CASE STUDY ON BIOTECH INNOVATION SYSTEMS

NORWAY

Vol. 1: Biopharmaceuticals

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Preface

The general key question for this country study is:

Can we identify important differences and similarities in the structure and dynamics of national biotech innovation system which explains the performance of this system, and what are the policy implications?

Given the specific characteristics of national innovations systems and the role public policies can play in the management of innovation processes in order to correct systems imperfections, a set of key questions specific for biotechnology innovations can be formulated. Starting from the general key question rendered above, the project focuses on more specific questions dealing with four main issues to be investigated:

systemic failures and fits,

system openness,

demand-side factors, and

systems policies.

Although the concept of national innovation systems addresses many research issues we think that these issues are in particular relevant to the biotechnology innovation system. First, systemic failures can be seen as symptoms of sub-optimal innovation systems and are judged as being a rationale for innovation policy actions, next to other rationales. However, an in-depth investigation of these systemic failures and their implications for policies is lacking so far for biotechnology. The investigation of these systemic characteristics is one of the main goals of the overall research project 'Case Studies in Innovation' as formulated by the OECD (DSTI/STP/TIP(2002)1) and therefore is a main issue in this project. Second, the concept of national innovation systems implies a definition based on a country's geographical boundaries. However, developments in high-technology sectors, in specific in biotechnology, are to an increasing extent realised by international research and business networks as can be found in international R&D co-operations, the presence of foreign companies such as major pharmaceutical multinational companies in a country. This national-international dimension of system openness is especially relevant to national policy-making. Third, demand-side factors play a major role in the successful development of new technologies with biotechnology as the most prominent example. However, in the literature and research on (national) innovation systems demand side factors have been relatively unattended. What are the effects of these demand side factors on the biotechnology innovation process and how should they be taken into account by the research, business and policy communities? We feel that an investigation of demand side factors and their influence on national innovation systems is needed. And fourth, a specific objective of the OECD 'Case Studies in Innovation' is to draw policy conclusions with regard to the balance between horizontal innovation policies and more customised measures that take into account the specific characteristics of innovation processes in the biomedical/biopharmaceutical innovation system (DSTI/STP/TIP(2002)1).

The report is organized in two volumes, where the first investigates the main biopharmaceutical sector study, and the second the more delimited and optional aquaculture sector study.

For an overview of main authorship responsibilities please cf. Appendix 3.

We would like to extend our sincere thanks to interview and survey respondents, as well as to the members of the project's reference group (Grethe Foss, Henrik Lund, Torben Hviid Nielsen, Thor Amlie, and Tronn Hansen) for valuable comments and suggestions.

Oslo, May 2004. The authors.

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Chapter 1: Introduction

In this chapter we first present the goals and approach of the study. The National Innovation Systems approach provides the framework for the study. Its main objective is to identify important differences and similarities in the structure and dynamics of the Norwegian biopharmaceutical innovation system that explains the performance of this system, and what are the policy implications. The chapter also provides an overview of Norwegian innovation system as background for the study. The main observation is that the oil industry and related industries drive the Norwegian economy to a degree where the structure of the economy is to a large degree defined by the presence of this industry.

1.1 Background and goals.

The national innovation systems approach (NIS) has grown in importance over the past decade. Its importance lies in being able to explain how the creation, diffusion and use of knowledge lead to economic growth and structural change. The approach focuses not only on the inputs and outputs in the innovation process but also the linkages or web of interaction within the overall innovation system. An understanding of these systems can help policy makers develop approaches for enhancing innovative performance and speeding up the pace of economic growth. Over the past ten years, the OECD has strived to improve our understanding of this approach and its relevance to policy making. The results of the NIS project were summarized in several OECD publications: *National Innovation Systems* (OECD 1997), *Managing National Innovation Systems* (OECD 1999), and *Dynamising National Innovation Systems* (OECD 2002).

Innovation systems can transcend national boundaries. Some generic or general-purpose technologies follow their own trajectories, which operate outside national boundaries. Malerba and Orsenigo (1996) show that innovative activities are more similar across countries in a specific sector then across sectors within a country. This suggests that technological trajectories may also be relevant for explaining the patterns of innovative activities within a particular industry and country. To address these patterns of innovation, the OECD Working Party on Technology and Innovation Policy (TIP) started a project in 2002, designated "Case Studies in Innovation" (DSTI/STP/TIP(2002)1), to investigate the policy implications from sectoral innovation systems. Biotechnology is a generic technology that will have important implications across both industrial and national boundaries.

This study analyses the Norwegian biotechnology innovation system, and, in particular, the innovative capacity and competitiveness of pharmaceutical firms doing biotechnology research and development (R&D). Following the OECD objective behind the project, the starting point for the study is *to identify important differences and similarities in the structure and dynamics of the Norwegian biotechnology innovation system that explains the performance of this system, and what are the policy implications*. Biotechnology is a generic technology that spans across many industries, and the pharmaceutical industry is just one of them. This necessarily involves analysing not only the intersection of biotechnology and the pharmaceutical industry, but also analysing the industry individually. The sub-sector is made

up of dedicated biotech firms, which are active in R&D and the use of biotechnology in developing new products and processes, and diversified biotech firms, which integrate biotechnologies in their existing R&D and production activities. Dedicated biopharmaceutical firms are primarily university spin-offs that transform the opportunities into potentially viable techniques and products. In contrast to the large pharmaceutical firms, these firms are largely Norwegian-owned, depending on collaborative agreements to access global technology and markets. They often get their funding from venture capital markets and public sources, but some of them have been successful in marketing products using biotechnology.

Biotechnology was chosen as a priority area in Norway in 1985. By that time the United States had already achieved a leadership position. But this does not preclude Norway from developing biotechnology because an important prerequisite for successful development is the availability of leading-edge scientific capabilities and the incentives to carry out leading-edge research and development. This will require access to the international scientific community and direct and active participation by the Norwegian dedicated biopharmaceutical firms in the network of scientists.

This study follows the main goals of the overall research project 'Case Studies in Innovation' and focuses on four systemic issues that are in particular relevant to the biopharmaceutical innovation system:

1. *Systemic failures:* Systemic failures are responsible for the sub-optimal performance of the innovation system and are judged as being a rationale for innovation policy actions. However, an in-depth investigation of these systemic imperfections and their implications for policies is lacking so far for biotechnology.

2. *System openness:* The NIS approach implies a geographical boundary. Developments in generic or general-purpose technologies, specifically biotechnology, are to an increasing extent realised by international research and business networks. These are generally found in international R&D co-operations or the presence of multinational corporations, such as major pharmaceutical firms, in Norway. This national-international dimension of system openness is especially relevant to national policy-making.

3. *Demand-side factors:* Demand-side factors play a major role in the successful development of new technologies. This is particularly important for the newly emerging biopharmaceutical industry. However, demand-side factors have been neglected to a great extent in the national innovation systems approach. This study will examine the effects of demand side factors on the biopharmaceutical innovation process and the importance they have for the research, business and policy communities.

4. *Systems policies:* A specific objective of the project is to draw policy conclusions with regard to the balance between horizontal innovation policies and more customised measures that take into account the specific characteristics of innovation processes in the biomedical/biopharmaceutical innovation system.

1.2 Approach.

To facilitate comparability across countries, the report adopts the OECD definition of biotechnology: "The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services." A pharmaceutical enterprise doing biotechnology research would adopt one of five technologies or processes:[1]

1. DNA (the coding): genomics, pharmaco-genetics, gene probes, DNA sequencing/synthesis/amplification, genetic engineering;

2. Proteins and molecules (the functional blocks): protein/peptide sequencing/synthesis, lipid/protein engineering, proteomics, hormones and growth factors, cell receptors/signalling/pheromones;

3. Cell and tissue culture and engineering: cell/tissue culture, tissue engineering, hybridisation, cellular fusion, vaccine/immune stimulants, embryo manipulation;

4. Process biotechnology: bioreactors, fermentation, bioprocessing, bioleaching, bio-pulping, bio-bleaching, biodesulphurisation, bioremediation and biofiltration; and

5. Sub-cellular organisms: gene therapy, viral vectors.

The biopharmaceutical sub-sector includes those actors and activities of R&D-organisations, companies and others that are involved in or address one or more of the biotechnology activities mentioned in the OECD definitions.

