, bankruptcy) of the biotech companies (Life Sciences Monitor, 2005).

Four different business models distinguish the dedicated life science companies; the ´tool company´, the ´product company´, the ´service company´ and the ´hybrid company´ (biopartner, 2004). The ´service dedicated biotech company´ is specialized in research and development of drugs and try to attain agreements with large pharmaceuticals, as the service companies generally have limited resources (Mamou, 2004). The ´tool dedicated biotech company´ has another form to secure their continuity; at first through subsidy and after the start-up through royalties and licensing. This different income structure is a result of the nature of the tool companies, which is focused on ´platform technologies´. These technologies are characterized by a range of scientific investigations that are more focused on the long-term. Large pharmaceutical try to find radical innovations that will boost their sales and income through the cooperation with these dedicated 'tool' biotech companies, e.g. Viagra. These co-operations enable the large pharmaceuticals to streamline some stages of their research, e.g. the screening of compounds that may lead to a medicine. Due to this long-term focus, direct income is not obtained to cover the short term expenses of the tool company, hence the need for subsidy and other similar forms of income. The ´product dedicated biotech company´ is committed to further development and sales of products. These activities grant the product companies with direct income. The ´hybrid dedicated biotech company´ is a combination of two of the above described business models.

The remainder of this thesis will focus on how life science firms that perform R&D manage their costs and income and whether their operational processes as attaining income and performing R&D is managed in a efficient matter. This of course to investigate whether life science firms are performing just as well on in practice as they do theoretically. With theory is meant publications etc, while practice means the actual operational performs (R&D performs, income and costs). Therefore, in order to see whether the biotech firms that perform R&D are managed in an efficient matter, this report will continue its focus only on biotech firms that perform R&D, which are the 'dedicated' and ´diversified´ life science companies. Of course due to the characteristic of next life science companies that they do not perform R&D, they are excluded from the remainder of the report.

1.4. Assessment of the biotech industry

Although no common used assessment exists of the biotech industry, most assessments used by scholars show a number of similar indicators for assessment. The European commission for example developed a ´Biotechnology Innovation Scoreboard´ (BIS), which functions as a benchmark exercise that measures innovation in biotechnology across Europe:

Biotechnology Innovation Scoreboard (BIS) of the European commission

Indicator	EU leaders (nos. 1, 2)
PhD graduates in life sciences per capita	France, Ireland
Government biotechnology research and development expenditures as a percentage of gross domestic product	Belgium, United Kingdom
Biotechnology publications per capita	Sweden, Denmark
Citations per publication in biotechnology	United Kingdom, Germany
Biotechnology EPO patent applications per capita	The Netherlands, Denmark
Biotechnology USPTO patents granted per capita	Denmark, Finland
Dedicated biotechnology firms per capita	Sweden, Ireland
Biotechnology venture capital as a percentage of gross domestic product	Belgium, Germany
Drug approvals per capita	Denmark, Ireland
Field trials in GMO crops per billion gross domestic product in agriculture	Belgium, Sweden
Public understanding of biotechnology	Sweden, The Netherlands

Source: European Commission Enterprise, 2003

The scholars that criticize the Biotechnology Innovation Scoreboard say that the number of publicly available indicators varies between countries. This in turn causes an inconsistent measurement of the R&D levels (as in some countries certain indicators are not measured), employment and outputs (European Commission Enterprise, 2003). Another argument against the BIS is that innovation indicators as collaboration between public and private organizations are lacking.

The OECD agrees to several indicators of the BIS for the assessment of a biotech industry; total expenditures on biotechnology R&D by biotechnology-active firms and by public sector, total number of biotech firms, number of dedicated biotech firms, number of biotech start-ups, people employed, sales, granted patents and application patents (OECD, 2005). In turn because two different international representative institutions (the OECD and the European commission) agree on similar variables, these variables are selected for the assessment of a biotech industry in this report:

Private and public expenditure on R&D, patents, financial status (availability of venture capital, debt and equity), people employed (in total and in R&D), number of start-ups, revenue, number of biotech companies.

To evaluate the selected indicators of the OECD for assessment of the R&D; the use of patents and R&D as indicators could be questionable, as the level of R&D expenditure does not guarantee a certain level of performance. A high expenditure of R&D could also simply implicate an inefficient R&D process. Patents do not say much about the potential of the innovation. A biotech company could have twenty patents with very low profits. While visa versa a biotech company could have only two patents, while making an enormous profit.

1.4.2. Measuring the efficiency of a biotech firm

The Dutch institution ´Wetenschappelijke Raad voor Regeringsbeleid´ emphasizes on the following indicators for assessment; the R&D investments, the number of patents, the number of new products (Wetenschappelijke Raad voor Regeringsbeleid, 2003). Yet the scholar Fuchs add besides the number of patents; the indicators R&D personnel and access to laboratories (Fuchs, 2003). While Cooke et al. set the following indicators; employment, turnover, R&D expenditure, number of patents (Cooke et al., 2007).

The OECD provides a similar set of indicators as the ones put above, and additionally adds some different ones; turnover of the organization, investment in R&D, number of R&D researchers, number of personnel, number of establishments of the firm, number of patents (both granted and applications), number of publications, number of established cooperation for R&D projects with other organizations (OECD, 2004).

In turn, the variables that are mentioned by different sources will be used in the research of this thesis:

Employment (number of employees, number of managers, characteristics of management; educational background and work experience), financial resources (e.g. venture capital), investment in R&D versus turnover, granted patents, new products, obtaining capital.

1.5. Assessment of the efficiency of biotech managers

One indicator used in this report to assess the efficiency of life science firms managers is the *net profit margin*. This indicator shows the management´s ability to generate profit and is calculated by the net income divided by turnover (Berman et al. 2006). A decreasing profit margin shows that costs and expenses are rising faster than sales, which indicates an unhealthy sign. Relating the profit margin to management performance in the life science industry; a higher profit margin gives a good indication that the management of the biotech firm in question is managing in a better way than the management that have lower profit margins as result. With this indicator all income, including investment capital (e.g. venture capital), is seen as profit.

Another indicator to assess the efficiency of life science firms managers is the *return on investment,* in this report also referred to as ROI. The return on investment is calculated simply by dividing the capital gained from investment by the capital invested. The result of the ROI calculation is given with a percentage. In turn, the higher the return on investment, the better management performs. Management´s operating effectiveness is proven if the company can prosper, obtain funding and rewards the suppliers of its funds (Friedlob et al. 1996).

1.6. The global biotech industry

Table 3: Global biotechnology statistics

Global Biotechnology at a Glance in 2006	Global	USA	Europe	Canada	Asia-Pacific
Public company data					
Revenues (US$m)	73,478	55,458	11,489	3,242	3,289
R&D expense (US$m)	27,782	22,865	3,631	885	401
Net loss (US$m)	5,446	3,466	1,125	524	331
Number of employees	190,500	130,600	39,740	7,190	12,970
Number of companies					
Public companies	710	336	156	82	136
Public and private companies	4,275	1,452	1,621	465	737

Source: Ernst & Young
Numbers may appear inconsistent because of rounding
Employment totals rounded to the nearest hundred in the U.S., and to the nearest 10 in other regions

When assessing the markets of the global biotechnological industry individually, as mentioned before, the indicators will be used of the last paragraph; part ´1.4.1 Measuring the performance of the biotech industry´. These indicators appoint the US as having the best biotech market. Some of these indicators are shown in table 3 and 4 and in addition can be seen that the US is performing best on all the indicators in these tables, except for the number of firms in which Europe performs best. In the appendix fig. i., can be seen that Europe is spawning most new life science ventures in comparison to the US. While in the appendix, figure ii until iv, can be seen that the US performs best on sales, R&D (which also appears from table 2) and patents. The second best market in the world is Europe, which is clear from table 2 and the appendix i until iv, followed up by Asia. However the biotech markets of the US and Europe have by far the best results on the indicators used for assessment. This is also confirmed by Ernst and Young in their comparison of the three markets in 2006.

Table 4: Different indicators assessment Europe and US

	US	Europe
Product approvals	36 (2006), 33 (2005)	27
Capital raised increase	38% from 2005 to 2006	45%
Revenue growth in total	13% from 2005 to 2006	13% from 2005 to 2006**
Revenue in total	US$59 billion (2006)*	US$16.6 billion
Total capital		US$5.9 billion
Venture capital		US$1.9 billion
Compounds in pipeline		700 (public), 800 (private)

**The US revenue grew by 13% among public and private biotech companies to US$59 billion, and the industry made a truly historic move toward profitability.*

*** 2006 marks a four-year turnaround, from the 12% revenue decline recorded in 2003.*

The US life science market is experiencing a higher stage of maturity and decreasing number of patents of life science firms than the other biotech markets (Ernst and Young, 2006). Therefore, what characterizes the US life science is a restructuring of the market through mergers and acquisitions. In Europe restructuring is also occurring; "In 2005 there was cautious optimism in the European biotech industry — as the sector emerged from a prolonged period of restructuring," said Siegfried Bialojan, Germany Biotechnology Leader, Ernst & Young. "In 2006, double-digit revenue growth — and sustained success across multiple measures — prove Europe's biotech sector has bounced back." In the Asian-Pacific market (Japan, China, Australia, South Korea, India, Taiwan, New Zealand and Singapore), countries started to develop their biotech industry later than their European and US counterparts, however it is developing with a faster pace than the North-American and European countries. This is primarily due to low costs, strong government support, large talent pool and biodiversity (Ernst and Young, 2006). In the future both India and China are expected to emerge as leading players in the global biotechnology market (Ernst and Young, 2006). Foreign investment in the Indian and Chinese pharmaceutical-industry has historically been low, as neither country allowed patents on pharmaceutical products. Now, however, both countries permit drug patents, have established mechanisms for patent enforcement, and have reached compliance with the World Trade Organization and the Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) (Ernst and Young, 2006). These developments are drawing foreign investment. The future strength of India and China is their human capital (National Science Foundation, 2006).

1.7. Conclusion first chapter

The life science sector is a very broad sector, covering many different areas and having impact on many different sectors. In addition, the life science sector is still an upcoming market, however considered as an industry with an enormous potential and an essential part of a knowledge economy. In this chapter the biotech industry have been analysed through its four major industrial areas; AgBio/Agro-Food, Human Healthcare, Environment / Biodiagnostics and Service concerns / General biotechnology. As these four areas cover the whole life science industry, this report will analyze these four areas accordingly. Concerning the three life science company types that were covered, the focus will be on biotech firms that perform research & development, to investigate how biotech firms handle their costs and income with research and development. ´Next life science firms´ do not perform research and development and for that reason only dedicated and diversified life science companies will be investigated. Since globally the biotechnological industry is dominated by the USA with a distinguished differences over the rest of the world, the focus is narrowed to the two most important biotech markets, the US and Europe. This in order to investigate the generally known ´entrepreneurial spirit´ of the US and the relating behavior of the European biotech market to gain a similar success. This assessment will be described in the next chapter; ´ The biotech industry in Europe and the US´. The analysis of Europe and the US is followed by an analysis of a European representative, The Dutch life science market. During this analysis the Dutch biotech market will be described first, followed by a theoretical framework that covers the different areas concerned with managerial characteristics of efficient and less efficient functioning firms. This in turn results in the following research question:

Research Question: '*What are the determining differences in management skills between managers of more efficient and less efficient functioning biotech firms in The Netherlands?´*

In turn the research question links the theoretical framework discussed earlier to the empirical study in the final chapter, which should determine the managerial differences between more efficient and less efficient functioning biotech firms in The Netherlands.

CHAPTER 2: THE BIOTECH INDUSTRY IN EUROPE AND THE US

2.1. Europe vs. US - introduction

With the discovery of the DNA structure that resulted in the modern biotechnology in 1970, insights were created into disease processes and potential treatment. These insights were further advanced by ambitious and far-sighted scientists, who began to apply academic research to produce market products, which in turn resulted into the biotechnological revolution and introduced the fundamental change to the manner in which drugs are researched and developed and marketed. Biotechnology as an industry in Europe is relatively young, in which the earliest biotechnology companies emerged in the 1980's through entrepreneurs such as Sir Christopher Evans. (Biotechnology in Europe, CEBR). Through the 1990's, the attitudes towards investment and risk changed and biotechnology companies started to emerge more in Europe. Meanwhile the US biotech market already experienced growth since 1970. Many of the early breakthroughs in the biotech industry and the first true biotechnology company, Genentech Inc. started on the West Coast of the USA, e.g. California and Massachusetts. This region benefited from the brainpower that came from nearby universities and from debate over the new kind of research (The history of biotechnology, 2007). The relation between these different parties created the spawning of many small biotech firms, which in turn were an important factor behind the success and global leadership of the biotech industry in the US (Senker, 1998).

Table five on the next page provides the remaining indicators which are used as assessment of a biotech market, according to the last paragraph of part ´1.4.1 Measuring the performance of the biotech industry´. In part 1.5 ´the global biotech industry´, both the US and European biotech market were already discussed. In addition to part 1.5., table 5 adds new indicators, namely the financial indicators (venture, debt and equity capital) and the indicator ´start-ups´ which are now used to finalize the assessment of the US and European biotech market. As can be seen in table 5, the US life science market is outperforming the European life science market in every aspect, except for the number of life science companies.

Table 5: The differences in the biotech industry between Europe and the US in 2004;

	Europe	US
Number of Companies	2163 companies (2003: 2200)	1991 companies (2003: 1975)
People employed	96.500 (incl. 42.500 in R&D). In 2003: 96.000 employed (incl. 42.000 in R&D).	190,500 people (2003: 170,500)
R&D	€7.6 billion in R&D (€7.6 billion in 2003)	€21 billion on research and development (2003: €20 billion)
Revenue	€21.5 billion revenue (€20.5 billion in 2003)	€41.5 billion of revenue (2003: nearly €40.5 billion)
Venture capital raised	€1.1 billion in venture capital in 2004 (€787 million in 2003)	Raised €2.5 billion in venture capital in 2004 (2003: €2.2 billion)
Equity raised	€2.1 billion through equity in 2004 (€1.45 billion in 2003)	Sold €5.3 billion worth of equity – largely through the public markets (2004: €3.5 billion)
Debt financing raised	Raised over €1.8 billion in debt financing in 2004 (€1 billion in 2003)	Raised a further €6.6 billion of debt (2003: €6.0 billion)
New companies formed	119 new companies in 2004 (over 130 in 2003)	Formed 78 new companies

Source: Critical I comparative study for EuropaBio (2006)

2.2. Europe vs. US – First mover advantage

A first factor that have led to the beneficial differences for the US has been caused by the earlier market development of the US life science market, which started developing a decade earlier than the European life science market and thereby allowing a more rapid development towards maturity (COGEM, 2004).

The differences between the US and European life science market, will further be analyzed through a political, economic and social (PES) analysis.

2.3. Europe vs. US – Political differences

The most significant influences that cause the diminishing growth in the European biotech industry are: the lack of capital that allows biotech firms to grow and the complex government regulations towards the biotech industry (Ministerie van Economische zaken, 2005). This complexity of politics is generally caused by the administrative bureaucracy, complex laws, public attitude and the relatively long duration of licensing (Ministerie van Economische zaken, 2005).

2.3.1. Europe vs. US – Government legislation

A very important aspect of government legislation relative to the biotech industry is to increase the efficiency of the drug approval process, and thereby lower the development costs for the biotech industry. In the US there exist the US Food and Drug Administration (FDA), of which one task is to supervise the biotech market. One important contradiction between the European Union regulator and the US´ FDA is that the FDA does not regulate the prices in the US biotech market (The Economist, 2003). In the US, the biotech companies can set prices on market demand, while in the European Union the biotech companies have a limit when setting their price. This in turn makes the US biotech market far more beneficial in comparison to the European biotech market. In Europe, biotechnology-derived products have to go through the European Union regulator for the evaluation of medicinal products (EMEA) which has been working since 1995. This agency functions with a centralized drugs-approval process, which according to the chief executive of Serono SA, the Swiss company that is the third biggest in the global bio-industry, operates too bureaucratic with decision-taking. With the European agency ´EMEA´, decisions were made in private sessions. Contrarily to the US agency, the European agency does regulate the drug prices, which has negative impacts on the European biotech market. The success and survival of a firm in the biotech industry, indifferent of its nationality, depends on its ability to generate an annual income that is close to the average of most similar enterprises, and spend an eighteen to twenty percent of its turnover on R&D (Sasson, 2004). Both these ratios depend on the price of drugs. Ironically, the U.S. gained its advantage in biopharmaceuticals over Europe by the exorbitant costs of its inefficient health care system. In Europe, government interventions such as cost control measures, cut-backs on state-reimbursed pharmaceutical purchases, health care reform, and pressures on physicians to limit prescribing have greatly decreased profit margins for life science companies and thereby slowed down the growth of the European life science market (Williams and Gwilym, 1998). In France for example, where the government fixes the price, it is increasingly difficult for biotech companies to meet the needs of both shareholders and researchers. Due to this strict government regulation, currently most of the large European biotech companies wish to make 50% of their annual turnover on the US market, where the prices of drugs are free of regulation and profits are much higher (Mamou, 2004). As a result, the investment capital meant for the European life science market is also moving to the US life science market. The investments of large biotech companies are generally done in the area where the expected profits are highest, hence the movement of investment capital to the USA. Consequently the research-and-development centres of the large European biotech companies are not threatened, but they are exposed to the risk of being outpaced by US groups or companies. A recent study by Rexecode showed that the US share in global drug production was increased by 5.3% between 1986 and 2000, while it decreased by 3.1% in Germany and 1.7% in France (Mamou, 2004).

2.3.2. Europe vs. US – the patent structure

In this part, two patent application systems are discussed. In one patent application system, the first person that registers an invention to obtain a patent for it, will be granted the exclusive right to make and/or sell the invention. This patent application systems is used everywhere in the world, except for the US and Canada. The other patent application system, which is used in the US and Canada, already grants the exclusive right to make and/or sell the invention when a person made the invention. With the patent application system that is used in the US and Canada it is not obligated to register the invention in order to obtain the exclusive right to make and/or sell the invention. Generally the most important difference between the two patent application systems is that the one where registration is obligated, large biotech firms have the advantage over small biotech firms because it is costly to register an invention. In turn small biotech firms generally have much less funds available to register an invention than large biotech firms. Furthermore, the patent application system in which registration is obliged, encourages the filing of too many, poorly drafted, and premature patent applications, which will increase the costs of using the patent system for all, especially for the small, independent biotech firms (Coster, 2002). In addition the patent application system in which registration is obliged can be costly when there is a dispute about who invented the invention first, which in turn will be more costly and more difficult for smaller independent biotech companies to win. When comparing the number of life science patents in the US to the number of life science patents in the rest of the world (see appendix viii), it becomes clear that the US was leading with 3331 life science patent applications in 2003. The EU ranks second with 2576 patent application and third comes Japan, with 1035 applications. In Europe, Germany has most patent applications, namely 901 life science patent applications. The second highest number of patent application has United Kingdom with 416 applications and France has the third highest number of patent application in Europe, with 370 applications.

2.3.3. Europe vs. US – public research funding

Another difference between the US and European biotech market, is the government (basic) funding structure to support the public research institutions. In both Europe and the US there exists a very strong support, however with difference, for the public research biotech institutions. The US functions with a long-standing policy, with the aim to ensure the US pre-eminence in life sciences research and its applications. First of all, in the US, pension funds are allowed to invest heavily in the biotech firms, while this is not allowed in Europe. This way the US has already billions of US dollars more to invest in life science companies than Europe. Besides the pension funds, the US has other governmental departments that invest heavily in the life science sector. As these US governmental departments cover an economic area with the size of Europe, the investments are of greater size invested in one specific cluster. While in Europe each country invests in its own cluster and is therefore more divided than the US. The US National Institutes of Health, for example, granted $27.9 billion to researchers and universities in 2004. This budget was increased by the contributions of other ministries like the Departments of Defense, Interior and Agriculture, as can be seen in the appendix, figure iib. Another form of funding associated with research was the government subsidy provided to combat bio-terror. This has helped many biotechnology companies specialized in immunology to survive in the US (Mamou, 2004). From appendix, figure ii a, b and c, it becomes clear that the US biotech market has much more investment capital available. In Europe for example, governments invest much less in ´basic biotechnological research or basic research´ (this is research that is exploratory and primarily focused on the advancement of knowledge) than in the US (European Commission, 2004). Such large public investment by the US in basic research encourages private investors to invest also in the life science market (Sasson, 2004).

The majority of research centres in Europe and the US are involved in several areas of biotechnology research. The life science research centres in the US focus for a very high percentage on their expenditure to basic research (50%). European centres however spend over 30% of their budgets on human biotechnology, followed by basic research (17%), cell factory (15%) and plant (12%) and animal biotechnology (10%).

Before 2004 there existed a clear gap between the structures of the European and the US public research funding. In Europe, only half of the biotech research institutions foster the commercializing of their inventions, while in the US three quarters of the biotech research institutions foster the commercializing of their inventions (Peter, 2004). There existed notable exceptions in Europe of course, however the general situation was simply that the biotech research institutions in Europe did not seem commercial enough to become serious competitors of the US. The European research centres functioned more as excellent knowledge providers to the industry, a source of top-class education and training and an ardent publisher of scientific literature. In the US, the life science research centres focussed strong on fostering commercializing and basic research results, which in turn created an atmosphere of faster knowledge spillovers that flow from the US research centre via the spin-offs to the private market (Sasson, 2004).

In reaction to this, in 2004, initial steps were made by Europe to improve the legal and fiscal framework and access to capital for high-technology small and medium-sized enterprises like most of the developing European biotechnology companies. The European Commission presented an 'action-plan', intended to support entrepreneurship and start-ups in Europe (Gabrielczyk, 2004). In Belgium, biotechnology and high-technology SMEs were to benefit from a 50% reduction on their business´ income tax for company researchers who collaborate with public research institutions: the more the company invests in R&D, the more it will benefit from the tax exemptions to come into effect in 2005 (Gabrielczyk, 2004). The German government foresaw to establish a

€500-million fund by 2005-2006 for high-technology SMEs. This, together with the creation of special seed funds, was aimed at bridging the gap in equity financing for most of the research-orientated biotechnology companies with products under development (Gabrielczyk, 2004). As a result can be seen in table 1 that the number of start-ups in Europe has become higher than the US.