The report contains four different kinds of data to describe the biopharmaceutical and biomedical industries in Norway:

1. *Descriptive analysis of the national biopharmaceutical innovation system.* This includes the description of the biopharmaceutical innovation chain and of the types of actors and organisations involved. It serves to describe the main framework conditions that affect the outcomes of the biopharmaceutical innovation process.

2. *Interviews with biopharmaceutical companies, sector experts and demand side actors.* These interviews were conducted from May to August 2003 and included one major global pharmaceutical company, 3 dedicated biotech companies, 3 diversified biotech companies, 3 fish vaccine companies, 2 fish feed companies, 6 government ministries, 2 research organisations, 2 venture capital firms, MedCoast, the Centre of Excellence, the regulatory body, the Norwegian patent office, Norwegian Association of Pharmaceutical Manufacturers, the Research Council of Norway, the Regional Development Fund, and the Norwegian Trade Council. Primary source material (firms' annual reports and relevant White Papers and policy statements from ministries and regulatory bodies) as well as internet webites of the various enterprises were also used for further analysis.

[1] Approved by the OECD Working party on Biotechnology in 2001 as the provisional statistical definition.

3. *Bibliometric and patent analysis for measuring the national performance.* This analysis identifies the main type of actors and their relevance in the biopharmaceutical innovation process. In the patent analysis, data are used for patent applications at the European Patent Office. Fraunhofer ISI performed the data collection and calculations by using the OECD Patent database and the Science Citation Index databases in February 2003

4. The *2003 Biotechnology Use and Development Survey.* This survey was designed according to the model survey under discussion at the OECD (2003) and augmented with a more elaborate set of questions about the co-operation patterns of the biotech firms. The intention of the model survey was to complement the 2001 *R&D and Innovation survey*, which is based on the OECD Oslo Manual, and was carried out by Statistics Norway. Unlike the standard R&D and innovation survey, this survey was specifically targeted towards enterprises related to the pharmaceutical industry where biotechnology applications where known to exist (cf. Appendix 1). It was sent out to 27 dedicated and diversified firms that were identified from a list provided by the Norwegian Bioindustry Association,[2] of which 16 had filled out the questionnaire. This list contains not only firms in the pharmaceutical industry, but also those that focus more on diagnostics and medical devices. To complement this survey, *Statistics Norway* aggregated the 2001 *R&D and Innovation survey* to provide complementary data on biotechnology and biopharmaceutical.

The study is organized as follows. The remaining five chapters are organized around the four main issues contained in the studies. The following section summarizes the main characteristics of the Norwegian innovation system. Chapter 2 presents the main Norwegian public policies and policy instruments that relate to biotechnology in the period from 1994 to present. It also provides information about the main policy making organisations and executing agencies. The third chapter discusses the structure and performance of the pharmaceutical innovation system and its use of biotechnology. The assessment of specific framework conditions, and their availability and accessibility, which are judged particular relevant to innovation, are presented in chapter 4. In chapter 5, specific elements of the demand-side in innovation systems are discussed, that is the national health care system, regulation of market access, the character of the Norwegian pharmaceutical and biopharmaceutical product market, the role of users and the influence of socio-economic and ethical issues. Finally, the main conclusions on systemic imperfections, system openness and the role of demand are summarized and the policy implications drawn in chapter 6.

[2] A status report issued by the RCN, prepared by Ernst &Young in 1999 identifies 32 firms. A report prepared for OECD in April 2003 identifies approximately 34. The list of companies by Ernst &Young includes some successful firms (i.e. PhotoCure), which did not comply with the definition of biotechnology in the current study, and were not included in our survey.

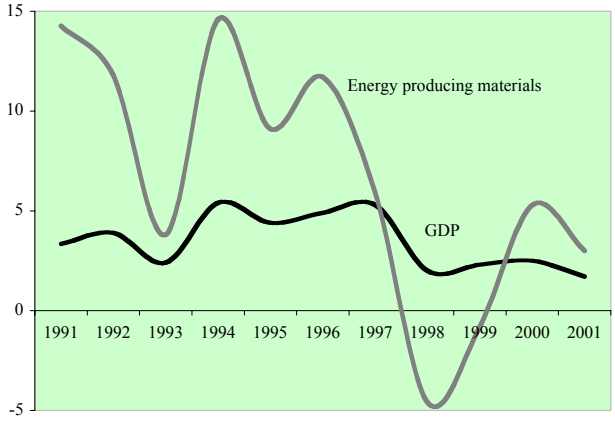
1.3 Main traits of the Norwegian economy

Norway is a small country with a population of slightly more than 4.5 million people (Population and Housing Census, 2001). In 2001, the OECD estimated its Gross Domestic Product (GDP) at €194 billion ($178.4 billion) in 1995 US dollars and exchange rates, or about €43 000 ($40,000) per capita. Civilian employment was 2.3 million, with about 3.8 per cent employed in agriculture, forestry and fishing, 21.5 per cent in industry and construction and the balance in services. Gross fixed capital formation was about 19 per cent of GDP, and general government current revenue was over 57 per cent, the highest among OECD Member States. However, there was also a general government surplus of 14 per cent of GDP because of oil revenues in that year.

The Norwegian innovation system relies heavily on natural resources, including oil, gas, hydropower and fishing. In 2001, oil and gas exports topped €86.6 billion ($77.6) and government oil revenues from these exports exceeded 15 per cent of GDP, which created large surpluses in both the government budget and trade balances. Little more than 63 per cent of the revenue obtained through exports was returned through the imports of goods and services in that year. An important consequence of these oil revenues is that the business cycle often moves in a different pattern from the rest of Europe. Figure 1-1 shows the evolution of GDP (measured as value added in 1995 prices) and its relationship to the energy producing sectors (NACE 10-12) from 1991 to 2001.

Norway created this competitive advantage in natural resources over time. Geography played an important role, encouraging the development of the fishing, wood, iron ore and shipping industries for several centuries and hydropower industry in the early 20th century. The discovery of oil and gas in the 1970s created dynamism over the past three decades that made Norway one of the wealthiest societies in the world, but also affected most other industries in the economy. Industries that were directly connected to the petroleum and gas industries often developed a competitive advantage, but those there were not were often faced by rising wage costs and exchange rate. The OECD (2002, p. 23) observed that competitiveness had deteriorated by 24 per cent between 1995 and 2001 in terms of unit

Figure 1-1: The growth of real GDP and energy producing sector in Norway, 1991 to 2001



Source: OECD Stan Database, 2002.