2.3.4. Europe vs. US – start-ups

The biotech start-ups firms are the most innovative biotech firms in medical biotechnology. Most innovations of biotech start-ups are a result from close collaboration with the universities. In the early modern biotechnological market, the universities across the US became origins for innovation, as entrepreneurial professors took their inventions (and graduate students) off campus to set up companies of their own. Since 1980, with the implementation of the Bay-Dole act, US universities have witnessed a tenfold increase in the patents they generate, spun off more than 2,200 firms to exploit research done in their laboratories, created 260,000 jobs in the process, and in 2002 contributed $40 billion annually to the US economy (Sasson, 2004).

Meanwhile also in the beginning of the 21^{st} century in Europe, the knowledge-driven economy started to develop with rapid pace. By the year 2000, the healthcare biotechnological industry had become a major growth industry. As a result massive public and private funds were invested into the sector and start-up companies emerged at an incredible rate. The capital injection in combination with the availability of experienced managers from a consolidating pharmaceutical sector resulted hundreds of biotech companies to emerge each year. Many regions in Europe started to focus on biotechnology and bio-communities started to emerge all over Europe, from Estonia to Spain.

In the US, the era of technology transfer was inaugurated by the Bay-Dole University and Small Business Patent Act of 1982 that permitted small businesses, universities and non-profit institutions to retain title to inventions resulting from federally funded grants and contracts. Theoretically Europe performed very well, as many of the original scientific discoveries that drove biotechnology were not made in the United States but rather in Europe, specifically Great Britain. The difference however appears in the transfer of knowledge spillovers from the public to the private market, whereas the U.S. because of its well-developed venture capital system and a greater acceptance of entrepreneurial endeavor has been much more adept at commercializing the original scientific discoveries (Sable, 2005).

2.4. Europe vs. US – Economic differences

2.4.1. Europe vs. US – private funding

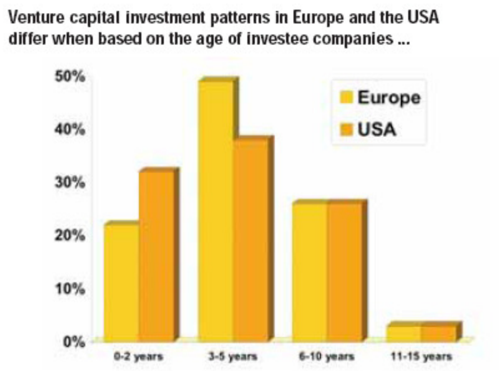
Biotechnology is a long term investment, in which it takes ten to fifteen years to gain the promised wealth. As a consequence the private investments in the early stage companies diminished significantly globally in 2001, along with the global economic downturn of that year. This slow down had a varying impact in Europe, clusters that had reached a critical mass diminished. As a result, some companies closed down, while other companies experienced simply a stop in their growth. The companies that stopped growing, minimized spending and transformed radically business models from platform technologies to product pipelines (series of products developed and sold by the life science company) to attract the reduced investment that remained available. ‘Platform technologies’ are technologies that enable the creation of products and processes that support present or future development. Access to appropriate platform technologies can reduce costs and avoid unnecessary duplication of facilities, increase international R&D competitiveness and provide an environment of effective networking and collaboration (The history of biotechnology, 2007). Thus life science firms with diminished growth changed their strategies from more exploratory research (platform technologies) to the actual development of goods for sale (product pipelines).

In 2001, the biotech industry in Europe was characterized by a more cautious venture capital market, where venture capital was and still is more difficult to obtain and in which companies are obliged to have a more global outlook as new regions start to become challenges. The more cautious capital market had the effect of diminishing funding for early stage investment and as a result reduced the rate of successful startup companies. This gap of financial support has started to be filled by public investment, especially for the newer biotechnological regions with planned, careful investment (The history of biotechnology, 2007).

Like American venture capitalists, European firms are returning to better days, although they never suffered as big a bust. Universities were becoming more reluctant to let academic research, whether in biology or engineering, mingle freely with commerce (Peter, 2004). Disputes over the fruits of intellectual property were becoming more common, and that is proving a barrier to venture capital investment (Sasson, 2004).

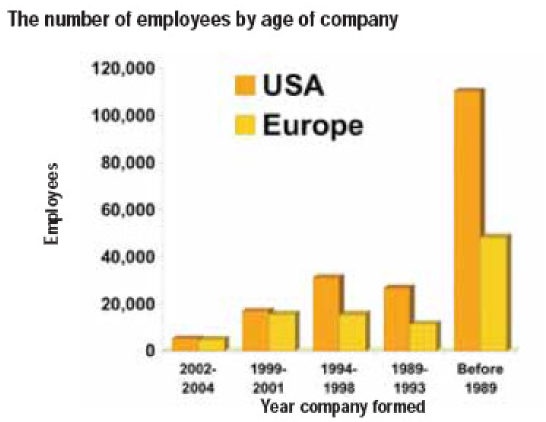
In turn as remains the case, the US still has a significant advantage over Europe (see appendix fig. 5). In 2004 the European biotech companies had much less venture capital (one fifth) available than the US biotech companies. Generally the European biotechnology industry is still not enough developed and is therefore to risky to attract the kind of substantial debt finance that is currently sustaining the US biotech market, which grows through growth-by-acquisition (Critical I comparative study for EuropaBio, 2006). The cooperation between politics, basic research and the biotechnological industry within a cluster is very important, however it would be meaningless without sufficient capital. In fact, the success of bio-industry is above all associated with an efficient capital market, according to David Pyott, chief executive officer of Allergan, the world leader of ophthalmic products and unique owner of Botox – a product used in esthetical surgery and the main source of the company's wealth. It would be impossible for any cluster to exist without a dense network of investors, business angels, venture capitalists and bankers, willing to invest in companies that form a part of the cluster (Mamou, 2004).

Concerning the willingness to invest in the life science sector, the US venture capitalists are characterized as generous, while the European venture capitalists are considered stingy and greedy.



Source: Critical I comparative study for EuropaBio (2006)

When looking at the age of the company and relate this to the investments of venture capitalists, there appear to be differences between Europe and the US. The venture capitalists in Europe invest less than the US in venture capital in start-up life science companies that exist one or two years (22% versus 32% of the total available capital for investors in US companies) and more than the US in mature life science companies that exist between three and five years old (49% versus 38%). In my opinion, it appears to be so, that European venture capitalists prefer to invest into companies that are more mature and have survived the critical start-up phase, while the US venture capitalists invest more in biotech start-up firms. In my opinion, through this early support from venture capitalists (for example through financial support, aid with management, access to new valuable contacts), biotech start-up firms have the possibility to develop their innovations better. It appears that the European venture capitalists let the biotech start-up firms grow themselves first. With the approach of the European venture capitalists, start-up biotech firms could go bankrupt just due to bad management, even when they have innovations with potential. In my opinion during the critical start-up years biotech firms can use all the help they can get, in terms of both financial and management support.



Source: Critical I comparative study for EuropaBio (2006)

In this figure can be seen that with age the firms develop into larger enterprises. Besides looking for new innovative behavior, the investors from both continents evaluate the biotech firms on a certain amount of substance and resourcing. From the appendix, figure 7 can be seen that the European venture capitalists invest nine percent of their portfolio in companies that were founded between 2002 and 2004, while the US venture capitalists invests twenty-two percent in these type of companies. However European investors have invested nineteen percent of their portfolio in biotech companies, that are very young, however had already grown to twenty people. In the US, this figure represents twenty-six percent of the portfolio. Concerning the company size, venture capitalists on both continents show similarities.

The focus of European start-ups remains on the venture capital set available in their own country rather than trying to compete on global markets. In Europe, banks still dominate early-stage investing with start-up biotech firms, while in the US venture capitalists supply the early-stage venture capital. Because banks are more risk averse than venture capitalists, the biotech start-up firms in the US obtain more venture capital than their European counterparts. In addition, European venture capital funds are still bonded by tax rules and regulations; for instance, many pension funds are not allowed to invest in assets that are deemed too risky, including venture capital (The Economist, 2004).

2.4.2. Europe vs. US – SME's

A brain drain of top-researchers from large biotech firms to small biotech firms is a very common occurrence. These top-researchers are attracted by the major changes that occur in cell and molecular biology. In turn these researchers become active in small companies where they pursue their research and try to contribute to drug discovery. Their objective is to repeat the occurrence of the late 1980s, where small companies have been very successful through developing treatments that did not yet exist.

Investment capitalists consider life science SMEs to have two common characteristics: to be a very risky investment and that the investments in life science SME´s show return after a long-term period (Sasson, 2004). To tackle these challenges, the US have been subsidizing and thereby stimulating the move from public research centres to the market. In Europe this has also started to occur since 2004 (Ministerie van Economische zaken, 2005). Through subsidizing, lightening the tax burden on innovative companies and improving the legal framework it has become easier in Europe for academic researchers to go into industry, which in turn has improved cooperation between public and private research (Francisco, 2004).

The gap between small biotech companies or start-ups and the bigger companies or large pharmaceutical companies has deepened. In 2003 about 60% of the 1,500 US biotechnology companies have between one and fifty employees, according to a study carried out by the US Department of Trade, and they must tighten their belt. At the other end of the spectrum, 1.9% of the companies have more than 15,000 employees as well as the same kind of revenue-earning as the conventional laboratories (Mamou, 2004).

The formation of new biotech companies is of course important, however the impact of these new biotech companies is very small. The life science start-up or young companies represent virtually a quarter (24%) of the total of European firms, yet they employ only just over 5% of the staff (see figure 2: The number of employees by age of company in the USA and Europe). Most people, of course, work in the largest, longest established firms: half of European employees do, and nearly 60% of US employees. The larger firms also contribute with higher proportion to revenue generation: in both Europe and the US, companies formed before 1990 earned four-fifths of the total revenue (see figure 2: The number of employees by age of company in the USA and Europe).

2.4.3. Europe vs. US – Mergers and Acquisitions and 'Elite biotech companies'

Although Europe possesses a high rate of world-class scientists, the European biotechnology market is generally characterized by a biotech market which lacks the right structure to compete with the US and faces financial crunch, which in turn may force many companies to seek mergers with stronger rivals (Firn, 2003). Actually, a key factor of the dynamism in the US biotechnology sector is the relentless movement toward partnerships, or even acquisitions, between the big pharmaceutical companies and biotechnology start-ups (Sasson, 2004). The main strategy that the big pharmaceutical companies follow is to find a few blockbuster drug innovations (innovations with annual sales above $1 billion). These blockbuster drug innovations allow the big pharmaceutical groups to be able to recoup the heavy investments made in research and development, and in the marketing and sales operations. In the study of Critical I (2006), an investigation was performed were 80% of the European biotech companies and 70% of the US biotechnological companies have been investigated, namely biotech companies which are 10 years old or younger (see appendix, figure 8). From figure 8 can be concluded that US biotech companies grow faster than their European counterparts. Later on in the theoretical part, the performance of firms will be related to mergers, acquisitions and other possible influential factors.

In terms of competition, the elite (large, multinational) European biotech companies can compete against US firms for finance, personnel and deals. However the main problem is that there are not enough elite biotech companies. Although Europe has more biotech companies quantitatively, the biotech companies have smaller equity (see appendix fig. 5). Meanwhile the US biotech firms employ twice the staff of Europe, spend about three times as much on R&D, and raise almost four times more venture capital (Critical I comparative study for EuropaBio, 2006). The shortage of European 'elite' life science companies is also because most large European pharmaceutical firms generate most of their profits in the United States because the profits are higher in the US, due to the unregulated prices as mentioned earlier in the report. This in turn has caused in turn a move of the large European pharmaceutical firms' R&D to the U.S.

2.5. Europe vs. US – The social differences

All surveys and enquiries of public perception or social acceptance of biotechnology (in both developed and developing countries) show an undisputable support for medical and pharmaceutical biotechnology, whose benefits are acknowledged by a high majority of respondents and interviewed people (Sasson, 2004). In people´s minds, health care is a top priority and anything that may improve it is obviously more than welcome. Increasing resistance of microbial pathogens and parasites to drugs does not deter the patients to consume the relevant drugs. The pharmaceutical R&D has the objective to lower this resistance, through the discovery of more efficient drugs, sanitary measures in hospitals to eliminate or mitigate diseases and by educating patients regarding drugs.

Other factors that create a better acceptance of society towards life science products in the US, are that medical doctors in the US are more willing to prescribe innovative ´new´ treatments, and direct-to-consumer advertising is not banned as it is in Europe (Business week, 2003). Besides the public acceptance, the overall social acceptance of medical and pharmaceutical biotechnology is also due to the reliability of the drug approval process and the credibility of the relevant agencies (e.g. the US Food and Drug Administration – FDA). Bio-vigilance is considered a good safeguard against an eventual health hazard, as it entails the immediate withdrawal of the suspected drug. Social acceptance issues in medical biotechnology arise more as ethical issues when one deals with the use of genomics information to discriminate people (in terms of recruitment, life insurance, etc.) because people are not equal with respect to their vulnerability to diseases. As mentioned in the ´government regulation´ in heading 2.1.1., the European approval of biotech products functions too bureaucratic, takes place behind closed doors, no one takes responsibility on approval committees, and the appeals are heard by the same committee. Meanwhile the US FDA functions in an opposite way, which in turn results in a more reliable and creditable drug approval process by the US.

In addition to the catch-up race of Europe towards the US, there is also another danger luring for the European biotech market. In the upcoming markets like Asia, the amount of venture capital set available for the financing of the life science market is growing with enormous pace. In addition, the acceptance of society in the upcoming Asian markets towards the biotech industry is higher, compared to Europe (COGEM, 2004).

This in turn is creating an upcoming competitive threat from these markets, which forces Europe to take action towards a better competitive position.

2.6. Conclusion chapter two

Worldwide, global corporate investment in R&D grew by 10 percent in 2007, and EU-based companies increased their investment by 7.4 percent. Although this percentage was better than the 5.3 percent growth reported in 2006, EU companies have had lower rates of growth in R&D spending in every edition of the Scoreboard than the US (Science business, 2007). Although there exist an upwards trend in R&D investment with the EU life science firms, the increase in the US is still higher. This indicates that the US was already investing a lot more than Europe, meanwhile they also maintain the growth rate at a higher level. In addition, the turnover of the US biotech industry is five times higher than the turnover of the European biotech industry.

In chapter two the institutional and market conditions were set out to explain why the US biotechnological market outperforms the European market. The institutional conditions are the conditions that are set by institutions, like regulations, and thereby form the state of the biotech market. In turn the market conditions are the conditions that result from the market itself, like the supply and demand of venture capital, and thereby form the state of the biotech market. These conditions are divided in this summary in ´institutional and market conditions´, in order to provide a clear summary of chapter two and in turn set the focus for the remainder of the thesis. In the remainder of the thesis and with the research, the main focus will be on ´market conditions´, due to the direct control that life science firms have over market conditions and indirect control over institutional conditions. The market conditions are under direct control by the life science firms themselves, which in turn makes the level of control high. Contrarily, the institutional conditions are controlled direct by the state and indirect by the life science firms, which is why the life science firms have less control over the institutional conditions.

2.6.1. Conclusions chapter two ´Market conditions´:

- The most important reason why the US life science market outperforms the European life science market is the lower amount of investment capital that is available in the European life science market. The US biotechnological market is better funded through investment capital. Therefore the European biotech market has less long term investment.
- Currently the cooperation between the life science institutions and life science companies is more similar in the US and in Europe, however Europe still has to catch up for the years they did not stimulate public research spin-offs. The transfer from the life science institutions to the life science companies is in the U.S. still in a more advanced stage, because of the Bay-Dohl act, the well-developed venture capital system and a greater acceptance of entrepreneurial endeavor in the US.
- The US government supports the US life science market through heavy public funding, much more than the European governments support their biotech markets. Therefore is the European biotech market not as responsive as the US market. This makes the US biotech market more interesting for venture capitalists.
- The US start-up biotech companies develop faster into large biotech firms than the European biotech firms.
- European biotech companies develop drugs with a slower pace than the US and have higher late -stage attrition rates.
- The US has more elite (large, multinational) life science companies, with a stronger base of capital and more employees, because the European biotech market is more fragmented into smaller life science firms instead of elite (large, multinational) life science firms.
- The US companies have been better than their European counterparts at the commercializing of their inventions.

2.6.2. Conclusions chapter two ´Institutional conditions´:

- The second most important reason why the US life science market outperforms the European life science market, is because the regulations for the biotech industry in the US are less strict than in Europe. The European government for example regulates drug prices and many pension funds in Europe are not allowed to invest in assets that are deemed too risky, including venture capital. While in the US, the pension funds invest heavily in risky biotech firms. This makes the US biotech market much more interesting for biotech firms.
- The acceptance of society towards biotech products is better in the US than in Europe.
- The US government invests much more in the US life science market than the European government invests in the European life science market.

CHAPTER 3: THE BIOTECH INDUSTRY IN THE NETHERLANDS

The Netherlands is an European country and in addition one of the European countries that is also underperforming with its life science industry, in comparison to the US life science industry.

The Netherlands is a small country, on which international and European developments have a large impact. The Netherlands is highly dependent on exports, through supplying other countries with goods and services. The Dutch life science sectors is therefore cooperating on a very international level, with many other European life science markets. Being competitive on the international market, is for a large part dependent of the innovativeness and knowledge intensity of The Netherlands. The knowledge intensity in the Dutch life science market is one of the best of Europe and even on a global scale, measured in number of patents and publications in scientific journals (which will be discussed in more detail on page thirty-six of this thesis). However the problem in The Netherlands, as in most European countries, is that the switch from the life science institutions to the private life science companies does not work optimal. The inefficient switch from institution to private firms in both The Netherlands and Europe is due to a variety of institutional and market conditions, which will be discussed in the remainder of this thesis.

3.1. Government regulation in The Netherlands

In The Netherlands genetic modification of animals is only allowed when the health of animals is not threatened, when there are no alternative ways to produce the biotech product and when it is 'ethical'. The latter means that The Dutch government only allows genetic modifying with animals for the production of medicines and not for the improvement of for example food products. This policy is unique in Europe and as a result companies move their establishments to foreign countries where the regulations are less strict. In The US and New-Zealand for example are genetically modified cows present. The Dutch government experiences a lot of pressure from the biotech industry and the EU, as other European countries have less difficulty with genetic modification of animals. Besides the stricter governmental regulations, the life science companies in The Netherlands also experience less efficiency in their operational business processes through the bureaucratic approval process in The Netherlands. This includes: requests for animal testing, field experimentation with genetically altered crops and clinical tests, which all require a very long and difficult process of approval. This also results in the move of biotech firms towards foreign countries. Almost a quarter of the Dutch life science companies moved their activities abroad or expanded their business abroad in the past few years (Niaba, 2005). About fifty-five percent of the Dutch life science companies considered or is already investing more abroad than in The Netherlands. These investments include besides starting up production facilities and sales organizations also investments in R&D. Most Dutch life science firms consider to move these R&D investments to: other EU-countries (48%), the US (43%) and Asia (20%). Concerning the decision to invest in a certain country, almost all Dutch life science companies (91%) indicate that the presence of a high knowledge-intensive infrastructure, a high level of R&D subsidies and the presence of sufficient qualified personnel are the most important factors. In turn Dutch biotech firms indicate that the Netherlands needs to revise their policy concerning biotech in order to make The Netherlands interesting again for new investments (Niaba, 2005).

3.2. The structure of the Dutch life science market

The Dutch life science market showed in 2001 a total of 423 life science firms (see table 4). The main focus of this thesis is on dedicated and diversified life science firms, which downsizes the main interest group to 149 life science firms.

Table 4: Life sciences companies in the Netherlands 2001

Type of life Sciences company Sector:	**Dedicated**	**Diversified**	**Followers**	**Totals**
Pharmacy/healthcare (incl. fine chemicals)	76	7	21	104
Agrofood	15	17	248	280
Machines & Instruments	8	1	3	12
Environment	9	-	2	11
Other	16	-	-	16
Total	124	25	274	423

Source: TNO-STB (2002), adaption of Biopartner data

The Dutch dedicated companies are specialized, R&D based companies, and are in general recent spinoffs from universities and other research institutes. In 2002 there were 124 dedicated companies in the Netherlands (see table 4) that in addition employed nearly 2500 people. The total turnover of the Dutch dedicated life science firms in 2002 was 122 million Euro, of which almost 60% percent (73 million Euro) was invested in R&D (TNO-STB, 2002). Table 4 above is used as indicator for the determination of the number of life science companies per type of company that is used for the investigation. Other studies show quite similar results to table 4, namely by counting 106 dedicated life science firms and 29 diversified life science firms (Enzing et al., 2002). Or by counting also 124 biotech companies in total active in The Netherlands in 2004 (Critical I comparative study for EuropaBio, 2006). In 2003 Ernst and Young counted 85 Dutch dedicated biotech companies. Two years later in 2007, Ernst & Young counted 77 dedicated biotechnological companies in The Netherlands, which are mostly start-ups (COGEM et al., 2007). As can be seen from these studies, similar but slightly different amounts of life science companies in The Netherlands are counted, due to different definitions that scholars use for biotech firms. According to Ernst and Young in 2007 (77) the number of new start-ups declined compared to 2003 (85). This period of consolidation was a result of lower economic growth, which in turn created a shortage of venture capital in Europe and the rest of the world. However it should be noted that the number of 124 dedicated life science companies used for the research should actually be set a bit lower.

The 'diversified' life science companies include large life science companies (often multinationals) that have at least ten employees and have a very diversified range of products in their portfolio such as Unilever, Akzo Nobel and DSM. Their R&D expenditure in the Netherlands alone is almost one billion Euro (TNO-STB, 2002). Due to the large size of the diversified biotech companies in terms of employees, the impact of these diversified companies on the life sciences sector in the Netherlands is very large.

3.3. The current situation of the biotech market in The Netherlands

With the quantity of life science companies, The Netherlands is ranked among the top in Europe (TNO-STB, 2002). However, besides the amount of life science firms, another aspect in which the Dutch life science market excels is the performance of the life science institutions. The Netherlands is home to universities and research institutions that belong to the best of the world. The scientific knowledge that a country possesses functions as a foundation for innovative prosperity. This scientific knowledge can be measured through the number of patents and publications in scientific journals. OECD statistics show that the US Patent Office has registered 100 biotechnology patents from Dutch companies and/or institutions in 2000. This relatively large number of patents makes The Netherlands the seventh country in the world in terms of number of patents, ahead of countries like Australia, Sweden and Switzerland. The number of Dutch biotechnology patents granted by the US Patent Office has risen by twenty percent between 1990 and 2000, which was globally during that decade one of the highest increases in granted patents. Concerning the publications in scientific journals, The Netherlands produces with only a quarter percent of the world population, two percent of all scientific publications and three percent of all global quotations refer to the two percent publications. In my opinion, according to these measurements, the Dutch life science institutions are performing very well.

3.4. Start-up biotech firms in The Netherlands

Although the Dutch life science institutions are performing very well, the Dutch private life science market is underperforming. One problem is that the private biotech industry in The Netherlands employs in total relatively few working people compared to other European countries (see appendix, figure 9 and 12). The R&D departments of private life science firms in The Netherlands (see appendix, figure 13) also have a small number of people employed. In addition, the turnover of the industry is also relatively low. When comparing the turnover to the US, the Dutch biotech industry only adds 0,07% to its gross domestic product (GDP), while the US biotech industry adds 0,38% to its GDP.

To improve the low job mobility and thereby the transition from institutions to the private life science firms, the Dutch government started to support the collaborations between scientists and business people in order to increase the number of spin-offs from the institutions towards the private life science companies. With this support, spin-offs from institutions were encouraged by means of subsidy programs, such as the ´research and development promotion act´ (a fiscal facility for research in companies and institutes) and the subsidy for technological cooperation. Furthermore, the ´Life Science Action Plan´ was implemented in 2000 specifically to support incentives for start-up companies. The action plan was followed by several other initiatives, for example ´Biopartner´, which had the objective to stimulate the life science sector and to encourage faster and more spin-offs from institutions into commercial life science companies.

Biopartner started to remove obstacles, like: lack of information, money, facilities and laboratory space. It is directed at bio-entrepreneurs during the 'seed', 'start-up' and 'solo' phases of the start-up process (the three first stages when starting a life science firm). The aim of the program was to have seventy-five new life sciences start-ups between 2000 and 2004. In 2003, three years after the program was started, sixty spin-offs from the institutions were established with the support of the program. Several strategies were deployed to attain the aim of the Biopartner program. One strategy was the creation of six centers, where new life science companies had the possibility to rent office space and laboratories (BioPartner Network, 2005). In addition, these centers offered the start-ups support to obtain the necessary permits and funds. The life science start-ups are also aided through the possibility to use advanced (and often expensive) equipment at universities and other research institutes. The Biopartner program also offers grants to potential biotech start-ups to set up a business proposal, in order to present the idea to a bank or venture capital firm. In addition, the Biopartner program include the ´BioPartner Start-up Venture program´, which provide funding as investment capital. The other characteristic is that the BioPartner Network helps to establish relationships between life sciences entrepreneurs and useful contacts, e.g. potential investors and government representatives.

The Biopartner program contributed to the enormous growth of the ‘dedicated’ biotech firms. In 2004 the dedicated life science companies were characterized in The Netherlands by a total turnover of 190 million Euros and an employment of 2150 FTE´s (BioPartner Network, 2005). Internationally The Netherlands is performing good with start-ups, by supplying 10% of all European start-ups (EuropaBio, 2006). While in turn the life science markets of other European countries is characterized by decline, for example in France and Germany the number of biotech companies decreased with 30% in 2001 and 40% in 2003, relative to the period 1998 – 2000. In Great-Britain the growth remained constant in the period 1998 – 2003. To relate the number of start-ups to the Europe versus US situation, it can be stated that The Netherlands has a high number of start-up companies relatively to other countries, whereas the European market also has a higher start-up rate for biotech companies relatively to the US biotech market (see appendix, Fig 1: Age of companies in the USA and Europe).

3.5. The financial picture in The Netherlands

As became clear from section 3.4., The Dutch government obtained its objective through the formation of more spin-offs from the institutions. These start-ups also need to attain growth, in order to become of significant meaning in the economy. As can be seen in the figure 28 of the appendix, for the start-up companies to attain growth, pre-venture and venture capital is crucial.

The LSP has 400 million Euros available to invest in the biotech industry, of which a part is invested in start-ups. The group that comes second, after the LSP, in terms of most funds available for investment in the life science sector, are funds like; Forbion (ABN Amro), Aescap, en Gilde (Rabobank). This group all together has an equal amount investment capital available as LSP, namely 400 million Euros. The group that comes third in terms of most funds available for investment in the life science sector are universities and city funds, which have investment funds that range between twenty or thirty million euro's, which are set available to invest especially in start-ups. In my opinion can be said that the Dutch market for venture capital is relatively well developed and that in The Netherlands sufficient venture capital is available. One of the world´s most successful life science venture capitalists, Atlas Venture, is based in The Netherlands. Already in 1997 venture capitalists in The Netherlands were investing about 40 million Euros (Fuchs, 2003).

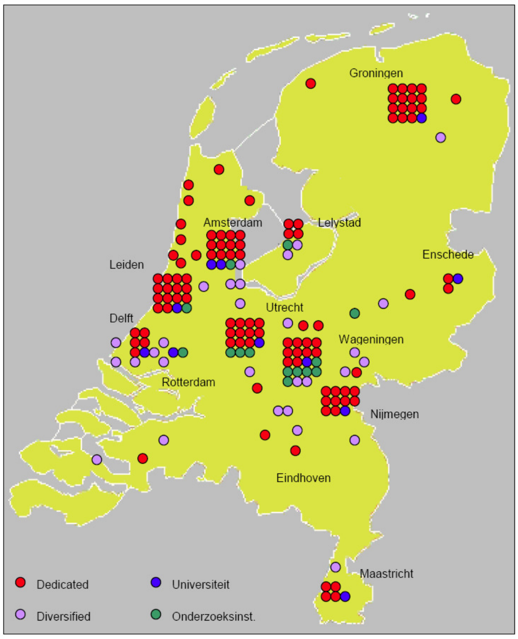
When trying to obtain external financial resources for the first time, start-up life science firms in The Netherlands experience a number of difficulties. Suppliers of financial capital have difficulties in assessing future risks of new products and services (Fuchs, 2003). In addition the suppliers of financial capital select start-ups that in reasonable time can attain notable growth through their product-portfolio of interesting products with future perspective. Suppliers of capital claim that many Dutch life science start-ups in The Netherlands are not able to attain notable growth in reasonable time through their product-portfolio of interesting products with future perspective. Suppliers of capital prefer companies to have many high-potential patents instead of one of two, or one or two patents that have the potential to be applied in many different research fields to attain diversification (Fuchs, 2003).

3.6. Innovativeness of the Dutch life science sector

The capital that a firm or country invests in R&D is crucial for its innovative ability (Nederlands Observatorium van Wetenschap en Technologie, 2007a). From the appendix, figure ix and x and figure 15 until 23 can be concluded that biotech firms in the Netherlands invest a low amount of money in R&D relatively to the biotech firms in other European countries. This in relation with the relative low amount of available R&D employees, results in relatively underperforming and inefficient R&D department of Dutch life science firms (Nederlands Observatorium van Wetenschap en Technologie, 2007a).

In The Netherlands different life science organizations are cooperating with each other and thereby forming clusters. Whereas these organizations are linked with each other by many formal and informal threads and thereby creating knowledge spillovers. A knowledge spillover is an internal knowledge spillover if there is a positive impact of knowledge between individuals within an organization that produces goods and/or services (Carlino, 2001). The life science clusters that exist in The Netherlands, are established in university regions, namely around Leiden, Utrecht, Amsterdam, Rijnmond, Wageningen and Groningen (see fig. 2 below and 24 of the appendix).

Fig. 2: Biotech clusters in The Netherlands



Source: Enzing et al., 'Life Sciences in Nederland', 2002

Within these clusters are many small and young life science firms established with strong links to nearby universities. In contrast, the older and larger life science companies are located throughout the country, on locations that have good infrastructural accessibility, such as rail and road, rather than proximity to universities or research institutes (see fig. 2 above).

The role of small biotech firms and large biotech firms in the Dutch life science industry does not show the same situation as the US or UK life science industry. In the US and UK biotech market the new life science start-ups and small firms play a dominant role. The role of the start-ups and small firms in The Netherlands have been almost zero. In the Dutch life science market, almost the entire turnover and employment available in the Dutch life science market is generated by the large (multinational) companies, e.g. Unilever, DSM, AKZO-Nobel (Fuchs, 2003).

3.7. Management in the Dutch life science sector

The biotech institutions in The Netherlands have the task to develop the Dutch life science industry. Biotech managers in The Netherlands can also influence the development of the biotech firms and thereby also the development of the Dutch biotech industry. Eric Claassen, who operates as entrepreneur, is responsible for seven biotech start-ups and is also professor of ´knowledge valorisation´ at the Erasmus University in Rotterdam and the ´Vrije Universiteit´ in Amsterdam, acknowledges that biotechnological companies need expertise at the head of the company, which includes managers that already have run a biotechnological company, and knows how to stir the company into the right direction. In addition, venture capitalists regard the presence of high-quality management capabilities in start-up firms a crucial condition for providing financial capital. With a slight of doubt by the venture capitalists about the management in the start-up life science firms, requests for venture capital are rejected. In The Netherlands ninety-five percent of the requests for venture capital by start-up biotech firms are rejected, in most cases because suppliers of venture capital consider the management of start-up biotech firms inadequate to guarantee the required rate of return (Fuchs, 2003).

In addition, start-up biotech firms do not focus much on attracting capable management. The focus lies more on research and development and obtaining investments from suppliers of financial capital (Philpott and Cassells, 2004).

3.8. Summary chapter three

In this chapter it became clear that the Dutch life science market excel in the performance of the life science institutions. The Netherlands is home to universities and research institutions that belong to the best of the world. Although the Dutch life science institutions are performing very well, the Dutch private life science market is underperforming. One problem is that the private biotech industry in The Netherlands employs in total relatively few working people compared to other European countries. The R&D departments of private life science firms in The Netherlands also have few working people. In addition, the turnover of the industry is also relatively low. When comparing the turnover to the US, the Dutch biotech industry only adds 0,07% to its gross domestic product (GDP), while the US biotech industry adds 0,38% to its GDP. The development structure of the life science industry in The Netherlands does not show the same situation as the US or UK life science industry, in which the new life science start-ups and small firms play a dominant role. The role of the start-ups and small firms in The Netherlands have been almost zero. In the Dutch life science market, the turnover and employment is mostly concentrated in large (multinational) companies, e.g. Unilever, DSM, AKZO-Nobel (Fuchs, 2003). The academic mentality is characterized by a reluctance to take (financial) risks and thereby academic scientists are reluctant to start a biotech firm (Fuchs, 2003). In order to improve entrepreneurship, the Dutch government has tried to stimulate start-ups and improve cooperation between different life science organizations. Suppliers of financial capital regard the presence of high-quality management capabilities in start-up firms a crucial condition for providing financial capital. In addition, ninety-five percent of the life science start-up firms in The Netherlands is considered to have a lack of management capabilities (Fuchs, 2003).

CHAPTER 4

THEORETICAL FRAMEWORK ABOUT THE MANAGAMENT IN THE DUTCH LIFE SCIENCE SECTOR

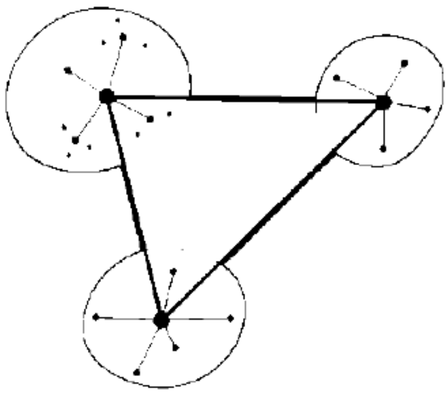
4.1. A polynuclear region

The innovations in small and large biotech companies are a key indicator to measure the entrepreneurial performance of management in both small and large life science companies (Miller, 1989).

Cook (2002) states that both small and large firms experience pressures to compete through innovativeness and therefore firms are mandatory to raise quality and reduce costs, which in turn is the responsibility of managers. The role of management in biotech firms has changed from 'coordinating the on-going internal activities of the firm through a command and control structure' to 'supporting different departments in the organization for both the internal and external exchanges' that are essential to a firm's survival and success (Cohen and Levinthal 1990, p. 131). In both cases, acquiring tacit knowledge from outside the firm is reliant upon its absorptive capacity, which is to be configured by the management of the firm.

Firms that are larger in size in terms of employees and financial capital are more innovative in terms of more significant innovations (Mohen et al., 2006). In turn firms that are larger in size in terms of employees and financial capital have more cooperation intensity (Tether, 2002). That smaller life science firms have less cooperation intensity can be explained by the fact that small life science firms do not want large life science firms to become too decisive about their research strategy (Tether, 2002). In addition firms that are larger in size in terms of employees and financial capital are also more productive with their Research and Development (Schumpeter, 1942; Galbraith, 1952; Arrow, 1962). The medium sized life science firms have the highest R&D activity (Worley, 1961). A more recent study, performed by Lewin and Massini (2003) proved that larger firms in terms of employees and financial capital spend more on research and development, but that the small life science firms are more efficient in research and development. Therefore, as discussed in the previous paragraph, in order to acquire tacit knowledge from outside the firm, the management of the start-up life science firms should focus on cooperation with medium and larger sized firms. Acquiring tacit knowledge from outside the firm, might also add to innovative and managerial improvements. In order to acquire tacit knowledge for innovative and managerial improvements, cooperations are formed with other life science firms on a local, regional, national, continental or international level. Most of these cooperations in The Netherlands, are in my opinion formed on a regional level, where most of the life science firms are established. This region in The Netherlands is referred to as ´the Randstad´. The Randstad, where most of the Dutch life science industry is located, is a polynuclear regional agglomeration of 3,200 square kilometer in the western Netherlands with 7.1 million inhabitants (45% of the population). A polynuclear region (see figure 3) such as the Randstad in the Netherlands is an urban network of cities/nodes connected by facilities (links, arcs, ties, relationships) through which entities such as goods and services pass (Batten, 1995).

Fig 3: A polynuclear region



Source: Batten (1995)

The Randstad consists of Utrecht, Amsterdam, Rotterdam, Leiden, Dordrecht, Haarlem, Flevoland, The Hague, and Delft. Furthermore the Randstad is a centre for health care in The Netherlands, containing ten university hospitals (a university hospital or teaching hospital combines assistance to patients with teaching to medical students and is often linked to a medical school) in close proximity to each other. Leiden has a substantial science park that functions as an anchor for the growth of the life science industry in the region. Polynuclear regions are focussed on networked interrelations and territorial concentration between clusters of firms, services and research institutes, relations of trust, and formal and informal networking (Meijers et al., 2004). The individual but networked cities within the Randstad region function as one cluster through cooperative research, and thereby provide greater agglomeration or external economies for the companies that operate within the region, in terms of better infrastructure and institutions (higher education). Another advantage of the polynuclear region is that it promotes innovation in the geographical proximity and interaction among each of the nodes. Which in turn reduces transaction costs and foster development of business networks that promote trading linkages amongst firms and thereby facilitate the exchange of knowledge and expertise.

Through the encouragement of interaction between neighboring locations, each location will specialize in areas in which it has competitive advantage. In addition, this will leave individual firms and the Randstad region as a whole with a stronger competitive position (Bailey and Turok, 2001). The emphasis of the specialization for the whole Randstad region is on entrepreneurship, commercializing and governmental intervention rather than on functional specialization (Sable, 2005).

According to the Ruimtelijk Plan Bureau (2006), which is a Dutch agency that investigates the urban planning of the Dutch life science sector, 75% of the cooperative research relations of life science firms in The Netherlands is with foreign organizations. The bulk of the life science companies in The Netherlands, the big and medium-sized life science companies, are geographically not closely situated to the research centers in The Netherlands. Therefore their relations for cooperative research are more internationally focused instead of regional (Fuchs, 2003). The life science firms that are closely connected to research centers in The Netherlands are the life science start-ups and some successful medium-sized life science firms. In fact the character of the Dutch life science clusters are mainly determined by the growth and development of these life science start-ups and successful medium-sized life science firms in The Netherlands that are close to universities or research centers. Although there are much more small biotech firms than large biotech firms in The Netherlands, in terms of growth and development of the Dutch life science industry as a whole, the role of the life science start-ups has been almost zero. The life science companies that do play a role in terms of employment and turnover are the large (multinational) life science companies (Fuchs, 2003). The large multinational life science companies however play only a small role in the development of the Dutch life science clusters, due to their international relations for cooperative research, instead of regional ones.

Cooperation between public and private life science organizations are considered important to expand the base of knowledge. However while performing the cooperative with universities, private life science organizations feel that universities do not always write their patent applications in the right manner, which makes the applications useless for commercializing. Private life science firms also feel that universities take too much time in decision making about whether to cooperate with a private life science firm (de Man and Duysters, 2003).

For the development of a new technology, both large and start-up life science firms often cooperate with universities. In addition, a large part of the start-up life science firms are a spin-off from the university research groups. Another factor for most small and start-up life science firms to find research cooperations with large life science firms is the lack of investment capital and the required knowledge to grow. Eventually these cooperations can result in a take-over of dedicated firms by diversified life science firms. For the large biotech firms, these research cooperations provide a cheap manner to assess the value of technological advancements made by dedicated firms. The large number of technologies and hype-sensitivity in the life science industry, cause the effect that larger life science companies can not and will not invest in all technologies. Instead research cooperations are set up with many different small life science firms at the same time. In the case that from one of these research cooperations results an innovation with the potential to create a large enough return on investment, the large biotech firm can take over the small biotech firm. Or in case the small biotech firm does not show potential, the alliance will be broken off by the large biotech firm. The large/diversified life science firms invest between ten and twenty-five percent of their available R&D budget on alliances with small/dedicated life science firms. Dedicated life science firms invest much more of their budget on research cooperations, as almost every R&D project of dedicated firms is performed through alliances. The most important cooperations in the life science sector are those between universities and private (dedicated and diversified) life science firms and between dedicated and diversified firms that are focused on new technologies, often on the basis of licensing. Concerning the take-over of dedicated by diversified life science companies, the expectations are that these will be done mostly by foreign companies, due to the limited overlap between the Dutch life science sector and other sectors in The Netherlands. In case these foreign companies move the R&D outside the Netherlands, the danger of a brain drain (the move of knowledge workers abroad) exists (de Man and Duysters, 2003).

Most partnering in the Dutch life science sector occurs between public organizations and private firms, while alliances between private firms are more scarce. In my opinion, this lack of alliances between private firms could have been caused by a lack of large (diversified) life science firms in The Netherlands. In the US for example there exists a high number of alliances between private firms, in turn there are also much more alliances between large (diversified) life science companies and small biotech firms (de Man and Duysters, 2003). Another factor, in my opinion, that causes the lack of alliances between private firms in The Netherlands, is that life science firms in The Netherlands focus very little on how to improve their position in a network, to form the best possible alliances and thereby have the best results.

Small/dedicated life science firms that are spin-offs from universities are often considered to have poor management relative to the management of life science firms in The Netherlands. In turn, the management of these small firms is responsible for the company’s strategy, deployment of its resources, deployment of its personnel, the structure of the firm´s internal environment and thereby the management is in direct control of the small biotech firm (Vivian Moses et al., 1999). Different than in the US, third parties play a limited role in the management board of small biotech firms. Venture capitalists in the US for example play a significant role in the management board of the small US life science companies. While in The Netherlands venture capitalists do not participate in the management. In The Netherlands there is sufficient investment capital available for the Dutch biotech industry, what in my opinion lacks are third parties that are more experienced in the management of biotech firms and take part in the management board of the small biotech firms, like in the US, to aid with making the correct management decision (de Man and Duysters, 2003). As indicated by Moses et al. (1999), managers learn decision making through the experience of others. Managers who inspire excellence in others are performing the most important management task of all – they are exercising leadership. In addition, for managing activities an ability to shape a group of diverse people into a team is mandatory. Other requirements of management are the ability to delegate, leadership and inspiration. In order to acquire these managerial skills, textbooks and courses in management help, however more helpful is learning management by example from a good manager (Sheila Moses, 1995).

4.2. Testing the hypothesis

With the testing of the hypotheses, the management skills of managers in life science firms are tested. In chapter one, in point 1.4. and 1.5., the following key performance indicators were discussed to evaluate the management skills: *Granted patents, new products, net profit margin, return on investment*.

The first three hypothesis for the research of this thesis are;

H1: Deploying commercial business strategies[1] *causes a higher return on investment*[2] *with life science firms in The Netherlands.*

H2: The management skills of managers in life science firms in The Netherlands are of better result[3] *when they cooperate with life science firms outside The Netherlands.*

H3: The management skills of managers in life science firms in The Netherlands are of better result[4] *when interacting with third parties.*

4.3. Characterizing life science management

Most investors of financial capital consider the management of small life science firms as the key weakness (Sullivan, 1995). These are tasks in which management should have expertise and experience, along with considerable team based skills. That most investors of financial capital consider the management of small life science firms as the key weakness has several origins; one is the management skills that academics lack to manage a life science firm, theoretical or practical experience is a very rare characteristic of life science academics. The whole career structure is oriented on

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[1] O*utsourcing the commercializing process; sharing laboratory space with other firms; doing mutual advertisement/marketing/sales with partner; outsourcing research to other organization(s); hiring frequently new employees with lower wages that replace the employees with higher wages of the commercial department; establishing in a cluster, which saves for example on transport costs when cooperating with another firm; having access to a database in which we can see the work of other firms, which saves on e.g. search costs; cooperating with organization(s) that have establishments in different clusters; having different establishments in different clusters; hiring employees through our already employed employees; focusing on long-term employment in our organization.*

[2] The return on investment is calculated simply by dividing the capital gained from investment by the capital invested.

[3] In terms of: *Granted patents, new products, net profit margin, return on investment*

[4] In terms of: *Granted patents, new products, net profit margin, return on investment*

theory; passing exams and obtaining PhD's. Meanwhile little or no emphasis is put on management issues, e.g. networking skills, teambuilding. In addition, the managers that are most successful in this organizational structure are offered positions as managers. In result many of these inexperienced life science managers do not have the skills to secure a good transition from public to private, which then leads to extremely poor project management systems (Sullivan, 1995). Furthermore, in The Netherlands there exist a serious lack of experienced life science managers that have experience in management functions such as sales, promotions, and marketing, especially in small life science companies. The number of managers that possess these characteristics is increasing in the US and remains low in Europe. In my opinion, this is because the US biotech market is more interesting for experienced managers, due to less strict regulations and better compensations. In turn, small life science firms in The Netherlands are in need of good (experienced) management to obtain investment capital and thereby growth (Sullivan, 1995).