Table 1-1: Structure of Production in Norwegian Manufacturing, 1990 and 2000

		Total output		Value Added		Employment		Exports	
		share 1990	*change in share 2000*	*share 1990*	*change in share 2000*	*share 1990*	*change in share 2000*	*share 1990*	*change in share 1999*
Food, beverages & tobacco	15-16	23.4	–1.3	15.1	1.4	17.4	0.7	9.2	2.4
Textile & leather products	17-19	1.7	–0.4	2.2	–0.6	3.5	–0.8	1.4	–0.3
Wood & cork products	20	4.8	–1.0	5.2	–1.2	6.7	–1.4	1.9	–0.5
Pulp, paper, printing & pub.	21-22	13.5	–2.0	16.9	–1.8	16.4	–0.5	8.3	–1.5
Coke & petroleum products	23	6.0	–6.0	1.7	–1.6	0.6	–0.6	9.9	4.2
Chemicals ex. pharmaceuticals	24ex2423	6.9	–6.9	7.4	–7.3	4.6	–4.6	12.3	0.3
Pharmaceuticals	2423	0.9	0.9	1.4	0.6	0.8	0.4	1.5	0.8
Rubber & plastic products	25	1.9	–0.3	2.5	–0.5	2.2	–0.2	1.7	–0.4
Other non-metallic prod.	26	2.9	–0.1	3.9	–0.3	3.5	–0.4	1.1	–0.4
Basic metals	27	9.7	0.3	8	1.2	5.8	–0.8	20.8	–3.3
Fabricated metal prod.	28	4.0	0.2	5.6	0.4	6	0.3	2.7	–0.4
Machinery & equip.	29	6.0	0.4	7.9	–0.2	7.9	0.5	7.3	0.2
Office & computing mach.	30	0.8	–0.5	0.9	–0.8	1	–0.8	1.9	0.1
Electrical machinery	31	3.2	–0.7	3.7	–0.7	3.8	–0.6	2.2	0.7
Radio, tele. & comm. equip.	32	1.1	1.2	1.5	1.4	1.6	0.7	1.6	1.2
Medical & precision inst.	33	1.0	1.0	1.4	1.0	1.3	1.3	1.5	0.7
Motor Vehicles & Trailers	34	1.0	0.4	1.1	0.5	1.1	0.6	2.2	0.3
Building & repairing of ships	351	7.5	1.7	8.3	1.6	9.2	2.2	9.7	–4.8
Aircraft & apacecraft	353	0.8	–0.6	1.5	–1.1	1.4	–1.0	1.3	–0.4
Railroad & other transport	352+359	0.6	–0.4	0.8	–0.6	0.9	–0.6	0.1	0.0
Other manufacturing; recycling	36-37	2.4	0.8	3.2	1.0	4.1	1.2	1.3	0.7

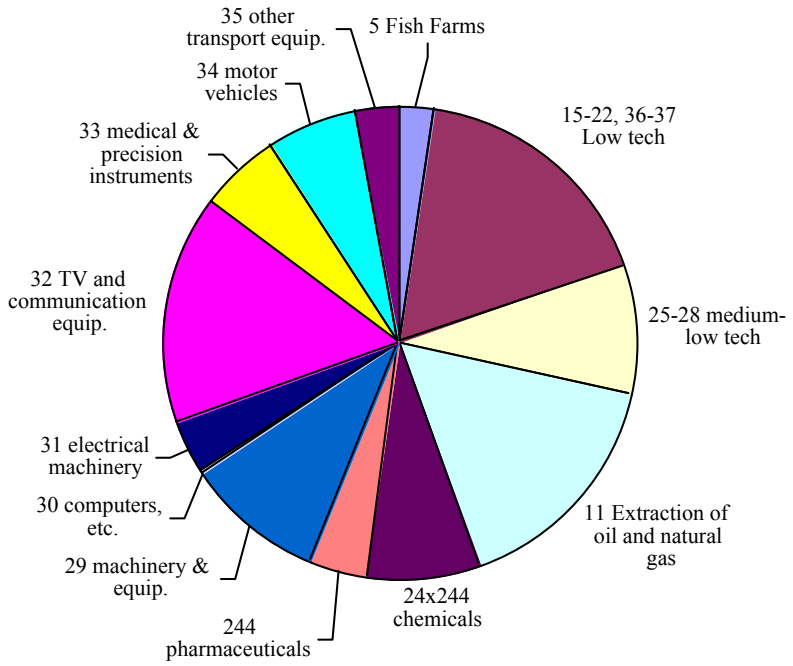
Source: OECD Stan database, 2003.

labour costs and by 7 in terms of wages per hour in manufacturing.[3] While there has been considerable productivity growth over the period, captured in the difference between the two measures of competitiveness, the information and communications (ITC) sector and biopharmaceutical industry remains small relative to its Nordic neighbours. This is partly because of technological trajectory followed by Norway.

Since Norway relies heavily on natural resources, it devotes a relatively low percentage of GDP to manufacturing. Without the petroleum sector, Norway's GDP would be much lower and the share of manufacturing would be higher. Declining competitiveness may have also influenced the growth of manufacturing over the past two decades. Manufacturing value added increased by an annual average of over one per cent from 1994 to 2001, but this followed twenty years of stagnation. Table 1-1 shows the industrial structure in 1990 and the change that took place during the decade. Food and beverages, pulp and paper, chemicals (including pharmaceuticals) and ship-building were the four main industries during the decade, with pulp and paper and chemicals losing the greatest share and ship building making the largest gains. Machinery and equipment remained rather constant because it is an important supplier to the petroleum sector. Pharmaceuticals made up less than one per cent of manufacturing output in 1990, but gained almost one percentage point during the decade.

[3] The relative trade-weighted unit labour costs also increased by 32 per cent during this period, but the OECD found that all but 2 per cent of this rise was offset by a decline in profit margins (OECD, 2002). The European Commission (2002) maintains that competition deteriorated by 15 per cent vis-à-vis other industrial countries.

Figure 1-2 Innovation expenditure by industry in Norway, 2001



Source: Statistics Norway, Community Innovation Survey, 2001

The extraction of energy producing materials and other miscellaneous mining output made up 57 per cent of Norwegian exports in 2001. Of the remaining commodities, foodstuffs (including fish and fish products), paper and wood-related products and metals were important (see table 1-1). Although the manufacturing sector did not lose export market share in 2001, its share in GDP declined since 1995, with manufacturing exports lagging market growth by almost 2 percentage points per year. Manufacturing exports were concentrated mainly in the low and medium-low technologies. The reason may be that the competitiveness of tradable goods deteriorated considerably from 1995 to 2001. However, the balance of trade in services was positive in recent years, mainly because of a large positive balance in sea transport, but the relatively large percentage of exports in business services indicates that Norway is developing a competitive advantage in certain high technology services.

The composition of business expenditures devoted to innovation, including research and development (R&D) activity the importance of the petroleum and natural gas sector. As figure 1-2 shows, the high tech sectors (NACE 244, 30, 32, 33) make up less than one-third of R&D activity in industry. When the petroleum and gas sector is excluded, the share rises to 38 per cent, which is well below the other Nordic countries and the United States (see table 1-2). Pharmaceuticals make up about 4 per cent of the innovation expenditures in industry, and about 2.5 per cent of total innovation expenditures by business enterprises. Innovation expenditures in various services make up about 40 per cent of total expenditures. The OECD (2003) points out that almost half of total R&D activities performed by business are carried out in the service sector.

Table 1-2: Structure of Norwegian Industry in comparative perspective, 2000.

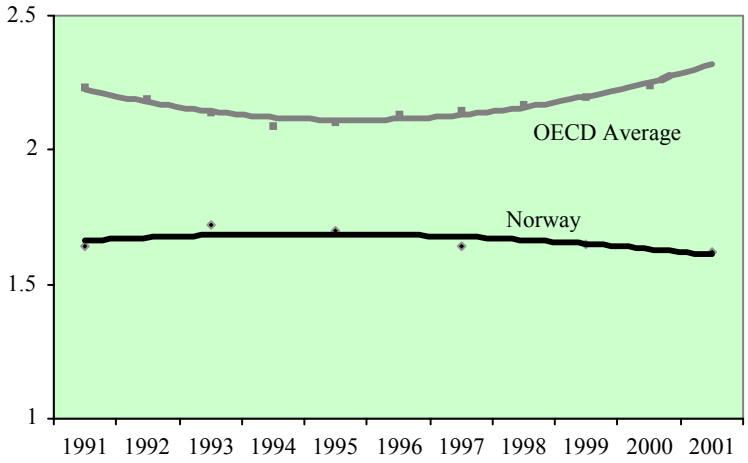
	Norway	Sweden	Denmark	Finland	USA
Structure of the economy:					
Agriculture and mining	17.5	2.1	4.1	4.0	2.5
Manufacturing	12.4	21.0	16.3	24.5	16.0
Services	70.1	76.9	79.6	71.5	81.9
Technological structure of manufacturing:					
Value added:					
High	7.9	16.9	23.6	14.5	23.0
Medium-high	12.5	30.7	19.4	25.9	26.1
Medium-low	30.7	20.4	19.1	23.2	20.1
Low	41.3	32	37.9	36.4	30.8
Employment:					
High	6.9	13.6	13.1	9.2	15.8
Medium-high	13.6	29.8	22.4	24.2	23.6
Medium-low	27.9	21.5	23.9	23.6	22.1
Low	47.5	35.1	40.6	43.1	38.6
R&D activity:					
High	39.4	57.6	56.0	63.4	59.9
Medium-high	28.9	34.1	27.9	21.4	31.2
Medium-low	20.9	4.2	9.3	7.4	4.3
Low	10.8	4.2	6.8	7.8	4.6
Exports:					
High	10.3	28.8	27.3	20.7	38.4
Medium-high	25.7	33.7	23.8	27.9	37.1
Medium-low	40.8	16.5	17.4	13.9	10.7
Low	23.1	20.9	31.5	37.5	13.9

Notes: Services include electricity and construction. R&D activity is from 1999. Technology groups are from OECD (2001).
Source: Own calculations based on OECD Stan database, 2003.