Academic scientists are often the ones that manage the biotech firm the first few years when it results as a spin-off from the research institution or university. As commercial influences may be limited at this point in time, the firm must focus on developing the technology to the level where venture capitalists could become interested to invest in the innovation and thereby in the firm. In order to develop the technology to the next level knowledge is to be acquired. To acquire this knowledge support is necessary from third contacts, such as other academic researchers, experienced biotech managers, suppliers of financial capital (Hine and Kapeleris, 2006). In my opinion it is necessary to focus, especially when the biotech firm is small and wants to obtain growth, on how to position the firm the best in a network (network strategy). When small life science firms that have reached the point where venture capital can be obtained, management of the small biotech firms should be able to provide: good leadership; experience in commerce, business and management; and should be able to gain the confidence and trust of colleagues and if present also the trust of the board of directors (Sheila Moses, 1995).

Managers of these small life science firms (that have reached the point where venture capital can be obtained) operate in a very individual and opportunistic manner. In addition many of these managers have little or no prior experience of appropriate management experience (Philpott and Cassells, 2004). Also do they lack the skills to: set up a good knowledge infrastructure, market the products of the firm and to structure and discipline the business environment. The managers of these dedicated life science firms (that have reached the point where venture capital can be obtained) are considered inadequate to create the right company structure as the companies develop (Philpott and Cassells, 2004). This includes the change from the pseudo-academic R&D norm to commercializing. As a result many small life science firms go bankrupt or get sold unintentionally (Philpott and Cassells, 2004). Suppliers of financial capital need assurance that their investment is in good hands and that the life science firm is properly managed. For that reason the suppliers of financial capital prefer that inexperienced managers of small life science firms appoint a CEO that does have the necessary skills and experience to apply the correct business structure and ascertain growth (Philpott and Cassells, 2004).

Life science managers control the internal situation of the firm. However what is less under control of the manager is the situation outside the firm, such as government regulation, competition and yet this situation outside the firms also has an impact on the firm and its business. Crucial for the manager is to recognize and understand the intimate relationships of the firm with the large number of influencers and stakeholder. This could be done through analyses of the situation outside the firm, from competitive intelligence to issues management. Life science firms that interact insufficient with their external relationships, are often not up-to-date about the latest changes in the biotech market. These changes gain momentum and ultimately destabilize the company, which in turn requires radical and painful measures to be implemented, which is called ‘crisis management’. Beyond knowledge and recognition, the manager must be able to communicate effectively with external groups (Vivian Moses et al., 1999). The relationship a manager has with its stakeholders and influencers, which are so valuable to a life science firm, can be obtained through relationships with: life science institutions, consultancy firms, other life science firms, suppliers of financial capital. In turn ´contacts of the management´ can all enhance a firms’ knowledge level through networks, collaborations, the hiring of new staff and so on (Hine and Kapeleris, 2006). Once a firm has acquired a star (manager), the likelihood that another star (manager) will follow and enter the firm is dramatically increased´ (Zucker et al., 2002).

Managers of private life science companies have to make sure that the shareholders have an accurate perception of the prospects of the company. Due to the insecure nature of the life science market, venture capitalist (shareholders) need to be constantly informed to know the status of the company. In turn to avoid that venture capitalists consider the life science firms too nontransparent. This includes also communicating with others parties that influence shareholders; investment counselors, stockbrokers, securities analysts and journalists (Vivian Moses et al., 1999). Large dedicated life science companies with earnings track record are easier for investors to assess than growth (dedicated life science) companies. Life science companies that are in the early stages of development have no historical records to evaluate the firm´s performance on. It is therefore much more difficult for investors to weigh these early stage life science companies. Valuation is also affected by the market's perception of the management – the skills, experience and capabilities of the company's leadership. In addition, the chairman of the life science firm Protheris and healthcare company SSL International doubts the effective management of dedicated life science managers and states; "There are a lot of very bright scientists around but for them, the controls and disciplines don't exist." More referring to specific tasks he said these managers lacked the discipline to raise money, control capital, handle distribution and manage effectively the sales and marketing tasks. He also believes that poor management will be one of the triggers for further consolidation in biotechnology. He said mergers were often opportunities to recruit higher caliber executives: "In many cases, the management is capable of handling things in a small business but they're not capable as their businesses begin to grow." (Vivian Moses et al., 1999).

As can be seen in the appendix, figure 25 until 27, The Netherlands is characterized by life science firms that grow with a very low pace. In addition life science firms tend to stay small, relatively to comparable countries (Hedgcoth, 2007). Older Companies – that are between 3 and 10 years – spend much more on R&D: this group of around twelve hundred companies accounts for over three billion Euros or forty percent of European biotechnology's research budget. This is 10 times as much as the contribution from the young life science firms and nearly as much as that from the long-established firms (Sasson, 2004). Small biotech companies and start-ups remain a driving force regarding the creativity of the biotech sector. Small life science companies can innovate in research areas where the diversified (multinational) life science firms do not research in. The complementing function of the small life science companies to the large life science companies in terms of research areas where large life science companies do not research in, results in a trend of alliances and mergers. These alliances and mergers are a result of the steady erosion of patents that large life science companies experience (Sasson, 2004). According to a study carried out by McKinsey in 2000, the number of new drugs marketed by each big pharmaceutical group has fallen from 12.3 over the period 1991-1995 to 7.2 over the period 1996-2000 (Mamou, 2000). In addition it is very costly for large life science companies to emphasize their research on many different research areas. In turn the strategy of the large life science company is to focus on a certain number of research areas and cooperate with small life science companies that specialize in the remaining research areas. This strategy is referred to as the 'blockbuster' strategy, i.e. the production of worldwide pharmaceuticals that can generate an annual turnover of more than $1 billion. Such blockbuster drugs entice the producers of generic drugs who can market a copy of a drug before its patent expires. But the race between the large life science laboratories and generic drugs companies is continuous if there is not a steady flow of new patents to replace those which fall in the public domain. There is in fact a slowdown in the production of novel medicines. This slower pace in innovation is unthinkable for an industry which produces less and faces increasing costs. The obvious response, as a counter-risk measure, is to take hold of the promising pharmaceuticals in the competitors' portfolio (Mamou, 2004). Many biotechnology start-ups try to conclude financial agreements with pharmaceutical groups in order to survive the first years on the private market. Dedicated life science companies seek alliances with large pharmaceutical firms or groups to validate their technology in the eyes of their current and future investors, to fund R&D and decrease the need for dilutive rounds of equity financing, and to have a commercial partner that can effectively sell their products on markets unreachable without a large sales force. In Europe, seventy-five percent of the dedicated life science companies have alliances with academic laboratories and pharmaceutical laboratories. The alliances with pharmaceutical laboratories represent the second source of financing for the dedicated life science companies (Francisco, 2004).

H4: The management skills of managers in life science firms in The Netherlands are of better result[5] *when having an appropriate educational background*[6].

H5: The management skills of managers in life science firms in The Netherlands are of better result[7] *when managers remain longer within the same life science firm.*

H6: The management skills of managers in life science firms in The Netherlands are of better result[8] *when managers have more experience in general management.*

H7: The management skills of managers in life science firms in The Netherlands are of better result[9] *when managers have more experience in the management of a life science firm.*

4.4. Conclusion chapter four

From chapter four it has been argued that managers of the dedicated life science companies in The Netherlands lack the management skills to lead the firm into the stage where venture capital is obtained. The problem is that venture capitalists consider the managers of dedicated life science companies in The Netherlands inadequate to guarantee a return on the venture capital. In order to be considered capable management that does guarantee a return on investment, the management skills have to be improved. There exist several possibilities to improve management skills, e.g. learn from more experienced managers, cooperate with diversified firms that have these more experienced managers, taking courses in management or management of life science firms or simply hire more experienced management. In the next chapter the strategies to improve management skills of life science managers and life science firm performance are researched.

[5] In terms of: *Granted patents, new products, net profit margin, return on investment*
[6] Education in: Finance, law, alliance management, commercializing, biotech, management in general, management in biotech.
[7] In terms of: *Granted patents, new products, net profit margin, return on investment*
[8] In terms of: *Granted patents, new products, net profit margin, return on investment*
[9] In terms of: *Granted patents, new products, net profit margin, return on investment*

CHAPTER 5

EMPERICAL FRAMEWORK ABOUT THE MANAGAMENT IN THE DUTCH LIFE SCIENCE SECTOR

5.1. Data description

Table four below shows the population size of the research.

Table 4: Life sciences companies in the Netherlands 2001

Type of life Sciences company Sector:	**Dedicated**	**Diversified**	**Followers**	**Totals**
Pharmacy/healthcare (incl. fine chemicals)	76	7	21	104
Agrofood	15	17	248	280
Machines & Instruments	8	1	3	12
Environment	9	-	2	11
Other	16	-	-	16
Total	124	25	274	423

Source: TNO-STB (2002), adaption of Biopartner data

As mentioned in chapter three, the population of the research exists of dedicated biotech firms and diversified biotech firms. Therefore the population size has been set on one hundred forty-nine biotech companies, of which one hundred twenty-four are dedicated biotech companies and twenty-five are diversified biotech companies. These one hundred forty-nine companies were contacted by telephone and later written by email to provide the link that gave access to the online questionnaire of this research. The responses were later analyzed with the program SPSS. The objective characteristics of the firm exist of the assessment indicators described in section 1.3. until section 1.5. of chapter 1. Which include:

The assessment of a biotech company:

Input indicators*: Employment (number of employees, number of managers, characteristics of management; educational background and work experience), financial resources (e.g. venture capital), investment in R&D versus turnover.*

Output indicators*: granted patents, new products, obtaining capital.*

And *the company type; dedicated, diversified and next life science firms.*

While for the assessment of management performance, the following indicators were used: *net profit margin* **and** *return on investment (ROI).*

For the remainder of this analysis, the research question; '*What are the determining differences in management skills between managers of more efficient and less efficient functioning biotech firms in The Netherlands?´* will be answered through the answering of the seven hypothesis. Both diversified and dedicated life science firms will be analyzed individually and a comparison between the two will be made.

5.2. Characteristics of the respondents

5.2.1. The response rate

What type of biotech firm is your organization?

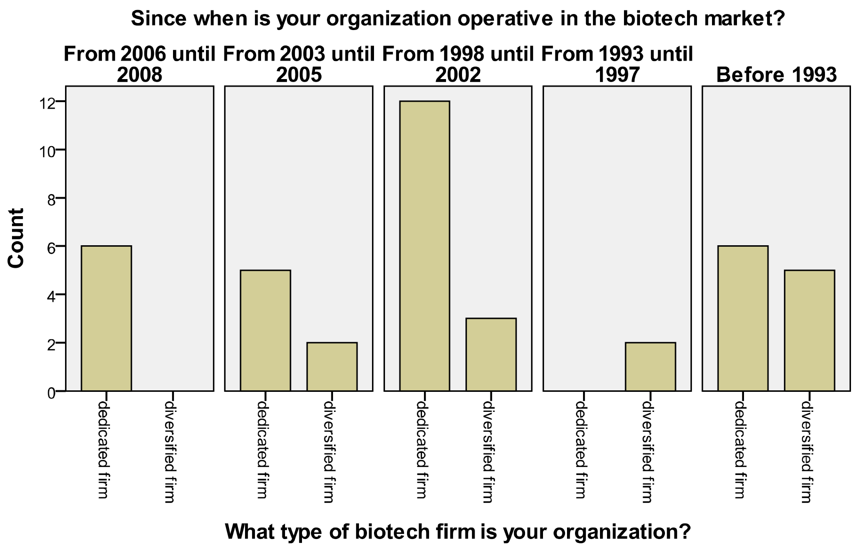
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	dedicated firm	29	69,0	70,7	70,7
	diversified firm	12	28,6	29,3	100,0
	Total	41	97,6	100,0	
Missing	99	1	2,4		
Total		42	100,0		

Twenty-nine dedicated biotech companies and twelve diversified biotech companies from the population responded to the questionnaire. This is a sufficient response rate for both dedicated and diversified life science firms as it covers over ten percent of the population. More precise, the dedicated life science firms represent 23,4% (29 of 124) of the total population, while the diversified life science firms represent forty-eight percent (12 of 25) of the total population. In order to avoid response bias (when respondents answer questions in the way they think the questioner wants them to answer rather than according to their true beliefs), the option ´dedicated life science firms´ is explained in the questionnaire as ´your core business is biotech R&D´. The option ´diversified life science firms´ is explained in the questionnaire as ´ besides biotech, your organization also focuses on other industries for R&D´. In addition, there has been made a third option also to avoid response bias, which is 'Next life science companies´, which is explained as ´your organization does not research in biotechnology, however make use of biotechnology which is developed by others´. These three options are very different from each other and give the respondent the possibility to chose the option that is according to their true beliefs.

5.2.2. Year of establishment

Most dedicated life science firms are young companies, not older than 10 years. While diversified companies are mostly older than 10 years. This is in line with the theory discussed in chapter 1 (section 1.3.1.), were it was stated that dedicated biotech firms represent generally start-ups or relatively young biotech firms and as these companies become more experienced and increase in size, they evolve towards diversified biotech companies (life science monitor, 2005).

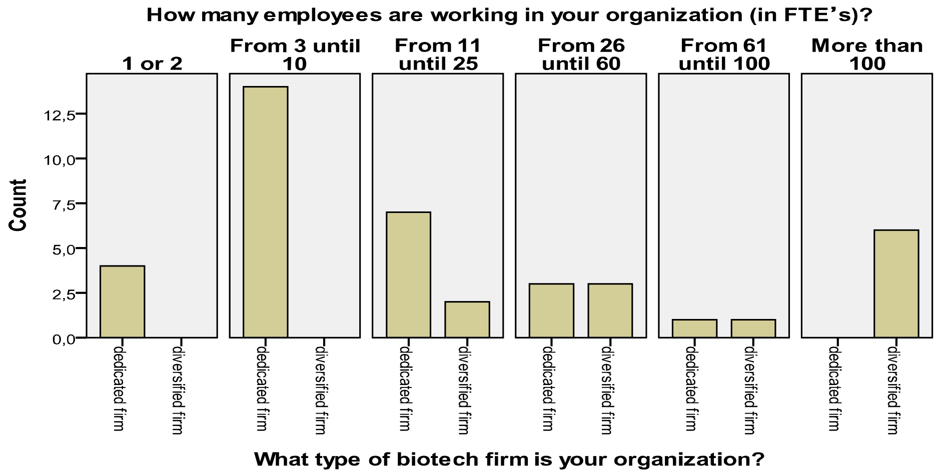
Year of foundation life science firms



5.2.3. Firm size

From the theory in chapter 1 (section 1.3.1.), it appeared that in general the dedicated biotech companies are represented by SME´s that employ below ten FTE´s. Meanwhile the diversified biotech companies are generally larger in size and employ at least ten FTE´s. The research shows a similar result; most dedicated life science companies have between three and ten employees, while even five diversified life science firms have one hundred employees or more.

Employment of life science firms



The objective of the frequency tables used in 5.2.2. and 5.2.3. is to give a clear view per different characteristic between dedicated life science firms and diversified life science firms. Due to the emphasize on each different characteristic, frequency tables were used instead of a crosstab. In my opinion, the size of the firm is more important than the age of the firm. In turn because dedicated firms are considered to have a low number of employees, which distinguishes them from the diversified firms. While there are life science firms that are operative for a longer period and remain dedicated life science firms. From the perspective of age, many dedicated firms are not distinguishable from diversified life science firms.

5.3. Testing of the hypotheses

In each problem, the question of interest is simplified into two competing hypotheses between which there is a choice; the null hypothesis, denoted H0, against the alternative hypothesis, denoted H1. The experiment has been carried out in an attempt to accept or reject a particular hypothesis, the null hypothesis, thus we give that one priority so it cannot be rejected unless the evidence against it is sufficiently strong. In order to test against the alternative hypothesis, a regression analysis was performed in SPSS. A regression analysis is a technique for the modeling and analysis of numerical data consisting of dependent variables and independent variables. The independent variable is typically the variable being manipulated or changed and the dependent variable is the variable that is explained in the model. In the model that is researched, the dependent variable is dependent on the independent variable(s).

The terms are set by these two variables; the independent variables and the dependent variables:

$y = \beta 0 + \beta 1x1 + \ldots + \beta ixi + u$

y is the dependent variable … (which the model should explain)

xi are the independent variables … (which are used to explain the independent variable in the model)

The linear regression model used in this research consists of two components:

1) The structural part $\beta 0 + \beta 1x1, + \ldots + \beta ixi$, which describes the systematic influence of *xi* on *y*.

2) The error term *u*: which contains all variables. The standard error shows the variance of the estimated coefficient. The lower the standard error, the better is the estimator.

When testing the validity of the regression model in this thesis, first the R square or coefficient of determination is evaluated. The R square measures the goodness of fit or the amount of the variation in the dependent variable explained by the independent variables. Besides the R square, the adjusted R square will also be evaluated to test the validity of the regression model. The adjusted R square provides a better measure than the R square by correcting for the number of observations and the number of independent variables.

The dependent and independent variables selected for this research where described already in chapter one:

Independent variables*: Employment (number of employees, number of managers, characteristics of management; strategies of management, educational background of management, duration of management, work experience of management, network of management), financial resources (e.g. venture capital), investment in R&D versus turnover.*

Dependent variables*: granted patents, new products, net profit margin, return on investment.*

Also mentioned in chapter one, was that the *net profit margin* is calculated by: dividing the net income by turnover (Berman et al. 2006). In addition, the ROI is calculated simply by dividing the capital gained from investment by the capital invested.

In order to avoid multicollinearity with the regression analysis, the **"backward model"** was used. By combining different variables, the backward model provides different p-values (significance level) for every combinations of variables. The backward model shows a large number of statistical non-significant variables and statistically significant variables. The variables that are tested for significance are the independent variables in the regression analysis. The non-significant variables have a p-value higher than 0.01 and the statistically significant variables have a p-value higher than 0.01. The independent variables that have the p-value lower than 0.01 are thus statistically significant and are considered to have a significant influence on the dependent variable. In turn the independent variables that are significant are investigated to determine their impact on the dependent variable.

5.3.1. Hypothesis 1: Management strategies

For hypothesis one, the following null and alternative hypothesis are used:

H0: $\mu1 = \mu2$ Deploying commercial business strategies does not cause a higher return on investment with life science firms in The Netherlands.

H1: $\mu1 \neq \mu2$ Deploying commercial business strategies cause a higher return on investment with life science firms in The Netherlands.

The independent variables are:

O*utsourcing the commercializing process; sharing laboratory space with other firms; doing mutual advertisement/marketing/sales with partner; outsourcing research to other organization(s); hiring frequently new employees with lower wages that replace the employees with higher wages of the commercial department; establishing in a cluster, which saves for example on transport costs when cooperating with another firm; having access to a database in which we can see the work of other firms, which saves on e.g. search costs; cooperating with organization(s) that have establishments in different clusters; having different establishments in different clusters; hiring employees through our already employed employees; focusing on long-term employment in our organization.*

The dependent variable is:

Return on investment.

To execute the analysis the following was programmed;

Analyze ⟹ regression ⟹ linear

R	R Square	Adjusted R Square	Std. Error of the Estimate
,915	**,837**	**,614**	1,179

By looking at the R Square of the model, it can be seen that the model explains 83.7% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 61.4% of the variance of the dependent variable.

The second table in the output is an ANOVA table. Anova is a technique for testing the hypothesis that sample means of several groups are derived from the same population. It compares the variances among the means to the variances within the samples. What it takes to be "large enough" for the difference to be statistically significant depends on the sample sizes and the amount of certainty that we desire in our testing (that is, *p* values or levels of statistical significance that we typically use with all of our significance tests). From the Anova table is determined which independent variables have a significance level that is lower than 0.01 and can therefore be used to draw valid conclusions from. The *F* statistic tests whether the R square proportion of variance in the dependent variable accounted for by the independent variables is zero. In case the null hypothesis is rejected, there is a regression relationship between the dependent variable and the independent variables. The result is a large F (H0: ß1= ß2 =… = ßm = 0) of 3.74, which indicates that the independent variables could be used to predict the dependent variable, return on investment. The p-value for the F-test is smaller than 0.01, namely 0.005. At least one coefficient differs statistically significantly from zero.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	114,522	22	5,206	3,744	,005
Residual	22,247	16	1,390		
Total	136,769	38			

Coefficients

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
nostrategytoimprROI	**-3,367**	,980	-,848	-3,437	**,003**
stratimprROIoutsourcecommercializing	**-4,627**	1,086	-,658	-4,259	**,001**
stratimprROIoutsourceresearch	**4,834**	,974	1,088	4,965	**,000**
stratimprROIcooperate with firms that are in different clusters	**-3,139**	,781	-,836	-4,019	**,001**
stratimprROI have different establishments in different clusters	**5,284**	1,406	,622	3,759	**,002**

So far the model has been considered valid. In turn, the next step is the analysis of the variables. In case independent variables were not considered statistically significant by the backward model, they were left out of the analysis. When looking at the coefficients (see above table), the variable ´having no strategy´ is significant when the significance or p-value is lower than 0.01. Which is the case for the variable ´no strategy´, as the significance is 0.003, meaning that the variable ***´no strategy´*** has a statistically significant influence. In addition, the coefficient is -3.367 (ceteris paribus, all other factors are the same). This means that when life science firms have no business strategy, the return on investment will be 3.37% lower than when the life science firms do have a business strategy. In turn, it is thus better to have a business strategy to improve the return on investment. The standard error of the coefficients of the variable ´no strategy´ is 0,98%. The standard error shows the variance of the estimated coefficient. The lower the error, the better is the estimator. In this case 0.98% is considered low, as it is less than 1%, which leaves still at least 3.37% - 0.98% = 2.39%.

In turn the conclusion remains the same, namely that no strategy has a considerable negative impact on the return on investment. Other variables that have a negative impact on the return on investment are:

- ***Outsourcing the commercializing of the products to other firms***; the p-value is lower than 0.01, namely 0.001. This in turn makes the variable valid to draw conclusions from. The coefficient is -4.627 (ceteris paribus, all other factors are the same) and the standard error is 1.086, which means that outsourcing the commercializing process to another firm has a negative impact on the return on investment. In turn when life science firms apply the strategy of outsourcing commercializing, the ROI diminishes with a margin between 5.71% and 3.54%, with an average of 4.63%. With the highest average, this variable is considered to be the worst strategy for life science firms to improve their ROI. In my opinion, this could be explained by the loss of profit that firms have when they do not obtain the income from commercializing.

- ***Cooperate with firms that are in different clusters***; the p-value is lower than 0.01, namely 0.001. This in turn makes the variable valid to draw conclusions from. The coefficient is -3.139 (ceteris paribus, all other factors are the same) and the standard error is 0.781, which means that when life science firms cooperate with life science firms from other clusters, the ROI diminishes with a margin between 3.92% and 2.36%, with an average of 3.14%. The emphasis for cooperation should therefore be more on cooperation with firms in the same cluster. In my opinion, this outcome is not what was expected, as it appears logic that firms with establishments in different clusters should transfer knowledge spillovers from other clusters. Apparently this is not the case and therefore it could be so that, to improve management skills, the cooperation should not be in the same cluster but outside the cluster.