When we group the manufacturing industries according to their research and development (R&D) intensity, the high-technology industries as a whole, including pharmaceuticals, had a relatively low share of value-added when compared with other Nordic countries and the United States. Table 1-2 shows this to also be the case for employment, R&D activity and exports. However, the R&D intensity, measured as the R&D expenditures as a percentage of value added, is similar to all of the countries in the table. This trend is significant because the high and medium-high technology manufacturing industries are generally seen as key contributors to competitiveness and growth.

The development of the Norwegian system of innovation and the competitive advantage of some industries helps to explain the evolution of R&D activity during the past decade. It also helps to explain why R&D activity as a percentage of GDP is significantly lower than the OECD average despite a policy target to reach this average by 2005 (OECD, 2002). Even more alarming is that the trend, depicted in figure 1-3, appears to be diverging from the average. One reason for the relatively lower R&D activity is that the industrial structure in Norway has a relatively lower share of R&D intensive industries, such as the defence, electronics and pharmaceuticals industries. If the defence-related industries are excluded from GERD, Norway compares more favourably to this average and is close to the EU average.

Figure 1-3: Evolution of GERD as a percentage of GDP in Norway and the OECD, 1991 to 2001.

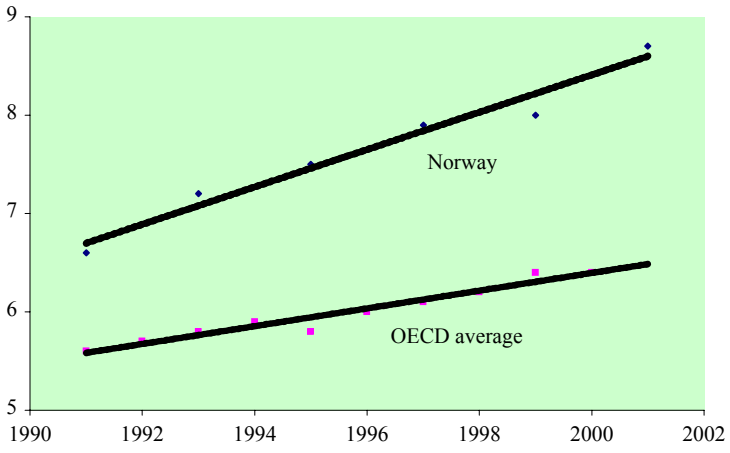


Note: The trend line was calculated using Microsoft Excel.
Source: OECD MSTI Database, volume 2003/1.

Moreover, Norway has a relatively higher R&D intensity in industries related to the petroleum and natural resource industries, most of which are not classified as high technology industries by the OECD (Knell, 2003).

Nevertheless, Norway compares very favourably with the OECD average when R&D activity is measured as the number of researchers as a percentage of the workforce. Figure 1-4 shows that Norway has about 1.5 more researchers per thousand workforce than the OECD average and the trend shows that the number of researchers should remain high. Some of the difference between R&D expenditures and R&D personnel may be due to the high priority given to the social sciences and humanities, where the link between research and productivity

Figure 1-4: Researchers per thousand workforce in Norway and the OECD, 1991 to 2001.



Source: OECD MSTI Database, volume 2003/2

Table 1-3: Gross Domestic Expenditure on R&D and Researchers, 2001

		Percentage of GERD financed by:		Percentage of GERD performed by:			Total Researchers
	million current PPP$	Industry	Govern-ment	Industry	Govern-ment	Higher Education	Full time equivalent
Norway	2,663.1	51.6	39.8	59.7	25.7	14.6	19,752
Denmark	3,204.1	59.0	31.2	64.9	19.4	14.5	18,944
Finland	4,676.8	70.8	25.5	71.1	18.1	10.2	36,889
Sweden	9,894.0	71.9	21.0	77.6	19.4	2.8	45,995
Total OECD	645,409.6	63.6	28.9	69.6	17.3	10.4	368,087

Source: OECD, Main Science and Technology Indicators, Volume 2003/1, p. 14.

is typically weaker than in areas such as science and engineering. This may also explain why the average number of triatic patents[4] granted per Norwegian researcher was only 5.4 patents per thousand workforce from 1993 to 1998, whereas it was 12.7 patents per thousand workforce in the OECD. Yet, this priority may also reflect the commitment of Norway to human development (UN, 2003).

The interrelation between the financing of R&D activities and the performing sectors are important for innovation system. As Table 1-3 shows, the government is a much more important source of finance for R&D activities than is typical in the OECD or even in the Nordic countries. The table also shows that the business enterprises also performs a much lower percentage of R&D activity than the OECD average and higher education and public research institutes perform a much higher percentage. This places added importance on the issue of complementarities between public and private R&D activity (David, et. al., 2000) and the relationship between universities and product and process innovation. Moreover, industry depended on foreign sources for more than 14 per cent of its business expenditures on R&D activity in 1999, which very high when compared with other countries in Scandinavia (OECD, 2003). Foreign capital was crucial to the development of a lot of the resource-intensive industries in Norway.

[4] Triatic patents include patenting activity in the European Patent Office (EPO), United States Patent and Trademark Office (USPTO), and the Japan Patent Office.

Chapter 2: Overview of national R&D, technology and innovation policies for biotechnology

In this chapter we first review the general historical background and main actors for policy-making and policy programme management. Thereafter we present policies for knowledge base support, policies for commercialisation support, and policies with a socio-economic or ethical dimension. Main actors for policy making are the Ministries, whereas the main actor for policy programme management is the Research Council of Norway. The latter body also has significant policy making roles. There is a great concern and enthusiasm within central government with regards to the development of coherent R&D policies, exemplified with the goal of reaching and eventually surpassing OECD average spending. However, one issue seems to be problems of coordination between various funding Ministries and other interest groups. Funding for knowledge base support increased in recent years, most notably the FUGE and the Centres of Excellence programmes, however ambiguities remain in the policies focused on the commercialisation of biotechnology. A new policy, implemented in 2004, will attempt to integrate the various government agencies into a new organisation, Innovation Norway. Norway also has a well developed – although somewhat complicated – system of ethics committees. At the same time there seems to be a lack of continued integration of biotechnology related concerns in horizontal policies, exemplified in this report through a review of the most recent policy on health and welfare issues.

2.1 Main actors involved in policy making and policy programme management

2.1.1 General historical background

The oil and gas industry was not only important for the Norwegian economy over the past three decades, but also in shaping policy. Nevertheless, during the mid 1990s Norwegian technology policy was centred on innovation and knowledge creation (Wicken, 2000). Instead of focusing on particular technologies, the government chose a more systemic approach to innovation that encouraged the generation and diffusion of technology. The numerous R&D and innovation promotion agencies were organised into two major organisations in order to improve the administration and coordination policies: the Research Council or Norway (RCN), and the Norwegian Industrial and Regional Development Fund. Although public funding of R&D activity increased through the 1990s, it still remained well below the OECD average. The government launched a new policy at the end of the 1990s (Norwegian Government White paper no. 39.1998-99) that set an ambitious goal of reaching the OECD average of R&D expenditures as a percentage of GDP by 2005. This required a considerable escalation in public expenditure, partly through the establishment of a research and innovation fund. Government funding for R&D activity increased by €133 million (NOK 1 billion) from 2001 to 2002, and the budget for 2003 provided an extra €80 million (NOK 640 million). It also aimed at encouraging new private initiatives. A fusion of science, technology and innovation policy, the White paper also targets education and research in universities, as well as R&D activity in four strategic areas: marine research, research on medicine and health, research in the intersection between energy and environment and ICT research. Two of the

priority research areas, marine research and medicine and health research are related to biotechnology, including biopharmaceuticals.