  The next step in the analysis is determining the variables that have a positive impact on the ROI, which are:

- ***Having different establishments in different clusters;*** the p-value is lower than 0.01, namely 0.002. This in turn makes the variable valid to draw conclusions from. The coefficient is 5.284 (ceteris paribus, all other factors are the same) and the standard error is 1.406, which means that outsourcing the commercializing process to another firm has a positive impact on the return on investment. In turn when life science firms have different establishments in different clusters, the ROI diminishes with a margin between 6.69% and 3.88%, with an average of 5.28%. With the highest average, this variable is considered to be the best strategy for life science firms to improve their ROI. In addition to the previous variable, where life science firms cooperate with other life science firms that are present in the same cluster, but do have establishments in the same cluster, this variable ´having different establishment in different clusters´ does generate a positive effect on the return on investment. In my opinion this is due to the proximity that life science firms have to each other and the more intensive relationship that managers have during the cooperation. This way managers learn from each other due to the more proximity.

- ***Outsource research;*** the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. The coefficient is 4.834 (ceteris paribus, all other factors are the same) and the standard error is 0.974, which means that outsourcing research to another firm has a positive impact on the return on investment. This means that when life science firms apply the strategy of outsourcing research, the ROI increases with a margin between 5.81% and 3.86%, with an average of 4.834%. The reason for the positive impact on the return of investments of life science firms, is in my opinion because of the specialization that each life science firm has into a certain area of investigation. Therefore, in my opinion, outsourcing the research to a life science firm that is specialized in a certain field of research should be more efficient than when life science firms perform their own research in fields where they are not specialized in.

When life science firms have different establishments in different clusters, the positive impact on the return on investment is highest. The highest positive impact on the return on investment is also obtained when life science firms outsource research to other firms. Outsourcing research has to do with specialization of other firms. By being specialized in a certain type of research field, a firm becomes evolved in cutting costs and increasing quality in the field its specialized in. Cook (2002) states about this that both small and large firms experience pressures to compete through innovativeness and therefore firms are mandatory to raise quality and reduce costs, which in turn is the responsibility of managers. Kanter agrees and states that the competitive value of innovation depends on the organizational capabilities like the effective management of resource allocation, human commitment (Kanter, 1983) and intra-organizational networks (Porter, 1985). In addition, Kandampully (1999) states that improving the firm´s network creates competitive advantage. Polynuclear regions, like the Randstad in The Netherlands, allow cities to develop and exploit complementaries or synergies between different locations. Through the encouragement of interaction between neighboring locations, each will develop specialization in areas which it has competitive advantage. In my opinion, being present in more locations and also knowing to which company to outsource, is therefore a very good explanation to improve the managerial ability and thereby the return on investment.

5.3.2. Hypothesis 2: Geographical distance to improve managerial ability

H0: $\mu 1 = \mu 2$ The management skills of managers in life science firms in The Netherlands are not of better result when they cooperate with life science firms outside The Netherlands

H1: $\mu 1 \neq \mu 2$ The management skills of managers in life science firms in The Netherlands are of better result when they cooperate with life science firms outside The Netherlands

The independent variables are:

The same city; the same province, but different city; the same country, but different province; another European country; outside of Europe

The dependent variables are:

Granted patents, new products, net profit margin, return on investment.

R	R Square	Adjusted R Square	Std. Error of the Estimate
,997	**,995**	**,978**	**,197**

ANOVA

Model		Sum of Squares	df	Mean Square	F	Sig.
	Regression	35,806	15	2,387	**61,485**	**,000**
	Residual	,194	5	,039		
	Total	36,000	20			

By looking at the R Square of the model, it can be seen that the model explains 99.5% of the variance of the dependent variable ´granted patents´. The model, corrected for the number of independent variables, explains 97.8% of the variance of the dependent variable. The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 61,485. The p-value for F-test is smaller than 0.01, namely 0.000. The H0-hypothesis can thus be rejected. At least one coefficient differs statistically significantly from 0. So far the model has been considered valid, by which the next step is the analysis of the variables.

Granted patents

When looking at the coefficients, the first variable:

- ***´Improving managerial ability by cooperation with other firms within the same city´*** is valid to draw conclusion from when the p-value is lower than 0.01. Which is the case for this variable, where the p-value is 0.000, meaning that the variable has a statistically significant influence. In addition, the coefficient is -4.718 (ceteris paribus, all other factors are the same)**.** This means that when managers of life science firms cooperate with management from other life science firms that are established in the same city, their amount of granted patents will be lower with 4.72 patents than when they cooperate with management that is from outside the city. The standard error of the coefficients of this variable is 0.392. The standard error shows the variance of the estimated coefficient. The lower the standard error, the better is the estimator. In this case 0.392 is considered low, which leaves still at least a result between 4.72 - 0.392 = - 4.33 and 4.72 + 0.392 = - 5.11 patents. In turn the conclusion remains the same, namely that cooperating with life science firms from the same city has a considerable negative impact on the granted patents.

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	Sig. B
(Constant)	7,176	,408		17,576	,000
distance between organizations that improve managerial ability same city	**-4,718**	**,392**	**-1,750**	**-12,043**	**,000**
distance between organizations that improve managerial ability same province different city	**-3,541**	**,291**	**-1,152**	**-12,149**	**,000**
distance between organizations that improve managerial ability same country different province	**-4,476**	**,352**	**-1,612**	**-12,712**	**,000**
distance between organizations that improve managerial ability other EU country	**7,224**	**,650**	**2,166**	**11,107**	**,000**
distance between organizations that improve managerial ability outside Europe	**,935**	**,226**	**,250**	**4,145**	**,009**

Other variables that have a negative relation with the granted patents are:

- ***Cooperation between life science firms that improve managerial ability in the same province however in a different city***; the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. The coefficient is -3,541 patents (ceteris paribus, all other factors are the same) and the standard error is 0.291, which means that when life science firms cooperate with other life science firms in the same province however between different cities, there is negative impact on the return on investment. In turn when life science firms cooperate with other life science firms in the same province however between different cities, the granted patents diminish with a margin between 3.83 and 3.25 patents, with an average of 3.54 patents.

- ***Cooperation between life science firms that improve managerial ability same country different province;*** the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. The coefficient is -4,476 patents (ceteris paribus, all other factors are the same) and the standard error is 0.352, which means that when life science firms cooperate with other life science firms in the same province however between different cities, the granted patents diminish with a margin between 4.83 and 4.12 patents, with an average of 4.48 patents.

The variables that have a positive impact on the granted patents are:

- ***Cooperation between life science firms from inside the EU to improve management skills;*** the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. The coefficient is 7,224 patents (ceteris paribus, all other factors are the same) and the standard error is 0.65, which means that when life science firms cooperate with other life science firms from the European Union, the granted patents increases with a margin between 7.87 and 6.57, with an average of 7.22 patents. With an average of 7.22 patents, cooperating with life science firms from other European countries, is the best strategy to increase an organization´s number of granted patents (in terms of geographical distance).
- ***Cooperation with organizations from outside the EU to improve management skills;*** as the p-value is lower than 0.01, namely 0.009. This in turn makes the variable valid to draw conclusions from. The coefficient is 0.935 patent (ceteris paribus, all other factors are the same) and the standard error is 0.226, which means that when life science firms cooperate with non-EU life science firms, the granted patents increase between 1.16% and 0.71%.

When testing for innovativeness, cooperation between life science firms from the same city, however from a different province has a very negative impact on granted patents. In turn, cooperating with life science firms from other EU countries results in the most granted patents. In my opinion, that cooperating with life science firms from other EU countries results in the most granted patents, could be explained by the lack of alliances between private firms in The Netherlands. Practices like alliance management, which concerns managing the cooperations for mutual research with other organizations that in turn create the opportunity of more granted patents, are learned from other managers. In turn when the alliance management is of good level, good and productive relationships are formed with other life science organizations. In result when these productive relationships are not formed, the effect on the granted patents will also be negative. Most partnering in the Dutch life science sector occurs between public organizations and private firms, while alliances between private firms are more scarce. In my opinion, this lack of alliances between private firms could have been caused by a lack of large (diversified) life science firms in The Netherlands. In the US for example there exists a high number of alliances between private firms, in turn there are also much more alliances between large (diversified) life science companies and small biotech firms (de Man and Duysters, 2003). The development structure of the life science industry in The Netherlands does not show the same situation as the US or UK life science industry, in which the new life science start-ups and small firms play a dominant role. The role of the start-ups and small firms in The Netherlands have been almost zero. In my opinion, in the UK the small life science firms are considered to be valuable research partners, while in The Netherlands the small life science firms are not considered valuable research partners but more firms that have a lack of management capabilities. Suppliers of financial capital regard the presence of high-quality management capabilities in start-up firms a crucial condition for providing financial capital. In addition, ninety-five percent of the life science start-up firms in The Netherlands is considered to have a lack of management capabilities (Fuchs, 2003).

New Products

R	R Square	Adjusted R Square	Std. Error of the Estimate
,809	**,654**	**,568**	**,921**

ANOVA

Model		Sum of Squares	df	Mean Square	F	Sig.
	Regression	25,674	4	6,418	**7,571**	**,001**
	Residual	13,564	16	,848		
	Total	39,238	20			

By looking at the R Square of the model, it can be seen that the model explains 65.4% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 56.8% of the variance of the dependent variable. The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 7,571. The p-value for F-test is smaller than 0.01, namely 0.001. The H0-hypothesis can thus be rejected. At least one coefficient differs statistically significantly from 0. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		B
(Constant)	4,356	,690		6,315	,000
distance between organizations that improve managerial ability same country different province	-2,254	,756	-,777	-2,982	,009

- ***Cooperation between organizations that improve managerial ability in the same country, but different province;*** the p-value is lower than 0.01, namely 0.009. This in turn makes the variable valid to draw conclusions from. The coefficient is namely -2,254 patents (ceteris paribus, all other factors are the same) and the standard error is 0.756, which means that when life science firms cooperate with other organizations in the same province however between different cities, the new products diminish with a margin between 3.01 and 1.5 patents, with an average of 2.25 patents. The other independent variables: *the same city; the same province, but different city; another European country; outside of Europe:* were not considered statistically significant. Therefore it is difficult to draw a conclusion from the effect of the independent variables on new products. However because the result of the variable *´Cooperation between organizations that improve managerial ability in the same country, but different province´* is negative, it does add to the conclusion of the granted patents; that cooperating outside The Netherlands is most beneficial.

ROI

R	R Square	Adjusted R Square	Std. Error of the Estimate
,965	,932	,830	,606

The model, corrected for the number of independent variables, explains 83% of the variance of the dependent variable. The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 9,148.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	40,301	12	3,358	**9,148**	**,002**
Residual	2,937	8	,367		
Total	43,238	20			

The p-value for F-test is smaller than 0.02, namely 0.001. The H0-hypothesis can thus be rejected. At least one coefficient differs statistically significantly from 0. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig. B
distance between organizations that improve managerial ability same country different province	**-1,478**	**,351**	**-,486**	**-4,215**	**,003**
distance between organizations that improve managerial ability other EU country	**4,126**	**,788**	**1,129**	**5,236**	**,001**

The variables that have a high enough p-value are:

- ***Cooperation between organizations that improve managerial ability same country different province;*** the p-value is lower than 0.01, namely 0.003. This in turn makes the variable valid to draw conclusions from. The coefficient is -1,478% (ceteris paribus, all other factors are the same) and the standard error is 0.351, which means that when life science firms cooperate with other organizations in the same province however between different cities, the ROI decreases between 1.829% and 1.127%.

- ***Cooperation with organizations from outside the EU to improve managerial ability;*** the p-value is lower than 0.01, namely 0.001. This in turn makes the variable valid to draw conclusions from. The coefficient is 4,13% (ceteris paribus, all other factors are the same) and the standard error is 0.79, which means that when life science firms cooperate with other organizations in the same province however between different cities, the ROI increases with a margin between 4.91% and 3.34% patents, with an average of 4.13%.

In conclusion can be stated that in order to improve the management skills of life science managers in The Netherlands it is best to cooperate with firms from other EU-countries and non-EU counties. In other words to cooperate with life science managers that do not operate in The Netherlands. This result adds to my previous conclusion of hypothesis one, that there exist a lack of qualified life science managers in The Netherlands and for that reason it is best to learn from qualified life science managers in other EU countries.

5.3.3. Hypothesis 3: Theory and practice to improve managerial ability

To test the third hypothesis, the following null and alternative hypothesis are formed.

H0: $\mu1 = \mu2$ *The management skills of managers in life science firms in The Netherlands are not of better result when interacting with third parties.*

H1: $\mu1 \neq \mu2$ *The management skills of managers in life science firms in The Netherlands are of better result when interacting with third parties..*

Independent variables: *through their own experience, through interacting with the management of diversified biotech firms, through interacting with the management of dedicated biotech firms, through interacting with the management of biotech firms with 10 FTE´s or more, through interacting with the management of biotech firms with less than 10 FTE´s, by interacting with management from non-biotech firms, through interacting with consultancy firms, by being in the management team of other biotech firms.*

Dependent variables: *Granted patents, new products, net profit margin, return on investment.*

Profit margin

R	R Square	Adjusted R Square	Std. Error of the Estimate
,878	**,770**	**,610**	**1,263**

The R Square of the model explains 77% of the variance of the dependent variable ´profit margin´. The model, corrected for the number of independent variables, explains 61% of the variance of the dependent variable. The standard error of this estimate is 1,263.

ANOVA

Model		Sum of Squares	df	Mean Square	F	Sig.
	Regression	122,902	16	7,681	**4,814**	**,000**
	Residual	36,698	23	1,596		
	Total	159,600	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 4,814. The p-value for the F-test is smaller than 0.01, namely 0.000. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig. B
Improve managerial ability through their own experience	**2,612**	,828	,546	3,154	**,004**
Improve managerial ability through interacting with management more than 10 FTE	**6,871**	1,398	1,228	4,914	**,000**
Improve managerial ability through interacting with management non-biotech firms	**-3,890**	,820	-,779	-4,743	**,000**

- **Improve managerial ability through their own experience**; the p-value is lower than 0.01, namely 0.004. This in turn makes the variable valid to draw conclusions from. The coefficient is 2,612% (ceteris paribus, all other factors are the same) and the standard error is 0,828%. This means that when life science managers learn from their own experience, they create a profit margin between 1.78% (2.612%-0.828%) and 3.44% (2.612%+0.828%).

- **Improve managerial ability through interacting with management more than 10 FTE***;* the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. The coefficient is 6,871% (ceteris paribus, all other factors are the same) with a standard error of 1,398%. This means that when life science managers learn from large life science firms with more than 10 FTE´s, they create a profit margin between 8.27% (6.871%+1.398%) and 5.47% (6.871%-1.398%). This result immediately causes the rejection of the H0-hypothesis. The management skills of managers in life science firms in The Netherlands are of better result when interacting with other parties. The profit margin increases 6,871% when life science managers interact with another party, while it only increases 2,612% when firms learn from their own experience. The high increase of 6,871% in profit margin also indicates that, interacting with life science firms that have more than ten FTE, is very beneficial. In my opinion, interacting with large life science firms is beneficial because life science managers learn a lot from the experience of large life science firms. Large life science firms have already passed several growth stages and in turn can teach the less experienced life science firms how to obtain continuity.

- Improve managerial ability through interacting with management of non-biotech firms*;* the p-value is lower than 0.01, namely 0.000. This in turn makes the variable valid to draw conclusions from. This in turn makes the variable valid to draw conclusions from. The coefficient is -3,89% (ceteris paribus, all other factors are the same) with a standard error of 0,82%, thus the profit margin decreases between -4.71% and -3.07%, when life science managers interact with non-biotech firms. This means that is it not beneficial for life science managers to interact with non-biotech firms. In my opinion, the life science market is an unique market, in which managers need experience on how to secure continuity for their firm. This experience is learned best from experienced life science managers that have survived in the life science market and have experienced how to cope with the life science market.

In conclusion can be stated that the best management performance results when life science managers interact with large biotech firms. In The Netherlands there exist a scarcity of private-private alliances, which could have been caused by a shortage of large (diversified) life science firms. Whereas in the US for example there exists a high number of private-private alliances, as more large (diversified) life science companies exist. Universities are often considered to have poor management relative to the management of diversified firms. This also counts for dedicated life science firms that are spin-offs from universities. Other than in the US, venture capitalists do not have an active role in the management of biotech firms. Venture capitalists in the US for example play a significant role in management support of the dedicated life science companies. Venture capitalists in The Netherlands are also not committed to build up a network around the dedicated life science companies they participate in. Venture capital is sufficiently present in The Netherlands, what lacks however is ´smart money´: investors that participate in the management of the dedicated life science firms (de Man and Duysters, 2003).

5.3.4. Hypothesis 4: Education and management performance

To test the fourth hypothesis, the following null and alternative hypothesis are formed.

H0: $\mu 1 = \mu 2$ The management skills of managers in life science firms in The Netherlands improve not better when having an educational background.

H1: $\mu 1 \neq \mu 2$ The management skills of managers in life science firms in The Netherlands are of better result when having an educational background.

Independent variables: Education in: Finance, law, alliance management, commercializing, biotech, management in general, management in biotech.

Dependent variables: *Granted patents, new products, net profit margin, return on investment*.

R	R Square	Adjusted R Square	Std. Error of the Estimate
,625	**,391**	**,280**	1,212

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	31,051	6	5,175	**3,525**	**,008**
Residual	48,449	33	1,468		
Total	79,500	39			

By looking at the R Square of the model, it can be seen that the model explains 39.1% of the variance of the dependent variable ´granted patents´. The model, corrected for the number of independent variables, explains 28% of the variance of the dependent variable. The model is statistically significant, due to the p-value which is lower than 0.01, namely 0.008.

Profit margin

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig. B
Improve managerial ability through courses in management of biotech firms	**-3,914**	1,209	-,516	-3,238	**,004**

- **´Improve managerial ability through courses in management of biotech firms´** is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.004, meaning that the variable has a statistically significant influence. The coefficient is -3,914% (ceteris paribus, all other factors are the same) with a standard error of 1,209. This means that the managers of life science firms that follow courses in life science management the profit margins will decrease between -5,12% and -2.71%. In my opinion, managing the costs and the profit in life science firms is not learned best through courses, however best through the learning from more experienced managers. In addition these more experienced managers have gained the experience to cut costs and increase income from practical experience and thereby actual cases. In turn these costs savings and income increases are in my opinion learned better from practical experiences than theoretical courses.

New Products

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig. B
Educational background manager commercializing (e.g. marketing, communication)	**3,287**	**,959**	**,932**	**3,426**	**,002**

The only variable that is considered significant with new products is **Educational background manager commercializing (e.g. marketing, communication).** This variable is statistically significant as the p-value is 0.002, which is lower than 0.01. In addition this variables is positively correlated with the number of new products by 3.287, with a standard error of 0.959 new product, thus the new products increase between 2,33 new products and 4.25 new products. In my opinion the commercializing of products can be learned from commercializing courses. The commercializing courses involve marketing practices that are very well analyzed and explained during the courses. Contrarily to the profit margin, where costs savings and income improvement are different for every situation and every life science firm, the commercializing process is a less unique practice. In turn by being less unique, commercializing is a practice that can be learned through both practical experience and education.

Granted patents

R	R Square	Adjusted R Square	Std. Error of the Estimate
,934	**,873**	**,708**	**,686**

By looking at the R Square of the model, it can be seen that the model explains 87.3% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 70.8% of the variance of the dependent variable.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	54,782	22	2,490	**5,296**	**,000**
Residual	7,993	17	,470		
Total	62,775	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 5,296. The p-value for F-test is smaller than 0.01, namely 0.000. The H0-hypothesis can thus be rejected. At least one coefficient differs statistically significantly from 0. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	B
Educational background manager in biotech	**1,233**	**,408**	**,351**	**3,019**	**,008**
Educational background manager management in general	**2,221**	**,576**	**,740**	**3,859**	**,001**

From the coefficients results that the following variables are significantly correlated with new products:

- **Educational background manager in biotechnology;** This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.008, meaning that the variable has a statistically significant influence. The coefficient is 1,233 patents (ceteris paribus, all other factors are the same) with a standard error of 0,408. This means that when life science managers have had an education in biotechnology, the number of patents is between 0.83 and 1,638 patent higher than when managers do not have had an education in biotechnology. In my opinion, when life science managers have had an education life science, they have more knowledge on how to manage the innovativeness of the firm. This includes actions like: setting up more prosperous alliances with other firms, how to make the R&D department of the firm more innovative, select fields of research that grant the possibility to create innovations with more potential.

- **Educational background manager general management;** is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.001, meaning that the variable has a statistically significant influence. The coefficient is 2,221 patents (ceteris paribus, all other factors are the same) with a standard error of 0,576. This means that when managers of life science firms have had education in general management, the granted patents are between 1.64 and 2,8 patent higher than in the case they did not had an education in management. In my opinion the same argument can be given as with the previous variables, when managers have an education in biotechnology. Namely that due to the theoretical background of management, life science managers know how to manage the firm and how stir it into the right direction.

In order to obtain a good level of new products, life science firms need to change the culture away from the pseudo-academic R&D norm to more commercializing. This move towards commercialization is still not occurring in many small life science firms and as a consequence many small biotech firms go bankrupt or get sold unintentionally (Philpott and Cassells, 2004). In my opinion and which was also apparent from the results above, commercializing skills can be obtained through education in commercializing. In addition learning from practice and thereby from other more experience life science firms is in my opinion also a good manner to improve commercializing skills.

5.3.5. Hypothesis 5: Duration management and management performance

To test the fifth hypothesis, the following null and alternative hypothesis are formed.

H0: $\mu1 = \mu2$ The management skills of managers in life science firms in The Netherlands do not are of better result when managers remain longer at the same life science firm.

H1: $\mu 1 \neq \mu 2$ The management skills of managers in life science firms in The Netherlands are of better result when managers remain longer at the same life science firm.