The way subsidies are given to private enterprise also changed at the end of 2001. A grant system (FUNN) was administered by the Research Council of Norway (RCN) until 2001 that granted 25 per cent subsidies for R&D purchases from universities and public R&D laboratories, with a limit of €124.000 (NOK 1 million) per enterprise. This grant system was replaced in January 2002 with a tax relief scheme for small and medium enterprises with sales that are less than €10.6 million (NOK 80 million) and less than 100 employees ("Skattefunn"). The tax credit is set at 20 per cent of R&D expenses and can be applied for up to €0.53 million (NOK 4 million) expenses for internal R&D and €1 million (NOK 8 million) expenses for external research. This change in policy instruments was done primarily to provide more objectivity in the decision to carry out R&D activities. A large proportion of the government's R&D spending consists of direct block grants to universities and public research institutes. About 25 per cent of government finance for R&D activity is provided to universities and public research institutes by various ministries through the RCN.

2.1.2 Actors

Several institutions at different levels provide public funding for R&D activity. Apart from the ministries such as the Ministry of Education and Research and the Ministry of Industry and Commerce, the two key organisations at state-level are the Research Council of Norway (RCN) and the Norwegian Industrial and Regional Development Fund (SND).

The Research Council of Norway (RCN)

The RCN is the most important actor in shaping research policy in Norway. Run under the auspices of the Ministry of Education and Research, the RCN acts as a main research policy advisor and allocates research grants on the basis of guidelines drawn up by the Norwegian government (RCN, 2002a). Approximately one third of Norway's public sector research investment is channelled through RCN. The remaining is transferred directly from the ministries to the relevant research institutions. In 1999, the total expenditure on R&D was €2.4 billion (NOK 20.3 billion), of which public sector allocations accounted for roughly €1.02 billion (NOK 8.5 billion). In 2002 the Research Council of Norway had a budget of €0.47 billion (NOK 3.6 billion (RCN, 2003a)). The RCN not only manages these funds but also advises the government on research policy and has a strategic responsibility for the research institutions. Its 3 main functions are:

1. Government adviser, identifying present and future needs for knowledge and research.

2. Funding agency for independent research programmes and projects, strategic programmes at research institutes, and Norwegian participation in international research programmes.

3. Co-ordinator, initiating networks and promoting co-operation between R&D institutions, ministries, business and industry, public agencies and enterprises, other sources of funding, and users of research.

The Executive Board of the Research Council of Norway is responsible for the Council's policy at the national level. Six research boards, one for each research division, submit annual strategic plans and budgets to the main Executive Board for final approval.[5]

Most RCN-funds are distributed through competitive means, using peer review of applications. Funding is allocated to research programs, independent projects, infrastructure, grants and fellowships. RCN negotiates its budget annually with each of funding ministries, which generally allocate funds for designated purposes. Ministry of Industry and Commerce is the largest contributor. The expenditure to be allocated to biotechnology research by RCN in 2002 was budgeted to €46.2 million (NOK 347 million). This included funding of Functional Genomics (FUGE), a new governmental initiative on genomics (RCN, 2003b).

User-driven research is the cornerstone of the Research Council's collaboration with Norwegian business and industry. Industrial enterprises set their priorities and provide an average of 35 to 40 per cent of the funding required for research in these fields. Among the Research Council's important partners in these efforts are employer and employee organisations, government authorities, research institutions, and bodies such as the Norwegian Industrial and Regional Development Fund (SND).

Norwegian Industrial and Regional Development Fund (SND) 1993-2003

The main objective of the former SND was to promote economically profitable business development and offers company financing, venture capital investment and financing of regional development projects. A public enterprise since its formation on 1 January 1993, it has been the government's primary instrument for promoting enterprise development throughout Norway. As an instrument for national and regional economic policy, the SND offers expertise and funding to companies in their early stages of development and promotes new and innovative business development by finding, refining, funding and following up interesting projects and enterprises. This also entails developing and carrying out regional and national projects and programmes, financing viable small and medium-sized companies, and improving female participation in industry, among other things.

SND was established as a decentralised regional office system. The 17 regional offices, one in each county, and the head office situated in Oslo jointly possess equally broad and in-depth competencies. The head office constitutes a national competence and resource centre for business and regional development. It also carries the responsibility for management and control, as well as the follow-up of operations and results for the entire SND system. The regional offices were local resource centres for Norwegian trade and industry, and the majority of all applications are handled and decided here. The regional offices constitute the customers' main entrance to both SND and its partners, and formed a gateway to all public financial instruments.

SND had in 2001 the responsibility of channelling further the sum of €0.57 million (NOK 4.6 billion) for R&D purposes in more than 9.000 projects. This also includes funding

[5] The Research Council was undergoing structural and organisational change. The new structure was implemented in 2003, and will focus on three major areas: basic research, innovation and research policy.

for the agricultural and fisheries sectors. Of this amount, 67 per cent was allocated to innovative projects and to newly established enterprises and existing companies. Although the amount allocated to innovation area within the national venture capital scheme and development grants as a whole does not show any fundamental change, the share of innovation linked to actual new establishments is increasing. While there is no public data on the amount of SND funds allocated to biotechnology, it was estimated that €3 - €4 million (NOK 20-30 million) was allocated in 2002, while the total amount allocated to innovation projects in total was €74.9 million (NOK 600 million) (interview, June 2003).

Innovation Norway

On 1 January 2004 SND merged with the Norwegian Export Council, the Norwegian Tourist Board and the Government Consultative Office for Inventors, SVO to create a new public organisation, 'Innovation Norway'.

Other related policy actors

Other important actors in biotechnology innovation are organisations and institutions that contribute to shaping the government's policy by playing an advisory role in various issues. Such organisations are non-governmental organisations (e.g. Norwegian Bioindustry Association, Association of Pharmaceutical Manufacturers, Cancer Society), governmental organisations (e.g. Biotechnology Advisory Board, Ethic Committees, Institute for Public Health), and initiatives for international cooperation (Medcoast, Scanbalt and The Trade Council of Norway, where the latter merged as mentioned above into 'Innovation Norway' on 1 January, 2004.

2.1.3 Public financing of biotechnology

The main funding organisations of biopharmaceutical research in Norway are the Ministry of Education and Research, the Ministry of Health, the Ministry of Environment and the Ministry of Industry and Commerce. The Ministry of Agriculture and the Ministry of Fisheries also play an important role in funding research in biotechnology, but research in these fields is not relevant in this context. The funding is channelled through The RCN, several institutes and universities. In addition, the Norwegian Industrial and Regional Development Fund played a role in funding of biotech project as co-funding, mostly for applied research and development projects.

In 2001 the total public expenditure on biotechnology R&D is estimated to be €85 million (NOK 686 million).[6] Public expenditure represents about 40 per cent of total R&D expenditure. Biotechnology expenditures were split about equally between higher education, industrial and institute sectors. The expenditure to marine biotechnology is not included in this amount.

The RCN is responsible for one-third of the research funding in the biotech area. Traditionally, all six divisions were funding biotech research, but from the September 2003

[6] According to statistics from Norwegian Institute on Studies in Research and Higher Education (NIFU), prepared to OECD, Directorate for science, technology and industry.

the RCN was reorganised into three main departments (basic research, applied research, strategic planning), which might simplify the application procedures. *FUGE - functional genomics in Norway,* represents, as described more in detail in section 2.2.1, a cooperative effort between Norwegian universities, research institutes and the industrial sector. *The Norwegian Industrial and Regional Development Fund (SND)* had, as described in section 2.1.2, in 2001 the responsibility of administering more than 9.000 projects.