Independent variables: *Less than 4 years, from 4 years until 9 years, from 10 years until 15 years, from 16 until 25 years, from 26 until 35 years, more than 35 years*

Dependent variables: *Granted patents, new products, net profit margin, return on investment.*

Profit margin

R	R Square	Adjusted R Square	Std. Error of the Estimate
,825	**,681**	**,539**	**1,372**

By looking at the R Square of the model, it can be seen that the model explains 68.1% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 53.9% of the variance of the dependent variable.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	108,282	12	9,023	**4,794**	**,000**
Residual	50,818	27	1,882		
Total	159,100	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 5,296. The p-value for F-test is smaller than 0.01, namely 0.000. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta	t	B
Duration manager less than 4	**-2,074**	**,602**	**-,503**	**-3,446**	**,002**
Duration manager from 4 years until 9 years	**-2,753**	**,630**	**-,676**	**-4,373**	**,000**

Duration of a manager in a company is less than 4 years; This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.002, meaning that the variable has a statistically significant influence. The coefficient is -2,074% (ceteris paribus, all other factors are the same) with a standard error of 0,602. This means that when life science managers are less than four years present in a life science firm, the profit margin is between -1,472% and -2,676% lower than when managers are not less than four years present in the life science firm.

- ***Duration of a manager in a company is between 4 and 9 years;***
  This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.000, meaning that the variable has a statistically significant influence. The coefficient is -2,753% (ceteris paribus, all other factors are the same) with a standard error of 0,63. This means that when life science managers are between four and nine years present in a life science firm, the profit margin is between -2,123% and -3,383% lower than when managers are not between four and nine years present in the life science firm.

Both two variables above have a negative impact on the profit margin. In turn when managers are less than nine years active in a biotech company, the impact on the profit margin is negative. About the duration of managers that are longer than nine years active in biotech firms there is no information available. Therefore long term duration (longer than nine years) of managers in biotech firms can not be compared to short term (shorter than nine years) duration of managers in biotech firms. The only conclusion that can be drawn is that short term duration (shorter than nine years) of managers in biotech firms has a negative impact on profit margin. In my opinion this could be explained by the fact that the respondents of the questionnaire are generally managers of small biotech firms that only exist for a few years. These small biotech firms that exist only for a few years are generally managed by academic scientists. Academic scientists are often the ones that manage the biotech firm the first few years when it results as a spin-off from the research institution or university. Many of these managers have little or no prior experience of appropriate management experience (Philpott and Cassells, 2004). They also lack the skills to: set up a good knowledge infrastructure, market the products of the firm and to structure and discipline the business environment. In turn the impact of these managers that have a duration of less than nine years in the biotech firms is negative.

ROI

R	R Square	Adjusted R Square	Std. Error of the Estimate
,797	**,635**	**,452**	**1,509**

By looking at the R Square of the model, it can be seen that the model explains 63.5% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 45.2% of the variance of the dependent variable.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	102,732	13	7,902	**3,473**	**,003**
Residual	59,168	26	2,276		
Total	161,900	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 5,296. The p-value for F-test is smaller than 0.01, namely 0.003. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta	t	B
Duration manager from 4 years until 9 years	**-2,008**	**,599**	**-,489**	**-3,351**	**,002**

Duration of a manager in a company is between 4 and 9 years; This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.002, meaning that the variable has a statistically significant influence. The coefficient is -2,008% (ceteris paribus, all other factors are the same) with a standard error of 0.599. This means that when life science managers are between four and nine years present in a life science firm, the return on investment is between -1,409% and -2,607% lower than when managers are not between four and nine years present in the life science firm.

About the duration of management is not very much to say, as there is no clear relation or positive result and additionally there is not sufficient significance for all periods in which a manager can be present in a life science. The only trend that is lightly displayed is that when managers of life science firms remain less time in the biotech firm, the effect on the profit margin is less negative. This contradicts the H1-hypothesis and therefore the H0-hypothesis can not be rejected. In my opinion, this result could be explained by the motivation that new managers have to prove themselves in the beginning. In addition, new managers that are hired, are hired for a certain expertise and selected on their accomplishments at other organizations. Meanwhile the managers that are managing the firm for a longer period, are most probably operative in the firm since the firm was in the early growth stages. In turn these managers that are already longer in the firm have probably a less strict evaluation than the managers that is newly hired. The difference is between the competitive group of managers from which the new manager is hired and really has to outstand with the management skills versus the already present manager who remains present because he or she adds for example experience or a network to the firm.

5.3.6. Hypothesis 6 and 7: Experience management and management performance

To test the **sixth hypothesis**, the following null and alternative hypothesis are formed.

H0: $\mu1 = \mu2$ The management skills of managers in life science firms in The Netherlands are not of better result when managers have more experience in general management.

H1: $\mu1 \neq \mu2$ The management skills of managers in life science firms in The Netherlands are of better result when managers have more experience in general management.

Independent variables: *No experience, Less than 5 years, From 5 years until 9 years, From 10 years until 15 years, From 16 until 25 years, From 26 until 35 years, More than 35 years*

Dependent variables: *Granted patents, new products, net profit margin, return on investment.*

R	R Square	Adjusted R Square	Std. Error of the Estimate
,990	**,980**	**,901**	**,399**

By looking at the R Square of the model, it can be seen that the model explains 98% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 90.1% of the variance of the dependent variable.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	61,500	31	1,984	**12,450**	**,000**
Residual	1,275	8	,159		
Total	62,775	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 5,296. The p-value for F-test is smaller than 0.01, namely 0.000. So far the model has been considered valid, by which the next step is the analysis of the variables.

Granted patents

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta	t	B
No experience manager in managing firms	**3,165**	**,709**	**1,010**	**4,465**	**,002**
Experience manager in managing firms from 5 until 9 years	**-2,692**	**,588**	**-,897**	**-4,576**	**,002**

- **No experience manager in managing non-biotech firms.** This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.002, meaning that the variable has a statistically significant influence. The coefficient is 3,165% (ceteris paribus, all other factors are the same) with a standard error of 0.709. This means that when life science managers have no experience in managing non-biotech firms, the granted patents will be between 3,874 patents and 2.456 patents higher than when managers are experienced in managing non-biotech firms.

- **Experience manager in managing non-biotech firms from 5 until 9 years.**

This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.002, meaning that the variable has a statistically significant influence. The coefficient is -2,692% (ceteris paribus, all other factors are the same) with a standard error of 0.588. This means that when life science managers have between five and nine years experience in managing firms, the granted patents will be between -2,104 patents and -3,28 patents lower than when managers are not between five and nine years experienced in managing firms.

The result from above two variables could be explained by the fact that the managers that were questioned are managers of biotech firms, however the result is: having experience in managing non-biotech firms does not aid biotech managers to perform better with the management of biotech firms.

Profit margin

R	R Square	Adjusted R Square	Std. Error of the Estimate
,860	**,740**	**,494**	**1,437**

By looking at the R Square of the model, it can be seen that the model explains 74% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 49.4% of the variance of the dependent variable.

ANOVA

Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	117,787	19	6,199	**3,001**	**,009**
Residual	41,313	20	2,066		
Total	159,100	39			

The test statistic of the F-test (H0: ß1= ß2 =… = ßm = 0) is 5,296. The p-value for F-test is smaller than 0.01, namely 0.009. So far the model has been considered valid, by which the next step is the analysis of the variables.

Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	B
Experience manager in managing firms more than 35 years	**-6,268**	**1,820**	**-,828**	**-3,445**	**,003**

- **Experience manager in managing firms more than 35 years***;* This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.003, meaning that the variable has a statistically significant influence. The coefficient is -6,268% (ceteris paribus, all other factors are the same) with a standard error of 1,820. This means that when life science managers have more than thirty-five years experience in managing non-biotech firms, the profit margin will be between -8,088 patents and -4,448 patents lower than when managers do not have more than thirty-five years experience in managing non-biotech firms.

Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	B
Experience manager in managing firms more than 35 years	**-6,268**	1,820	-,828	-3,445	,003
Experience manager in managing firms from 26 until 35 years	**-3,016**	1,307	-,398	-2,309	,032
Experience manager in managing firms from 16 until 25 years	**-1,983**	1,030	-,456	-1,926	,068
Experience manager in managing firms from 10 until 15 years	**-1,591**	,875	-,333	-1,819	,084

Because the variable ´ **Experience manager in managing firms more than 35 years**´ is the only statistically significant variables, the significance level is set a bit higher, up to ten percent, just to investigate whether there can be seen some sort of trend from the data results. When setting the significance level up to ten percent, a trend is shown which can be seen in the table above. It can be seen that managers with more experience in managing non-biotech firms have a more negative impact on the profit margin. This can be seen in the B column, which is the second on the left. Here the impact goes stepwise down, from a -6,268% decrease in profit margin for the most experienced managers, to -1,591% for the least experienced managers.

In my opinion is the life science market an unique market, where in order to run a life science firm, work experience is needed not from any industry, but the life science industry. This in turn explains the result that managers with no management experience in firms (from all industries) have a more positive impact on granted patents of life science firms. This also contradicts the H1-hypothesis and thereby does not reject the H0-hypothesis.

To test the **seventh hypothesis**, the following null and alternative hypothesis are formed.

H0: $\mu1 = \mu2$ The management skills of managers in life science firms in The Netherlands are not of better result when managers have more experience in the management of a life science firm.

H1: $\mu1 \neq \mu2$ The management skills of managers in life science firms in The Netherlands are of better result when managers have more experience in the management of a life science firm.

R	R Square	Adjusted R Square	Std. Error of the Estimate
,860	**,740**	**,494**	**1,437**

By looking at the R Square of the model, it can be seen that the model explains 74% of the variance of the dependent variable. The model, corrected for the number of independent variables, explains 49.4% of the variance of the dependent variable.

Profit margin

Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	B
Experience manager in managing biotech firms from 16 until 25 years	**4,512**	**1,206**	**,945**	**3,742**	**,001**

Experience manager in managing biotech firms from 16 until 25 years; This variable is significant when the significance or p-value is lower than 0.01, which is the case for this variable. The p-value is 0.001, meaning that the variable has a statistically significant influence. The coefficient is 4,512% (ceteris paribus, all other factors are the same) with a standard error of 1,206. This means that when life science managers that have between sixteen and twenty-five years experience in managing biotech firms, the profit margin will be between 5,718 patents and 3,306 patents lower than when managers do not have between sixteen and twenty-five years experience in managing biotech firms.

Because only the variable ´experience manager in managing biotech firms from 16 until 25 years´ is statistically significant, the p-value margin is set a bit higher at five percent. This is done to determine whether a trend is shown when more variables are significant.

Model	Unstandardized Coefficients		Standardized Coefficients		Sig.
	B	Std. Error	Beta	t	B
Experience manager in managing biotech firms from 10 until 15 years	**2,514**	**1,187**	**,563**	**2,119**	**,047**
Experience manager in managing biotech firms from 16 until 25 years	**4,512**	**1,206**	**,945**	**3,742**	**,001**
Experience manager in managing biotech firms from 26 until 35 years	**6,038**	**2,135**	**,473**	**2,828**	**,010**

In this case a trend is shown, in which it can be seen that managers with more experience in managing biotech firms have a more positive impact on the profit margin. This can be seen in the B column, which is the second on the left. Here the impact goes stepwise up, from a 6,038% increase in profit margin for the most experienced managers, to 2,514% for the least experienced managers.

The theory states about inexperienced life science managers that they are largely individual, opportunistic and reactionary. These inexperienced managers are often founders of dedicated life science firms that spin-off from universities and are merely scientists that lack the skills to; set up a good knowledge infrastructure, a good IT-structure, structure and discipline the business environment and to market the products of the firm. These starters of university spin-offs are poorly equipped to deal with evolving the company structure as the companies develop. This evolvement includes the change of culture away from the pseudo-academic R&D norm to more commercializing. As a result many young life science firms go bankrupt or get sold unintentionally (Philpott and Cassells, 2004). To prevent this, investors (including large life science firms) that invested in the dedicated life science firms, need to be assured that their investment is in good hands and that the life science firm is properly managed. The investors generally consider the founding innovative scientists of the life science firm do not have the skills and experience to drive the business in the right direction. For that reason the investors prefer that the life science firm appoints a CEO that does have these skills and experience, which emphasizes the necessity for experienced life science managers.

The result, that more experienced life science managers perform better in life science firms, confirmed my previous statement which was put in the result of the profit margin of hypothesis six. In this statement the life science market was characterized as an unique market, where in order to run a life science firm work experience is needed not from any industry, but the life science industry. The result that more experienced life science managers perform better in life science firms, also rejects immediately the H0-hypothesis.

5.4. Conclusion chapter five

When biotech firms are present in multiple clusters and also know to which company to outsource their research, the return on investment is highest. In addition, when biotech firms in The Netherlands cooperate with life science firms from other EU countries the number of granted patents are highest. Furthermore to improve the management skills of life science managers in The Netherlands it is best to cooperate with firms from other EU-countries and non-EU counties. The best management performance results when life science managers interact with large and medium sized biotech firms. In short the focus of research cooperation should be on large and medium sized biotech firms outside The Netherlands. For biotech managers in The Netherlands, to improve their commercializing skills, education in commercializing is a very good way. Biotech managers in The Netherlands, when their commercialization skills are not developed enough and their company´s result is not optimal, are best of to take additional courses in commercialization, to improve their commercialization skills. However to run a life science firm the best way of all is to have previous work experience in the life science industry.

CONCLUSION

In the beginning of this report it became clear that the life science market is a relatively new market. The US life science market and the European life science market are the leading markets the two world, in which the US is even far more advanced than Europe. The US government invests much more in the biotech industry than the European governments, e.g. through capital, entrepreneurship, easy regulation. As a result in the US, the life science market is more advanced than in Europe, which includes e.g. the companies, management, company life cycles. During this thesis the management of biotech firms were investigate, hence the answering of the research question in the remainder of this conclusion:

Research Question: '*What are the determining differences in management skills between managers of more efficient and less efficient functioning biotech firms in The Netherlands?´*

In the first four chapters of this thesis it was found that life science managers who have done courses in management, have the best performance. During the investigation of this thesis, it was found that a theoretical background in management and biotechnology help biotech managers to perform better in their firms, however the best performance is obtained when biotech managers learn from through experience.

From the research of this thesis it became clear that managers of the biotech industry in The Netherlands, have the best performance in terms of profit margin, when interacting with large life science firms that contain more than ten FTE´s. This in turn is in my opinion due to the experience that biotech firms with more than ten FTE´s have build up during their growth. This experience in turn can learn biotech firms, that are in earlier growth stages, how to cope with their future growth stages.

As discussed in chapter three, there exist a shortage of large life science firms in The Netherlands, which in turn explains the lack of learning from experienced life science managers. In The Netherlands, the large life science firms are spread very diverse throughout different clusters. In addition, it is not just about cooperating with firms that are established in different clusters, but being actually present in the different clusters. By being present in different clusters, biotech firms are able to learn from more parties.

In the Netherlands there exist very few private-private cooperations between biotech firms. In addition, from the research it became clear that in order to improve the management skills best in terms of the return on investment, biotech managers cooperate with biotech firms from outside the European Union. While in terms of granted patents it is best to cooperate with biotech firms from other European countries or non-EU countries or in other words non-Dutch biotech firms.

In the US, venture capitalists play an active management role in the biotech firms where they invest in. In Europe, the opposite occurs, namely that the venture capitalists play a very limited management role. From the research of this thesis it became clear that cooperating with experienced non-biotech managers has a negative effect on management performance in terms of profit margin and granted patents. While cooperating with experienced biotech managers does have a positive effect on profit margin and granted patents. These experienced biotech managers could be present in large life science firms, venture capitalists or other organizations. The key is to find the experienced biotech managers and to form cooperations or make them part of the management.

In turn, in my opinion, it should be stimulated that the less experienced biotech managers are able to find the more experienced biotech managers to set up cooperations. In turn by stimulating the cooperation between large biotech firms and small biotech firms. In addition also stimulate experienced biotech managers (e.g. from large life science firms, venture capitalists) to form part of the management of biotech firms where the management is inexperienced.

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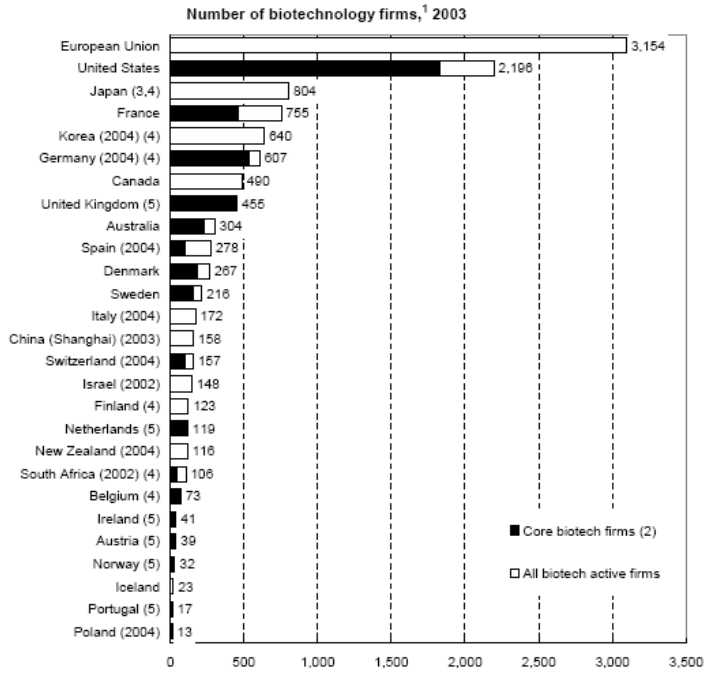
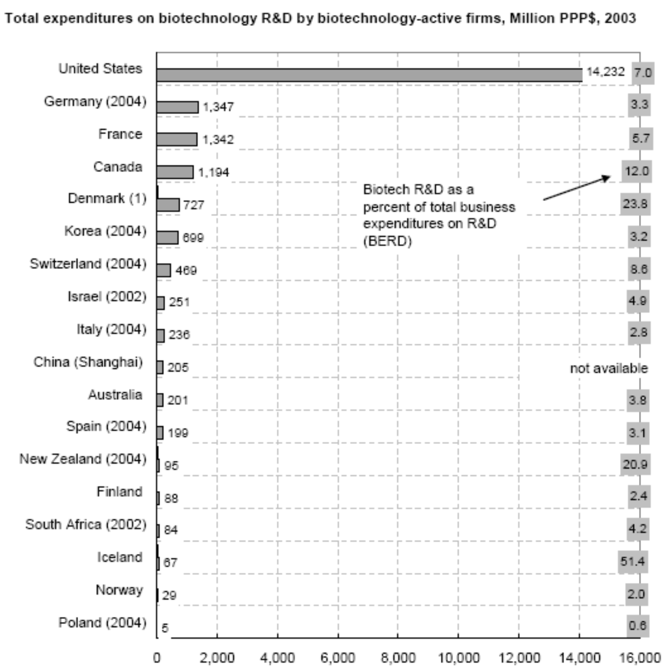
APPENDIX

Fig i: Number of private biotechnological firms in 2003



Source: OECD

Fig iia: Total expenditure R&D private sector in millions $, 2003



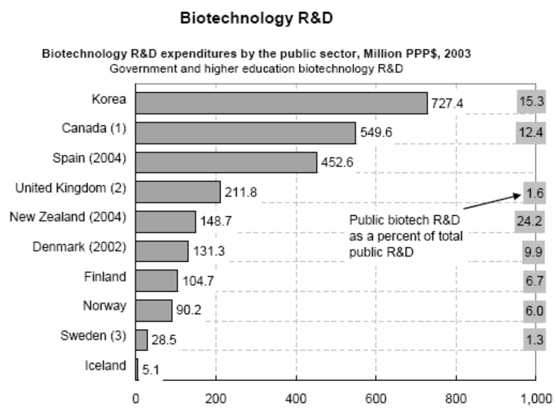
Source: OECD

Fig iib: Total expenditure R&D US public sector in millions $, 2005

Agency	Life sciences R&D ($m)	Share of total
All agencies	29,790	100%
Agency for International Development	167	1%
Department of Agriculture	1,443	5%
Department of Defense	694	2%
Department of Energy	288	1%
Department of Health and Human Services	25,497	86%
Department of the Interior	165	1%
Department of Veterans Affairs	307	1%
NASA	334	1%
National Science Foundation	578	2%

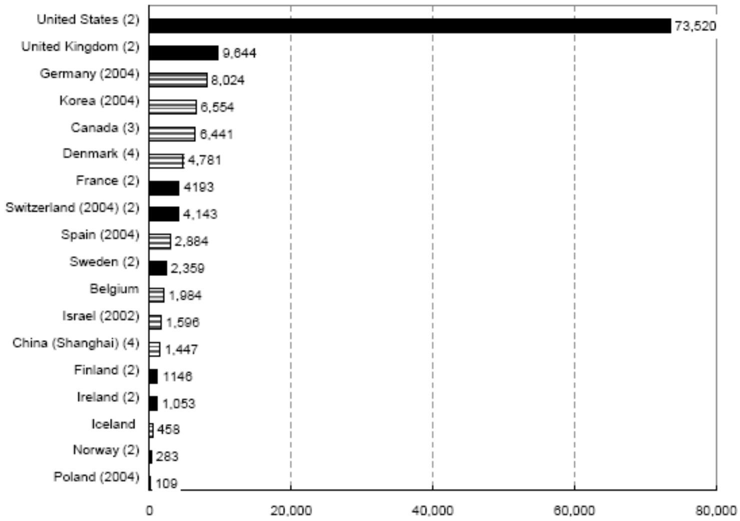
Source: American Association for the Advancement of Science. Reports I through XXXI. 2007.