The Norwegian Cancer Society (NCS) funds significant parts of basic biological research in Norway. NCS is a national voluntary organization with 170.000 members and a secretariat of 180 persons. One of the main activity areas of NCS is cancer research. The total amount spent on research in 2002 was €17 million (NOK 130 million). Public allocations to medical and health research are limited, but the support from the general population via NCS has helped to maintain a high international standard of cancer research. The Society supports clinical research on new forms of treatment, quality assurance of therapeutic results, and optimal palliative care. NCS also emphasises prevention and early diagnosis, and urges the establishment of national screening programmes.

The NCS gives substantial support to research on new methods of diagnosis, and steady progress is being made both within microbiology and diagnostic imaging. Other important studies focus on the biology of cancer, how the disease spreads in the body, and the importance of the immune system for development and treatment. In recent years there has been an explosion of knowledge within molecular medicine. Various new strategies for the treatment of cancer are being launched. NCS does not run its own research institutions. The activities are integrated with the research being done at universities, regional colleges and main hospitals.

One example on a half governmental, half private efforts is a venture capital funding agency named START (see section 2.2.2.). Half the capital base is a loan from the Government, channelled through Regional Development Fund (SND).

2.2 Main vertical policies and most important horizontal policies

The Norwegian government had long recognized the need to support certain “strategic” technologies such as biotechnology. From 1978 to 1991, Norway implemented a technology policy that targeted research efforts into certain strategic technologies where it had a natural comparative advantage, or was already competitive (Norwegian Government White Paper no. 54:1982-83). The Ministry of Trade and Industry targeted five technologies: IT, biotechnology, material technology, aquaculture and off-shore technology. The principal means of promoting R&D up until 1994 was to require the oil companies to invest R&D in Norwegian firms, which created a bias toward research institutes in the energy sector. Yet, public support for R&D activities in IT technology increased during the early 1990s and new institutions were created that facilitated the diffusion of technology, especially to SMEs.

2.2.1 Policies for knowledge base support

Sector-specific policy instruments

To strengthen the knowledge base in biotechnology, in addition to research programmes funded by RCN, the Norwegian government decided to establish three major measures: A functional genomics programme (FUGE), the research programme Prosbio, and a Centre of Excellence (CoE) in Molecular Biology and Neurology (CMBN).

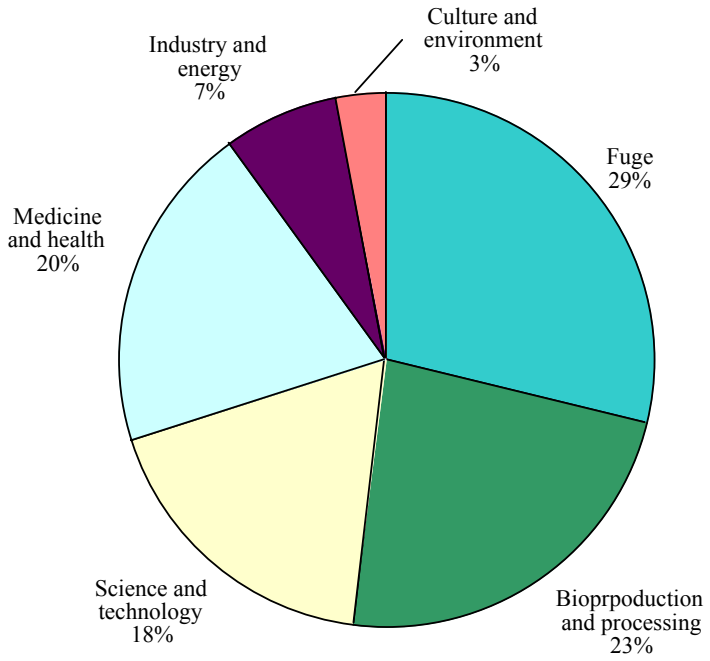
*FUGE (*National plan of Functional Genomics) was launched in January 2002 and is a long-term plan for reorganising and restructuring Norwegian biotechnology research. FUGE covers a range of disciplines within biotechnology research, and, according to the basic document on FUGE, the input into basic research, the increase of the research quality in biotechnology and a national coordination of functional gene research would help Norway to reach the international level in this field (FUGE, 2003a). The plan is a proposal for increasing the Norwegian research capacity in functional genomics, in order to enhance basic biological research, medical research and research in the marine sector. One objective is to promote enhanced ties between the research community and trade and industry. FUGE requested €40 million (300 million NOK) annually on average (increasing progressively from a lower sum) over 5 to 10 years for this purpose. Figure 2-1 shows how the distribution funds between FUGE and the six scientific divisions within the RCN.

PROSBIO (Innovation Programme for the Process and Bio-medical Industry) The Prosbio programme was started in 2002, with the aim of stimulating growth in several related fields including the bio-medical area. The programme endeavours to improve the knowledge base, enabling Norway to compete at an international level, by contributing both to the educational sector, research environments and to industry. The programme encourages the development of new production processes and new products in the biomedical and speciality chemicals fields by making funds available for various research projects. It supports both new and existing R&D projects in this area and it is expected to be particularly attractive to new research based firms and SME's operating with high risks, while it is also open to universities and research institutes. Special priority is given to collaborating groups either within Norway or internationally, where commercial firms, research institutes and universities all participate.

Centre of Excellence (CoE) in Molecular Biology and Neurology (CMBN), was appointed by RCN and is located at the University of Oslo and National Hospital (Rikshospitalet). It is one of 13 CoEs appointed by RCN in 2001. The Centre shall take on a leading role in elucidating the role of DNA repair and genome maintenance mechanisms in preventing neurological disease and brain ageing. The Centre will develop and apply stem cell technology and targeted repair to broaden the range of therapeutic strategies in neurological disease. The Centre consists of 11 research groups and about 100 scientists are involved in research.[7]

[7] The Centre and the research groups of the Centre receive funding from the following organisations The Research Council of Norway, University of Oslo, Rikshospitalet, Norwegian Cancer Society and European Union (CMBN, 2003).

Fig. 2-1: Distribution of funds between FUGE and six scientific divisions



The bio-medical aspect of the programme is intended to support firms involved in production of analytical systems, diagnostics, biological active substances for use in human medicines and for related software and hardware. Areas of particular interest are the use of bioinformatics in new medicines and treatments, signal transmission and immunology. So far around 20 projects in biotechnology have received support from Prosbio. The program is expected to run to 2010 with an annual budget of approximately €5.6 million (NOK 45 million) with around half of this sum expected to go towards biotechnology and bio-medical projects.

Nordic networks. Over the past decade each of the Nordic countries have built up research networks within their own borders in an effort to maximize their resources. More recently, the countries have turned their attention to their neighbours, seeking to create formal and informal connections with each other as well as with countries in the Baltic region. Medcoast Scandinavia is a new initiative to create a dynamic network among universities, industry, healthcare- and other organisations related to biomedical research and development in the Gothenburg - Oslo region ("The GO-region"). The region is made up of Oslo, Akershus, Østfold; Göteborg and Västra Götaland. The main goal of the initiative is to facilitate co-operation and knowledge sharing between industry, the academia and the public health care sector, and to enable the realisation of more innovations into commercial products and to strengthen the market shares for established companies. The GO region is an important region both in Scandinavian and international context. Almost quarter of the population Norway and Sweden, almost three million people live in this area. Oslo and Gothenburg are major centres

for education, industry, trade and transport. The GO region is thus perceived of as functioning as a gateway to the Nordic countries with its 25 million inhabitants.

MedCoast Scandinavia aims to harmonise efforts between Norway's FUGE and Sweden's SWEGENE, a Stockholm based private funded organisation that funds research and education. MedCoast hopes to collaborate with Medicon Valley, which helps to coordinate research activities in Lund, Malmø and Copenhagen (Nature, 2002).

2.2.2 Policies for commercialisation support

The public policy targeted to commercialisation support can be understood as various activities ranging from support to start ups to stimulation of product development in last phases, or even patenting practices at universities.