Fig iic: Total expenditure R&D public sector in millions $, 2005



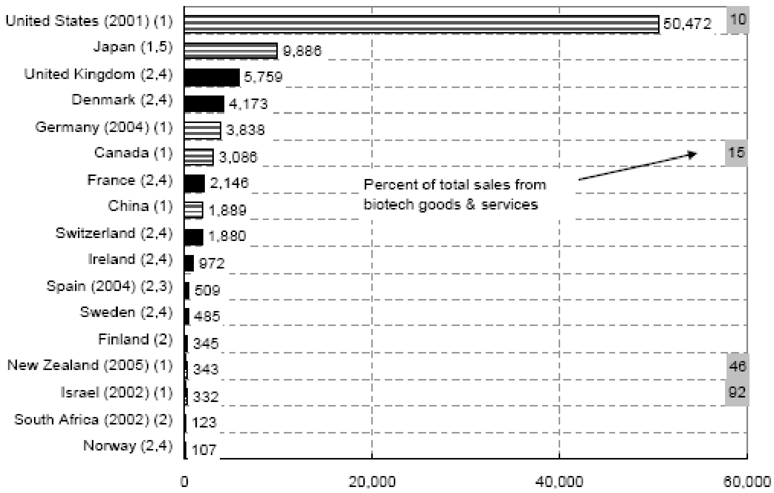
Source: OECD

Fig iii: R&D Employment biotech, 2003



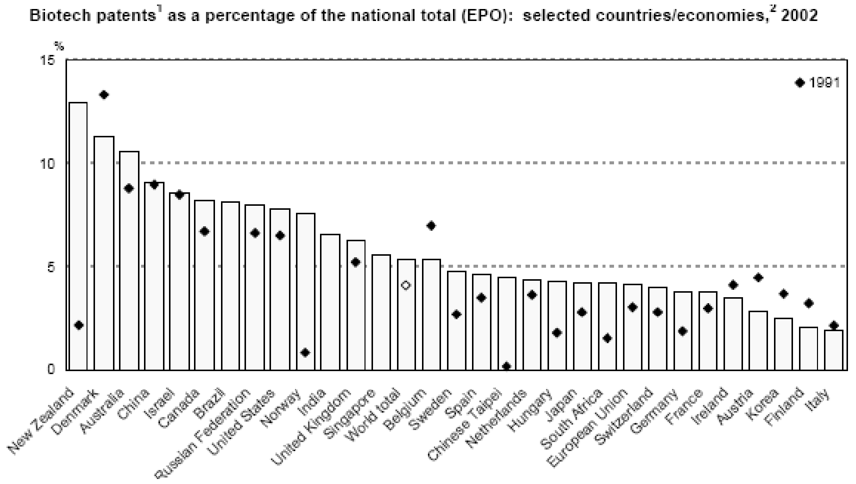
Source: OECD

Fig iii: Sales biotech firms, 2003



Source: OECD

Fig iv: Biotech Patents biotech firms, 2002



Source: OECD

Fig. v: Different bio-industries

DNA/RNA	Genomics, pharmacogenomics, gene probes, genetic engineering, DNA/RNA sequencing/synthesis/amplification, gene expression profiling, and use of antisense technology.
Proteins and other molecules	Sequencing/synthesis/engineering of proteins and peptides (including large molecule hormones); improved delivery methods for large molecule drugs; proteomics, protein isolation and purification, signaling, identification of cell receptors.
Cell and tissue culture and engineering	Cell/tissue culture, tissue engineering (including tissue scaffolds and biomedical engineering), cellular fusion, vaccine/immune stimulants, embryo manipulation.
Process biotechnology techniques	Fermentation using bioreactors, bioprocessing, bioleaching, biopulping, biobleaching, biodesulphurisation, bioremediation, biofiltration and phytoremediation.
Gene and RNA vectors	Gene therapy, viral vectors.
Bioinformatics	Construction of databases on genomes, protein sequences; modelling complex biological processes, including systems biology.
Nanobiotechnology	Applies the tools and processes of nano/microfabrication to build devices for studying biosystems and applications in drug delivery, diagnostics etc.

Source: OECD (2005) Statistical Definition of Biotechnology

Fig. vii: The biotechnology value chain

Phase	Tasks	Time	Actors
1) Research	Product discovery; identification of product for commercialization	0-3 Years	Research Universities and Start-Ups
2) Development	Clinical Trials; Involves animal and human testing for the product's safety and efficacy; Government Review and Approval	3-4 Years	Governmental Regulatory Agencies; Research Universities and Start-Ups
3) Manufacturing	Mass Production	Variable	Large Pharmaceutical Firms
4) Commercialization	Marketing and Selling	5 Years	Large Pharmaceutical Firms

Source: Boston consulting group and Lourdes Pagaran, 1993

Fig. viii: The biotechnology worldwide patenting record

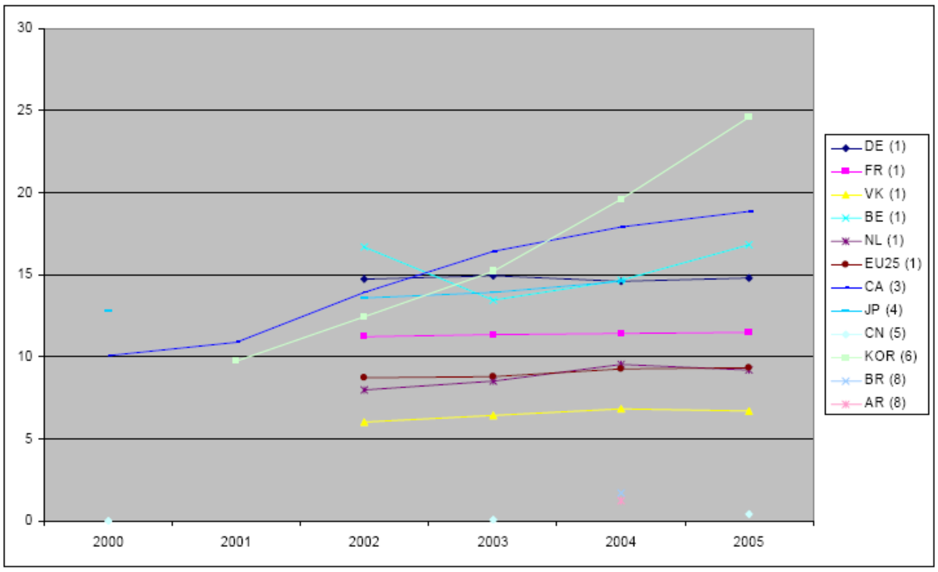
Biotechnology patenting – EU-27 ranked second worldwide

Table 6: Biotechnology patent applications to EPO by country[1], 1993, 1998, 2003 and AAGR

	Total			AAGR		
	1993	1998	2003	1993/1998	1998/2003	1993/2003
EU-27	920	2 155	2 576	18.6	3.6	10.8
Belgium	52	153	107	24.2	-6.9	7.5
Czech Republic	1	5	7	37.7	8.5	22.2
Denmark	75	120	169	9.9	7.1	8.5
Germany	202	564	901	22.7	9.8	16.1
Ireland	1	16	12	100.6	-5.7	37.6
Greece	2	2	7	6.9	23.1	14.7
Spain	9	32	66	27.9	15.5	21.5
France	157	329	370	16.0	2.4	9.0
Italy	42	70	124	10.5	12.3	11.4
Hungary	2	4	6	15.3	10.0	12.6
Netherlands	77	173	174	17.6	0.1	8.5
Austria	27	31	56	2.7	12.6	7.5
Poland	2	1	6	-15.7	44.2	10.3
Portugal	1	1	7	-3.1	47.4	19.5
Finland	20	37	38	13.4	1.0	7.0
Sweden	34	104	99	24.7	-0.9	11.1
United Kingdom	213	506	416	18.9	-3.8	6.9
Iceland	2	1	8	-19.8	67.5	15.9
Norway	10	19	21	13.9	2.4	8.0
Switzerland	36	75	133	15.9	12.0	13.9
Australia	54	116	165	16.5	7.2	11.7
Canada	66	231	224	28.7	-0.6	13.1
China	4	64	136	77.5	16.2	43.6
Israel	29	87	127	24.6	7.9	15.9
Japan	342	562	1 035	10.5	13.0	11.7
Korea	15	55	150	29.4	22.1	25.7
New Zealand	6	22	29	29.1	6.2	17.1
Russian Federation	12	30	35	20.9	3.0	11.6
South Africa	:	7	2	:	-19.5	:
United States	1 595	3 531	3 331	17.2	-1.2	7.6

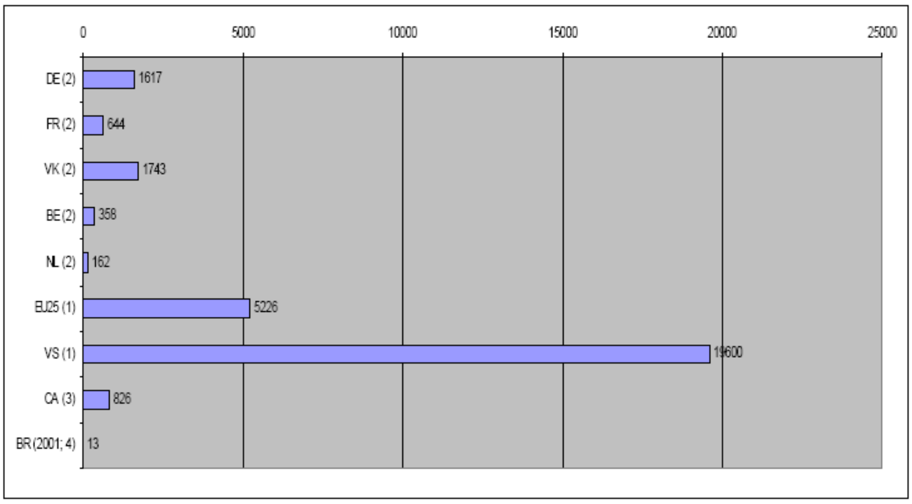
Source: Eurostat patent statistics

Fig ix: Public life science R&D expenditure in million PPP$ per million inhabitants 2000-2005.



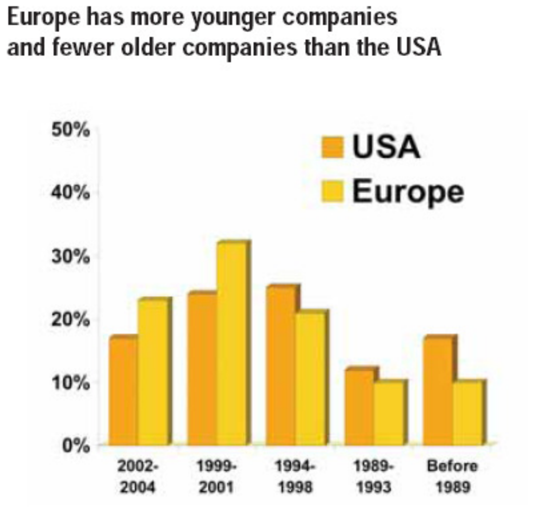
Source: TNO Innovation Policy Group, 2007

Fig x: Private life science R&D expenditure in million PPP$ per million inhabitants 2004.



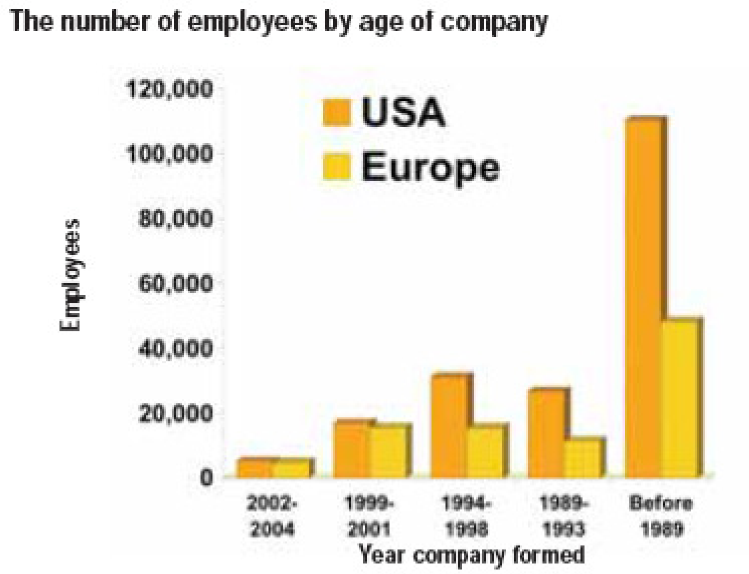
Source: TNO Innovation Policy Group, 2007

Fig 1: Age of companies in the USA and Europe



Source: Critical I comparative study for EuropaBio (2006)

Fig 2: The number of employees by age of company in the USA and Europe

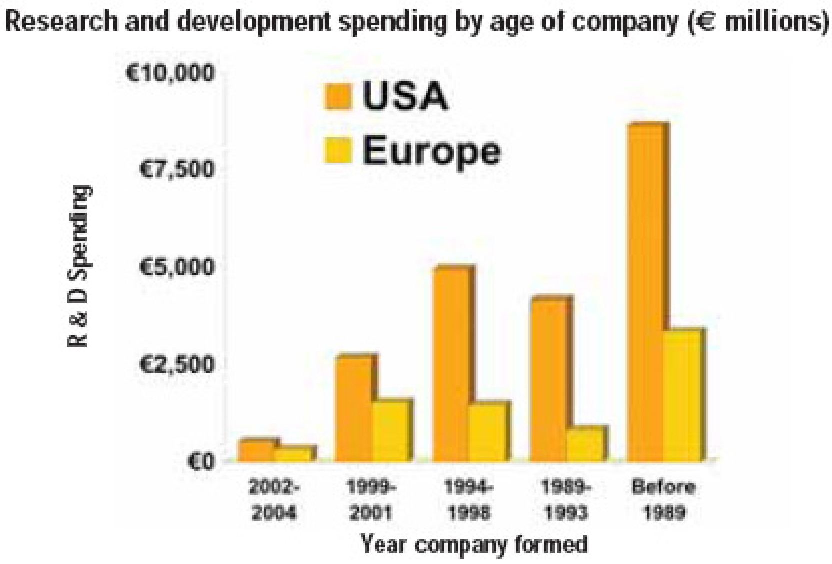


Source: Critical I comparative study for EuropaBio (2006)

Fig 3: The total revenue earned by age of company in the USA and Europe

Source: Critical I comparative study for EuropaBio (2006)

Fig 4: The R&D spending by age of company in the USA and Europe



Source: Critical I comparative study for EuropaBio (2006)

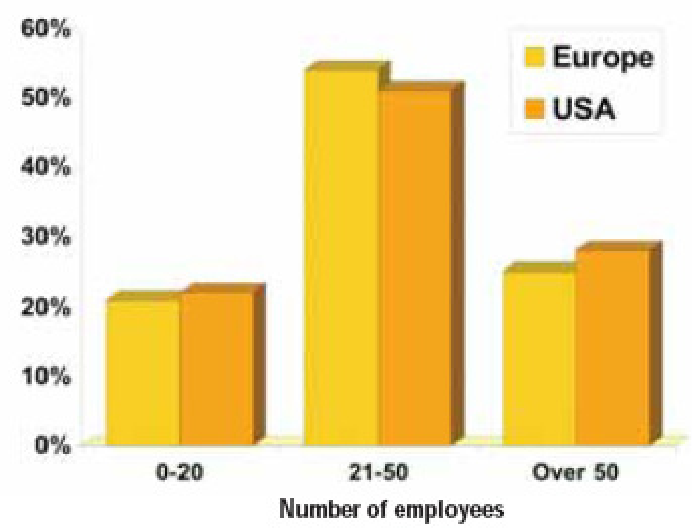
Fig 5: Total financial picture in the USA and in Europe (€ millions)

	Finance available 2002-2004 (total)				
Country	VC	Total Equity	Public Equity	Debt	Total
Austria	103	108			108
Belgium	127	175	23	26	201
Denmark	187	339	98	102	441
Finland	11	26		34	60
France	476	670	53	52	722
Germany	602	885	142	8	893
Ireland	19	211	190	1233	1444
Italy	28	47			47
Netherlands	28	63		3	66
Norway	7	9		1	10
Sweden	125	208	51	20	228
Switzerland	171	306	133	975	1281
UK	866	1868	346	539	2407
USA	7205	22500	9735	16872	39372
Europe	2748	4916	1036	2994	7910
Overall	9953	27416	10772	19866	47282
Europe %	28%	18%	10%	15%	17%

Source: Critical I Limited

Fig 6: Venture capital investments by year of foundation

Fig 7: Venture capital investments by company size



Source: Critical I comparative study for EuropaBio (2006)

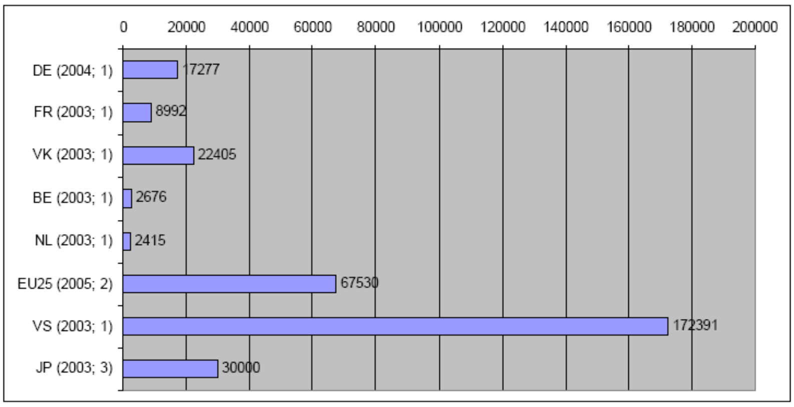
Fig 8: Growth of companies US and Europe with different company age

Older European companies tend to stay small:
Percentage of each age group with number of employees.
The largest class in each age range is highlighted.

Number of employees	Year company founded 2002-4	1999-2001	1994-1998
Europe			
0-20	**93%**	**68%**	**49%**
21-50	6%	27%	33%
Over 50	1%	5%	17%
USA			
0-20	**77%**	28%	30%
21-50	22%	**60%**	26%
Over 50	1%	12%	**44%**

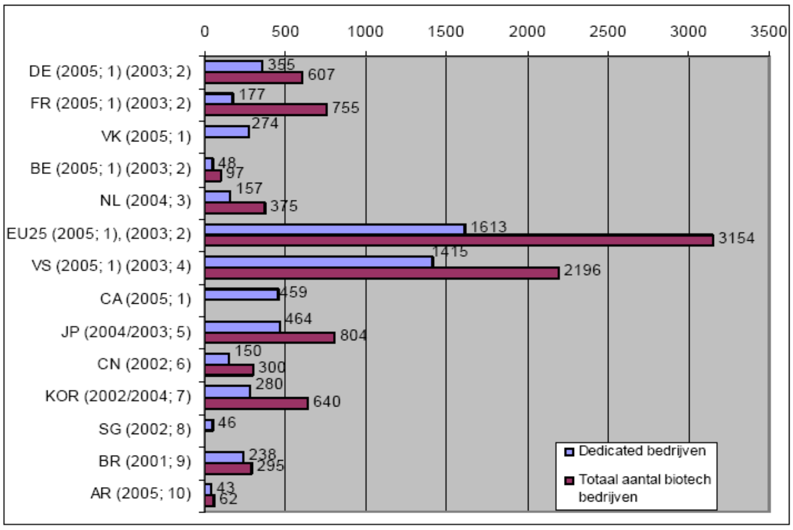
Source: Critical I Limited

Fig. 9: Number of employees working in biotech companies per European country in 2007



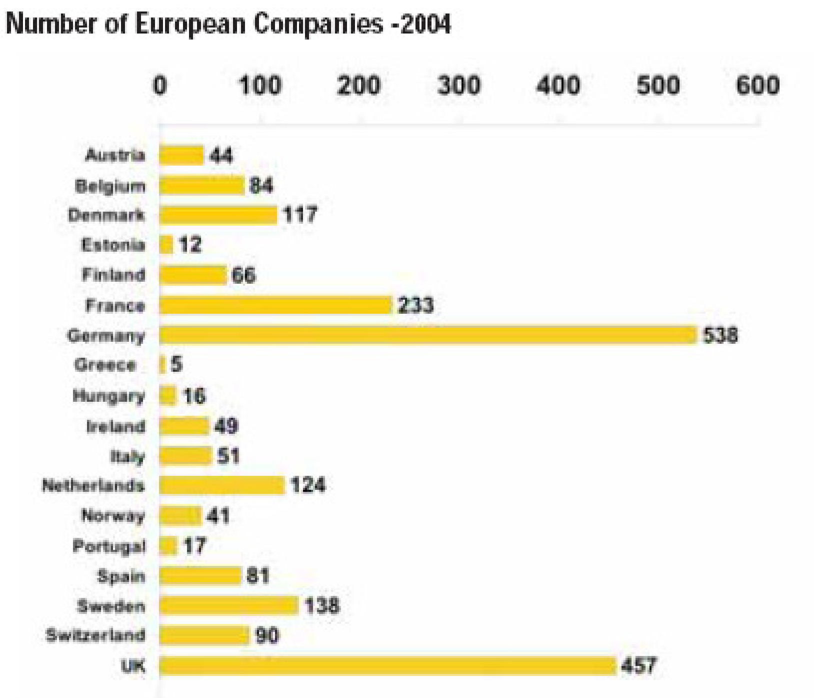
Source: TNO Innovation Policy Group, 2007

Fig. 10: Number of biotech companies per European country



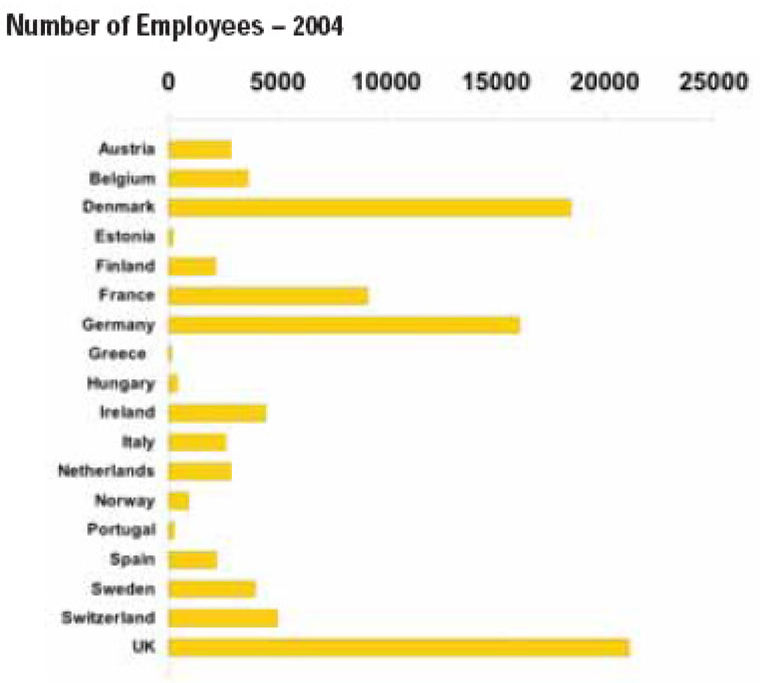
Source: TNO Innovation Policy Group, 2007