One example on a half governmental, half private efforts is a venture capital funding agency START. START was founded in 1998 and is a privately owned venture capital company with a capital base of €38 (NOK 320 million). Half the capital base is a loan from the Government, channelled through Regional Development Fund (SND). The fund has a 15 years lifetime, and proceeds from exits may be re-invested. START is Norway's leading seed and start-up stage investor. The venture capital company invests in start-ups and early stage firms with potential for high-growth and international expansion. The minimum unit investment is €0.24 million (NOK 2 million) and up to €3.6 million (NOK 30 million) may be invested in several stages.

The role of the former Norwegian Industrial and Regional Development has also been significant. In 2001, €0.57 billion (NOK 4,6 billion) for R&D and other types of support has been channelled to more than 9.000 projects (see 2.1.2. for details).

Ownership of patents, which are based on research at university facilities, has been an object for yearlong debate. Recently, the University Law has been modified. The new law pays more attention to commercialisation.

2.2.3 Policies with socio-economic and /or ethical dimensions

We firstly review Norway's general and specified policies with a socio-economic and/or ethical dimension with a relevance to biotechnology since the late 1990s based on the views expressed in two of the relevant policy initiatives during this period, The White Paper on Research (1998) and The White Paper on Health (2003). Secondly we present the two main technology evaluation boards, Norwegian Biotechnology Advisory Board and the Technology Board, and the RCN programme Ethics, society and biotechnology.

The White Paper on Research (1998) and The White Paper on Health (2003)

A memorandum by the Research Council of Norway (RCN) entitled Research for the Future precedes the White Paper on Research. Here it is stated that biotechnology-related research may contribute to the societal goals of value creation and sustainable development as well as to new scientific insights and development of the scholarly disciplines. More

concretely the RCN board committed itself to seven items, including the following three that relate to biotechnology:

1. Prioritize research directed towards medicine and health sector, food production, and marine biotech. Questions related to environment, risk and ethics were to be incorporated in these programmes.

2. Increase the funds for basic research within biotech

3. Strengthen research knit to the environment and ethics aspects in connection with risk assessment within modern biotech (RCN, 1998: 65)

The subsequent year, The White Paper on Research entitled *Research at a Watershed* was presented by the Norwegian Government Ministry of Church- Education, and Research Affairs and subsequently passed (Norwegian Government Ministry of Church- Education, and Research Affairs, 1999). The White Paper follows up on several of the recommendations by the RCN memorandum and identifies four areas for special attention: marine research, information and communication technologies, medicine and health, the crossroads between environment and energy.

Marine research is in the White Paper designated to be embedded in a value chain perspective, where one sees the whole production process as a whole: from fisheries and fish farming on the one side to marketing and sales on the other. The sector's understanding of consumer behaviour, consumer patterns and trade policies is to be improved. New processing methods are to be developed in order to secure a high quality of the products. Moreover, marine biotechnology research aimed at understanding how marine resources may be utilized in food products, pharmaceuticals and cosmetics is to be strengthened passed (Norwegian Government Ministry of Church- Education, and Research Affairs, 1999: section 4.4.1).

Medicine and health related research is to be strengthened on a broad basis in order to achieve "a better health sector and increased value creation". Contribution form the social sciences is also included in the proposal. Concrete measures include: (1) Making research positions more attractive in order to secure recruitment; (2) Creation of excellent research centres in order to achieve internationally strong research groups; (3) Research on preventive and health strengthening aspects, both on a general basis as well as on specified fields (e.g. women's special health issues, chronically ill, children. etc.); and (4) Ensuring that the emphasis on medicine and health contributes to increased levels of innovation in the business system, through linkages between university and business and incentives for commercialization including a change of legislation related to university produced intellectual results (Norwegian Government Ministry of Church- Education, and Research Affairs, 1999: section 4.4.3).

A majority of these plans have, as described elsewhere in this report, been implemented, including the centres of excellence programme and change in the commercialisation of university produced intellectual results legislation, although so recently that it is as of today not yet possible to assess their effects.

The Norwegian public policy relevant to this context is as of 2003 heavily focused on the last of the focus areas listed above, research on preventive and health strengthening aspects. The White Paper on Health entitled *A Prescription for a Healthier Norway* was presented by the Norwegian Government Ministry of Health Affairs and subsequently passed in 2003 (Norwegian Government Ministry of Health Affairs, 2003). The 5 main concrete areas of improvement or "knowledge development" include: (1) increased physical activity, nutrition, and lifestyle (8 measures); (2) social inequality and health (2 measures); (3) suicide (2 measures); (4) overview of illness prevention measures (2 measures); and (5) mental health (6 measures) (Norwegian Government Ministry of Health Affairs, 2003). The measures recommended in the most recent White Paper therefore follow a logical progression from the former recommendation with its heavy focus on the public's general health condition. At the same time it is hard to see any direct follow-up of previous declarations on increased focus on biotechnology-related research since the link to relevant fields is totally absent in the most recent White Paper.

Advisory boards and bioethics

The two policy instruments designated for evaluation of the ethical and societal impact effects of new technology are The Norwegian Biotechnology Advisory Board and The Technology Board. There is in addition an RCN programme starting in 2002 entitled Ethics, society and biotechnology.

The Norwegian Biotechnology Advisory Board was established in 1991. The main task of the Technology Board is "to evaluate the social and ethical consequences of modern biotechnology and to discuss usage which promotes sustainable development" (Norwegian Biotechnology Advisory Board, 2003a). The Biotechnology Advisory Board has approximately ten regular board meetings, publishes statements about relevant developments, as well as organizes two to three public conferences annually. It consists of 24 members appointed by the government. Through the direct appointment system the format thus differs somewhat from the Dutch and Danish layperson-based technology assessment format. Each member has a background that makes the person competent to discuss questions regarding modern biotechnology. 16 of the members are individual appointments, whereas 8 members represent different public organizations. There are in addition observers from 6 different Ministries. The secretariat has five employees assisting and coordinating the board.

The Technology Board was established in 1999. The six most important tasks of the Board are to: (1) address technological challenges and the possibilities of new technology in all areas of society; (2) aim to stimulate public debate and to support the political opinion and decision-making processes; (3) Monitor international technological development and the development of technology assessment methods (i.e. technology foresight methods, participatory methods etc.); (4) contribute so that Norway quickly addresses new technological challenges; (5) put special emphasis on lay-people's judgement, in assessment of new technologies; and (6) impart the results of their work to the Storting (The Norwegian Parliament), other authorities and society. The Technology Board consists of 15 members appointed for 4 years. 9 are within academia or research institutes (from both natural sciences, engineering and social sciences/humanities), and 6 from the private business sector or public administration. One of the main activity forms is to initiate and administer relevant surveys

and projects. The four main projects thus far are not directly relevant to biotechnology issues.[8] However, the Board has collaborated with The Norwegian Biotechnology Advisory Board in the organizing of one conference regarding GMOs (2000) and one conference on stem cells (2001).

The National Committees on Research Ethics includes one committee on Medical Research Ethics, and are designated as: (1) a resource of competence in ethics in all fields of scientific research; (2) a watchtower and an adviser at the national level; (3) an instrument to inform and advise scientific communities, government authorities and the general public; and (4) a coordinator of relevant national activities and represent Norway in related international fora.

The committees' work is aimed at researchers and research institutions, politicians and civil servants, relevant professions and organizations and the general public. The three committees are (1) The National Committee for Medical Research Ethics (NEM); (2) The National Committee for Research Ethics in Science and Technology (NENT); and (3) The National Committee for Research Ethics in Social Sciences and Humanities (NESH) (National Committees on Research Ethics, 2003).

The RCN programme Ethics, society and biotechnology is unique in the sense that it is designed to work across all of the divisions within the RCN (Ethics, society and biotechnology, 2003). The aim is to contribute to competence building within ethical, judicial and societal aspects of modern biotechnology by developing research-based knowledge on the field. In addition the programme aims at strengthening the communication between experts and citizens.