Fig. 11: Number of biotech companies per European country in 2004



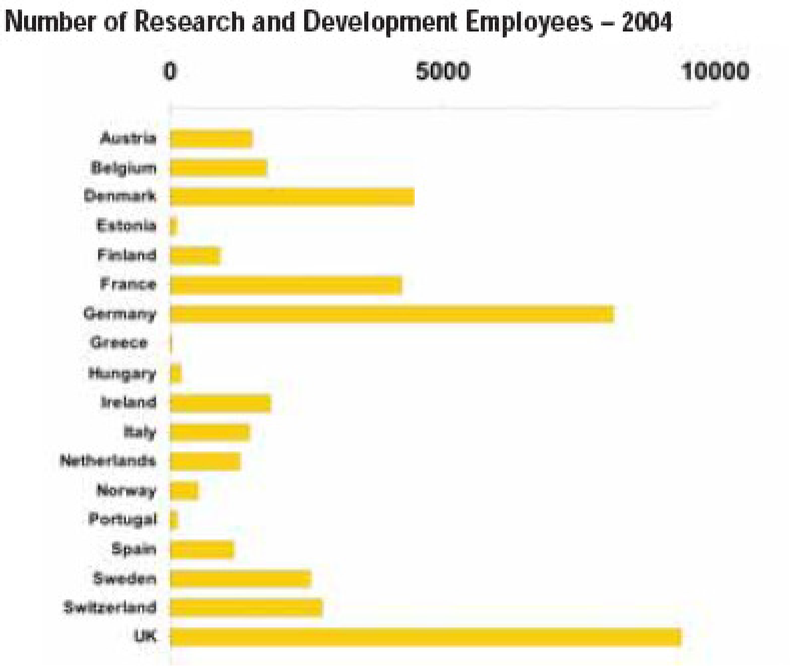
Source: Critical I comparative study for EuropaBio, 2006

Fig. 12: Number of employees working in biotech companies per European country in 2004



Source: Critical I comparative study for EuropaBio, 2006

Fig. 13: Number of R&D employees working in biotech sector per European country in 2004



Source: Critical I comparative study for EuropaBio, 2006

Fig. 14: Rate of new companies in the biotech sector per European country in 2004

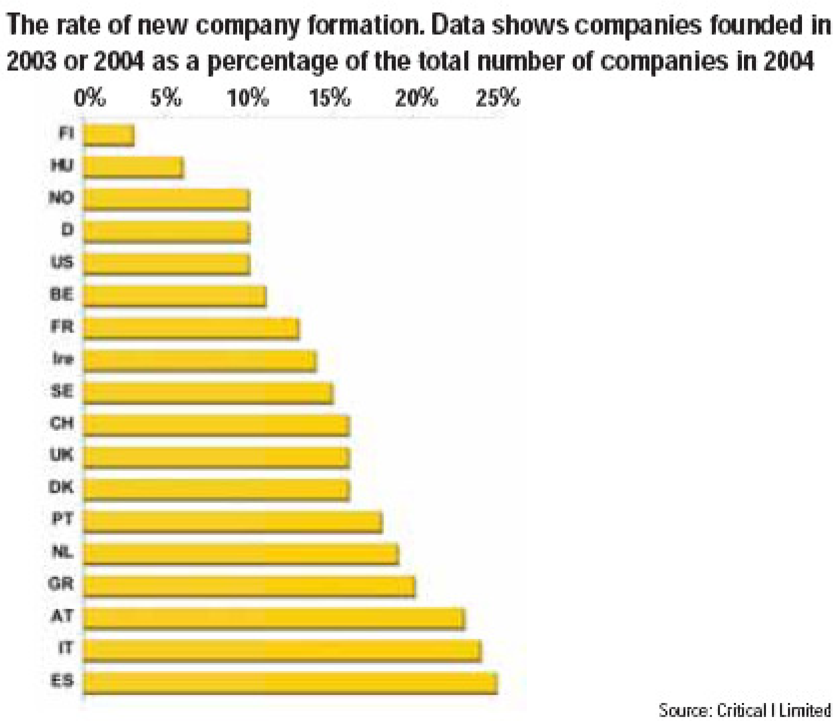


Fig. 15: Information biotech market Belgium in 2004 and 2003

(Financial data in €m)

2004 (2003)	
84 (79)	Companies
3654 (3070)	Employees
1767 (1392)	R&D employees
€315 (€232)	R&D Spend
€606 (€357)	Revenue
€124 (€50)	Total Equity (of which)
€100 (€26)	Venture Capital
€0 (€0)	Private placements
€0 (€23)	Public Equity Offering
€7 (€18)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 16: Information biotech market France in 2004 and 2003

(Financial data in €m)

2004 (2003)	
223 (225)	Companies
9142 (8373)	Employees
4246 (3651)	R&D employees
€589 (€516)	R&D Spend
€2197 (€1842)	Revenue
€226 (€155)	Total Equity (of which)
€194 (€90)	Venture Capital
€19 (€1)	Private placements
€0 (€52)	Public Equity Offering
€2 (€42)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 17: Information biotech market The Netherlands in 2004 and 2003

(Financial data in €m)

2004 (2003)	
124 (116)	Companies
2837 (2761)	Employees
1282 (938)	R&D employees
€147 (€99)	R&D Spend
€308 (€175)	Revenue
€47 (€15)	Total Equity (of which)
€14 (€14)	Venture Capital
€0 (€0)	Private placements
€0 (€0)	Public Equity Offering
€1 (€1)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 18: Information biotech market Sweden in 2004 and 2003

(Financial data in €m)

2004 (2003)	
138 (151)	Companies
3942 (4542)	Employees
2579 (2779)	R&D employees
€367 (€447)	R&D Spend
€854 (€766)	Revenue
€38 (€95)	Total Equity (of which)
€21 (€45)	Venture Capital
€9 (€0)	Private placements
€7 (€44)	Public Equity Offering
€16 (€1)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 19: Information biotech market Ireland in 2004 and 2003

(Financial data in €m)

2004 (2003)	
49 (42)	Companies
4436 (2941)	Employees
1839 (1080)	R&D employees
€284 (€288)	R&D Spend
€707 (€961)	Revenue
€7 (€198)	Total Equity (of which)
€15 (€1)	Venture Capital
€16 (€7)	Private placements
€1 (€189)	Public Equity Offering
€850 (€381)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 20: Information biotech market Germany in 2004 and 2003

(Financial data in €m)

2004 (2003)	
538 (575)	Companies
16094 (18410)	Employees
8138 (9226)	R&D employees
€1507 (€1568)	R&D Spend
€2910 (€3101)	Revenue
€401 (€239)	Total Equity (of which)
€244 (€193)	Venture Capital
€36 (€27)	Private placements
€120 (€3)	Public Equity Offering
€1 (€2)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 20: Information biotech market Switzerland in 2004 and 2003

(Financial data in €m)

2004 (2003)	
90 (93)	Companies
4990 (5503)	Employees
2796 (2778)	R&D employees
€795 (€736)	R&D Spend
€2367 (€1939)	Revenue
€261 (€43)	Total Equity (of which)
€126 (€43)	Venture Capital
€0 (€0)	Private placements
€133 (€0)	Public Equity Offering
€476 (€498)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 21: Information biotech market UK in 2004 and 2003

(Financial data in €m)

2004 (2003)	
457 (484)	Companies
21134 (22834)	Employees
9384 (9896)	R&D employees
€1557 (€1828)	R&D Spend
€4522 (€5073)	Revenue
€753 (€521)	Total Equity (of which)
€294 (€245)	Venture Capital
€239 (€141)	Private placements
€132 (€81)	Public Equity Offering
€461 (€5)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 21: Information biotech market Austria in 2004 and 2003

(Financial data in €m)

2004 (2003)	
44 (41)	Companies
2842 (2099)	Employees
1498 (1134)	R&D employees
€345 (€267)	R&D Spend
€481 (€314)	Revenue
€59 (€48)	Total Equity (of which)
€54 (€48)	Venture Capital
€0 (€0)	Private placements
€0 (€0)	Public Equity Offering
€0 (€0)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 22: Information biotech market Denmark in 2004 and 2003

(Financial data in €m)

2004 (2003)	
117 (121)	Companies
18461 (17902)	Employees
4459 (4265)	R&D employees
€994 (€1002)	R&D Spend
€5396 (€5011)	Revenue
€129 (€54)	Total Equity (of which)
€40 (€41)	Venture Capital
€0 (€0)	Private placements
€86 (€1)	Public Equity Offering
€5 (€66)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 22b: Information biotech market USA in 2004 and 2003

(Financial data in €m)

2004 (2003)	
1991 (1975)	Companies
190462 (179657)	Employees
79344 (77119)	R&D employees
€20958 (€20016)	R&D Spend
€41514 (€40609)	Revenue
€9621 (€7437)	Total Equity (of which)
€2550 (€2171)	Venture Capital
€1792 (€1403)	Private placements
€5262 (€3495)	Public Equity Offering
€6568 (€6020)	Debt

Source: Critical I comparative study for EuropaBio, 2006

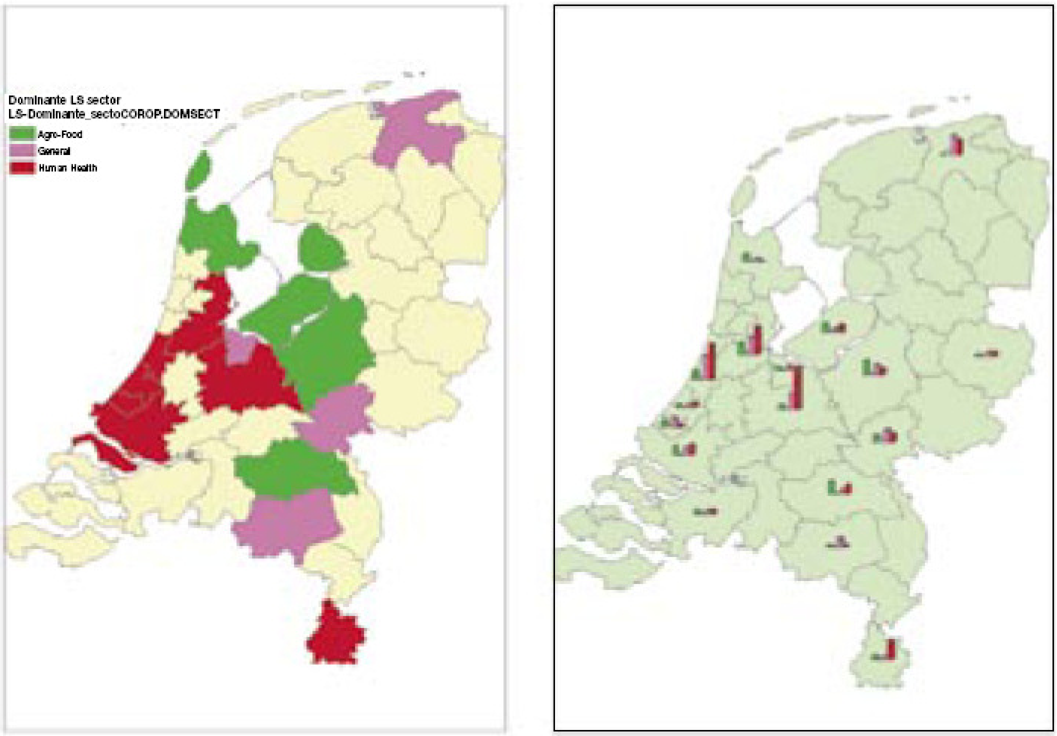
Fig. 23: Information biotech market Europe in 2004 and 2003

(Financial data in €m)

2004 (2003)	
2163 (2198)	Companies
96459 (96228)	Employees
42512 (40756)	R&D employees
€7617 (€7592)	R&D Spend
€21644 (€20691)	Revenue
€2090 (€1451)	Total Equity (of which)
€1111 (€787)	Venture Capital
€322 (€178)	Private placements
€481 (€395)	Public Equity Offering
€1824 (€1019)	Debt

Source: Critical I comparative study for EuropaBio, 2006

Fig. 24: Biotech sector spreading in The Netherlands (green: Agro-food, purple: General biotech, red: Human health)



Source: SenterNovem (2005), 'Dynamiek van de hooginnovatieve Life Sciences bedrijven in Nederland'.

Fig. 25: The typical Danish biotech firm

Denmark - the typical company

(Financial data in €m)

Age (years)	0-2	3-5	6-10	11-15	16+
Employees	16	16	28	41	122
Revenue	€0.28	€0.73	€1.99	€3.66	€44.31
Research strength (personnel)	6	13	19	27	44
Research strength (R&D budget)	€0.70	€1.82	€3.27	€4.23	€4.9

Source: Critical I comparative study for EuropaBio, 2006

Fig. 26: The typical Belgian biotech firm

Belgium - the typical company

	(Financial data in €m)				
Age (years)	**0-2**	**3-5**	**6-10**	**11-15**	**16+**
Employees	29	29	49	25	128
Revenue	€0.55	€2.04	€8.51	€5.08	€33.64
Research strength (personnel)	7	15	29	9	54
Research strength (R&D budget)	€0.94	€4.29	€4.71	€1.06	€9.9

Source: Critical I comparative study for EuropaBio, 2006

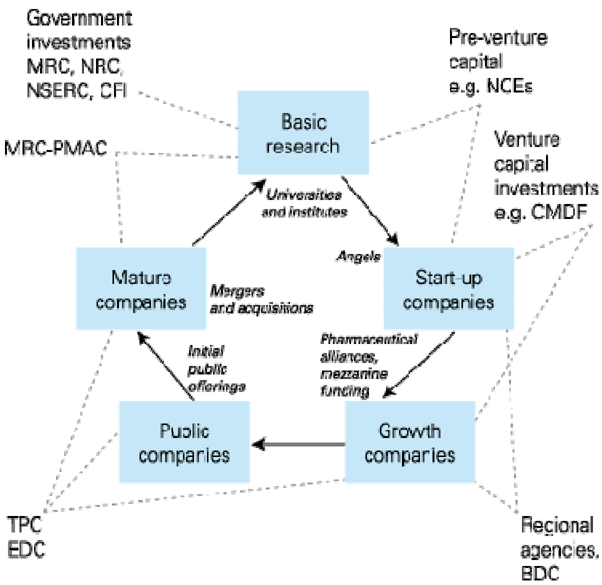
Fig. 27: The typical Dutch biotech firm

The Netherlands – the typical company

	(Financial data in €m)				
Age (years)	**0-2**	**3-5**	**6-10**	**11-15**	**16+**
Employees	14	14	15	26	42
Revenue	€0.2	€1.12	€1.46	€3.14	€11.71
Research strength (personnel)	3	8	8	8	15
Research strength (R&D budget)	€0.46	€0.98	€1.43	€0.77	€2.93

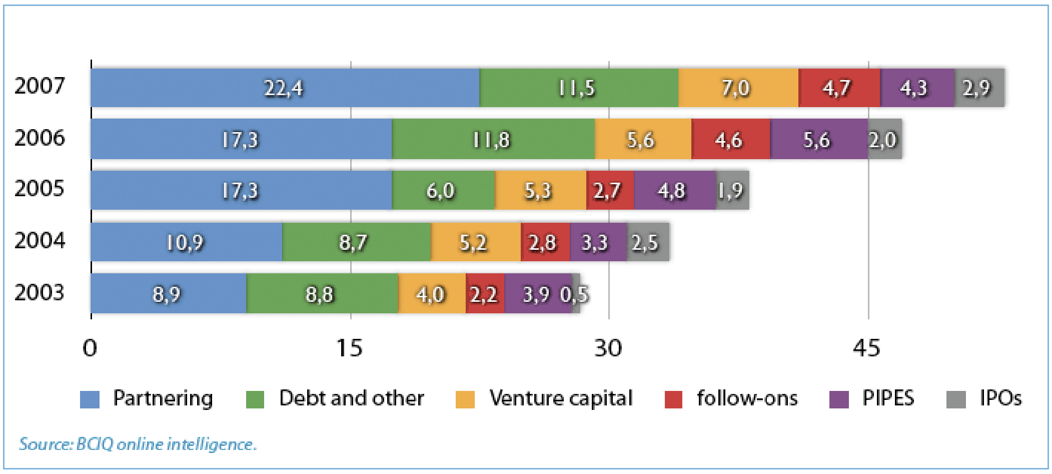
Source: Critical I comparative study for EuropaBio, 2006

Fig. 28: Financing schedule biotech industry



Source: http://biotech.gc.ca/archives/graphics/bh/fig1.gif

Fig. 28: Global biotech industry financing



Source: www.biodirectory.it

QUESTIONNAIRE

This questionnaire concerns the management of biotech firms. The questionnaire consists of 18 or 19 multiple choice questions (depending on answer given) and will take about **5 minutes** to complete **(half of the questions are simple questions about the characteristics of your organization, e.g. how many employees, when founded)**. You will get the results of this research if you complete the questionnaire before 25 November 2008. The participants of this questionnaire will remain anonymous.

Important**With the questions where is indicated *´Multiple answers possible´,* please answer the questions for each manager of your management team individually. For example in question 11 it could be so that one manager studied finance, while another manager studied management, finance and law, please fill in answer to the question ´finance, management and law´.

1. What is your position in the organization?

- Company owner
- CEO or Managing Director
- Division manager (e.g. sales manager, production manager, marketing manager)
- Other, namely:……………………………………….

2. Since when is your organization operative in the biotech market?

- From 2006 until 2008
- From 2003 until 2005
- From 1998 until 2002
- From 1993 until 1997
- Before 1993

3. What type of biotech firm is your organization?

- ‘Dedicated’ life science companies (your core business is biotech R&D)
- ‘Diversified’ life science companies (besides biotech, your organization also focuses on other industries for R&D)
- ‘Next’ life science companies (your organization does not research in biotechnology, however make use of biotechnology which is developed by others)

4. How many employees are working in your organization (in FTE's)?

- 1 or 2

- From 3 until 10

- From 11 until 25

- From 26 until 60

- From 61 until 100

- More than 100

5. How many new products *(estimation)* **to market did your organization bring forward during the presence of your current management?**

- I don´t know
- Not applicable
- 0
- From 1 until 3
- From 4 until 7
- From 8 until 15
- More than 15

6. How many *(estimation)* **granted patents (individually, thus divide group patents in individual patents) does your organization have during the presence of your current management?**

None

From 1 until 4

From 5 until 9

From 10 until 14

From 15 until 20

More than 20

7. What percentage *(estimation)* **of your turnover (*also incoming investment capital*) did your organization averagely spent on R&D during the presence of your current management?**

- I don't know
- Not applicable
- Nothing
- Less than 5%
- From 6% until 14%
- From 15% until 29%
- From 30% until 50%
- More than 50%

8. What percentage *(estimation)* **was your average profit margin (net income/turnover) during the presence of your current management?**

- I don't know
- Not applicable
- 0%
- Less than 5%
- From 6% until 14%
- From 15% until 29%
- From 30% until 50%
- More than 50%

9. What percentage *(estimation)* **was your average return on investment (money gained from investment/ money invested) during the presence of your current management?**

- I don't know
- Not applicable
- 0 %
- Less than 5%
- From 6% until 14%
- From 15% until 29%
- From 30% until 50%
- More than 50%

10. Which strategy(s) does your management deploy to improve the return on investment (to make the use of the investment more efficient)? *(multiple answers possible)*

- No strategy
- We outsource the commercialization process
- We share laboratory space with other firms
- We do mutual advertisement/marketing/sales with partners
- We outsource research to other organization(s)
- We hire frequently new employees with lower wages that replace the employees with higher wages of the commercial department.
- We are established in a cluster, which saves for example on transport costs when cooperating with another firm
- We have access to a database in which we can see the work of other firms, which saves on e.g. search costs
- We cooperate with organization(s) that have establishments in different clusters
- We have different establishments in different clusters
- We hire employees through our already employed employees
- We focus on long-term employment in our organization
- Other:…………………………………………………………………………

11. How many managers are in the management team of your organization?

- 1 or 2

- From 3 until 5

- From 6 until 10

- More than 10

12. How long are the managers from your management team active as managers in your organization? *(Multiple answers possible)*

- Less than 4 years
- From 4 years until 9 years
- From 10 years until 15 years
- From 16 until 25 years
- From 26 until 35 years
- More than 35 years

13. What educational (including extracurricular courses) background(s) does your management team have? *(Multiple answers possible)*

- Education related to finance
- Education related to law
- Education related to alliance management (R&D management)
- Education related to commercialization (e.g. marketing, communication)
- Education related to biotech
- Education related to management in general
- Education related to management in biotech
- Other:…………………………………………………….

14a. How much experience does your management team have in total in managing firms (including biotech firms and firms from other industries)? *(Multiple answers possible)*

- No experience

- Less than 5 years

- From 5 years until 9 years

- From 10 years until 15 years

- From 16 until 25 years

- From 26 until 35 years

- More than 35 years

14b. How much experience does your management team have in managing biotech firms? *(Multiple answers possible)*

- No experience

- Less than 5 years

- From 5 years until 9 years

- From 10 years until 15 years

- From 16 until 25 years

- From 26 until 35 years

- More than 35 years

15. What do the managers of your management team add to your organization besides their management expertise? *(Multiple answers possible)*

- Investment capital

- Connections with other organizations for mutual R&D research where the manager(s) is also in the management board, namely:..

- Connections with other organizations for mutual R&D research where the manager(s) is not in the management board

- Connections for venture capital

- Connections for other form(s) of investment capital, namely:...

- They bring in new products to market

- They bring in other managers

- They bring in R&D personnel

- They bring in other personnel than R&D, namely:..

- Patents from other firms

- Other:..

16. Through which way does your organization hire its management? *(Multiple answers possible)*

- Via the management of our own organization
- Advertisement
- Through a fare or other organized interaction program
- Intermediary firm / Consultancy firm
- Via the employee(s) of our own organization
- Through a merger(s) with another firm
- Other:……………………………………………………………….

17. Which sort of investment capital did your organization obtain during the presence of your current management team? *(Multiple answers possible)*

- Government subsidy

- Investment from business angels

- Venture capital

- Investment from a large pharmaceutical

- Investment from a manager that entered the company and brought in capital

- Investment from an organization we merged with

- Other:…………………………………………………………

18. By which way does your management learn to improve their managerial ability? *(Multiple answers possible)*

- Through courses in general management (end of questionnaire)
- Through courses in management of biotech firms (end of questionnaire)
- Through their own experience (end of questionnaire)
- Through interacting with the management of diversified biotech firms
- Through interacting with the management of dedicated biotech firms
- Through interacting with the management of biotech firms with 10 FTE´s or more
- Through interacting with the management of biotech firms with less than 10 FTE´s
- By interacting with management from non-biotech firms
- Through interacting with consultancy firms (end of questionnaire)
- By being in the management team of other biotech firms
- Other:……………………………………………………………………………

19. What is the geographical distance between your organization and the organization your management interacts with to improve their managerial ability? *(Multiple answers possible)*

- The same city
- The same province, but different city
- The same country, but different province
- Another European country, namely:…………………………………(please name the country)
- Outside of Europe, namely:…………………………………(please name the country)

Thank you for your time and effort. End of questionnaire.