[8] The four main projects thus far as of 2003 are Sustainable technology politics, Software development politics, Digital networks in Norway, and Mobile phones and health issues.

Chapter 3. Structure, dynamics and performance of the biopharmaceutical system

This chapter focuses on the structure, dynamics and performance of the biopharmaceutical system. It begins by describing the actors involved in the national public R&D system. Section 3.2 then considers the pharmaceutical and biopharmaceutical business systems in Norway, focusing on entry and exit, acquisitions, R&D co-operation and the international dimension of the system. The chapter then analyses the performance of the biotech innovation system by examining the science, inventive and innovative activities in the biopharmaceutical industry and biotechnology as a whole. Although the biopharmaceutical system is small and dependent mostly on small, dedicated biotechnology firms with primarily Norwegian ownership, it started relatively late compared with the United States, United Kingdom, Sweden and Denmark. Nevertheless, bibliometric and patenting activities indicate that Norway is average when compared with the OECD and EU, and that the industries are very innovative. One important trend is that Norway has been creating strategic partnerships with enterprises and organizations in these countries. From this point of view Norway should see other countries as the target for setting policies to improve the public and business systems in biotechnology.

3.1. National public R&D system

The innovation process in biotechnology depends crucially on developments in basic science. This means that publicly funded basic research is essential if Norway is to succeed in creating a viable biopharmaceutical industry that can introduce new products and processes. One of the important characteristics of the Norwegian research system is the high percentage of public funding. In 2001, the government financed almost 30 per cent of total R&D activity, or about 11 percentage points above the OECD average (see table 1-3). Both universities and business enterprises obtain significant funding from the Norwegian government, which appears as the difference between the amount financed and the amount performed by these sectors.

Table 3-1 summarizes the Norwegian biopharmaceutical innovation system. The table identifies the various sub-systems (the national public R&D system, the business system, and the environment) and actor types, including examples and their role in this context.

Universities

As mentioned in chapter 1, higher education performed just under 15 per cent of R&D activity in the Norwegian economy in 2001 (see table 1-3). In Norway all institutions of tertiary or higher education are subject to the authority of the Ministry of Education, Research and Church Affairs. Higher education in Norway is mainly offered at state institutions, notably four universities, six university colleges, 26 state colleges and two art colleges. They are all covered by the same Act, which came into force on January 1, 1996. The degrees and titles that each institution can award and their professional and educational programmes, as well as the duration and specific requirements concerning breadth and depth are all laid down

in a Royal Decree of 10 May 1996. A degree candidate may combine studies from

Table 3-1: Structure of Norwegian biopharmaceutical innovation system

	Actor type	Role / examples
The national public R&D system	Universities	Education and research: 4 national comprehensive universities, Norwegian University for Agricultural Studies (NLH), Norwegian College for Veterinary Studies (NVH)
	Government research institutes	Research: Matforsk (food research), Aquaforsk (aquatic research), Havforskningsinstituttet (marine research)
Biotechnology business system	Firms: Medium size and large pharmaceutical companies	Research: mainly clinical
	Firms: Dedicated biotechnology firms	Research: mainly development
	Research organisations	Contract research: SINTEF (large scale research foundation) Unimed division, Medinnova, smaller scale CROs
	Public bodies for policies	Policy and funding: Ministry of Trade, Ministry of Education and Research, Ministry of Health, Ministry of Environment, Ministry of Fishery, Ministry of Agriculture Funding: SND, Research Council of Norway Advise and surveillance: Medicines Control Agency, National Health Agency (Statens helsetilsyn), Biotechnology Advisory Board,, Ethics Committees
The environment	Regulations and regulating authorities	Legislation: Biotechnology Act, Act on GMOs, other relevant Acts
	Semi-public stimulation programs	Funding, investment and investment aid: START, Argentum, Teknoinvest, Neomed
	Stimulation programs by the government	Funding and organisation of research: FUGE, Centres of Excellence, FORNY ("Renew), MEDKAP ("Commericalisation of medical research")
	Technology Transfer Offices	Technology transfer/commercialisation aid: Medinnova, National Cancer Hospital (Radiumhospitalet) Research Foundation, science parks and private incubator facilities
	Business support organisations	Business interest groups: Norwegian BioIndustry Association
	Initiatives for international co-operation	Linkage aid: Trade Council of Norway, MedCoast, Scanbalt Interest group: Life Sciences Norway

Note: Note that the examples are not exhaustive.
Source: Based on our field research.

universities and colleges, as the courses offered are at the same academic level. Network Norway was set up to promote cooperation and a more rational division of labour between the Norwegian universities and colleges. In June 2001, the Norwegian Parliament (Storting) passed an extensive reform of higher education. The reform introduces a new degree structure, the possibility for certain colleges to become universities, a new organisational structure,

more programmes in English, greater participation in international programmes and exchange agreements as well as many other changes.

All four of the national and comprehensive universities, located in the cities Oslo, Bergen, Trondheim and Tromsø, have programmes and conduct research in areas relevant to the development and maintenance of a biopharmaceutical innovation system at large. Each of them specialize in particular fields related to biotechnology. The largest programme that focuses specifically on biotechnology is at the National University of Science and Technology in Trondheim, where over 65 teaching and research staff are located in the Deaprtment for Biotechnology. The University of Oslo also sponsors the Biotechnology Research Centre of Oslo, the Centre for Molecular Biology and Neuroscience, which specializes in DNA repair and genome maintenance mechanisms and with its five university hospitals, the Faculty of Medicine has been an important focal point for clinical trials. Biochemistry, Pharmacy, Medical Biochemistry, and Molecular Biotechnology are taught in Tromsø and the University also has The Norwegian Structural Biology Centre. The University of Bergen has the Broegelmann Research Laboratory, which specializes in immunology research and Sars International Centre for Marine Molecular Biology, which specialises in marine biotechnology. Other universities also have courses within the relevant disciplines, as do regional colleges although predominantly not on the post-graduate level in the latter case. Two specialised universities that also conduct biotechnology research are the Norwegian University for Agricultural Studies and the Norwegian College for Veterinary Studies.

Public research institutes

Another actor within the national public R&D system is the institute sector consisting of public or semi-public research institutes. These are divided in accordance to their research area, such as genome, food-related research, marine related research, as well as other fields. The main public research institutes doing research in biotechnology are Haukeland Hospital; the Institute for Cancer Research, Norwegian Radium Hospital; the Institute for Experimental Medical Research, Ullevål University Hospital; National Hospital; National Institute of Public Health; Regional Hospital of Tromsø; Regional Hospital of Trondheim; and Ullevål Hospital. In addition, the Norwegian Institute of Public Health is managing a large database for doing the genetic epidemiologic research.

The Business system and environment

The business system consists, firstly, of firms of different types. One of the most unique aspects of the Norwegian system within this field is, as described elsewhere in this report, the limited presence of foreign owned large pharmaceutical firms combined with the presence of a number of locally developed dedicated biopharmaceutical firms. This set-up and distinction between the two is reinforced by their respective different roles when it comes to types of research conducted, where the former group hardly conducts any research at all in Norway or conduct clinical trials to a larger or lesser degree, whereas the latter conducts applied research of different types. The business system also includes organisations specialising in carrying through the considerable number of clinical trials conducted in Norway. Finally, a business system actor type, which in logical terms overlaps towards the public sub-system as well as

towards what we refer to as the environment, is the portfolio of public bodies for policies formulation and enactment. This ranges from actors that have a role in policy-making and original source of public funding (government ministries) and the channelling of funding (SND, Research Council of Norway), to miscellaneous agencies and bodies for advice and surveillance.

The environment in which businesses operate may obviously be divided into a number of sub-categories. Firstly, there is the institutional set-up at large in the form of legislation. Secondly, there are several different types of stimulation programs by the government. These typically include not only the administration of funds channelling, but also learning and organisational aspects such as trying to achieve clustering effects by way of inclusion in the stimulation program. One prominent example is the functional genomics program (FUGE) described in detail elsewhere. Some recently started institutions funded by FUGE include The Centre for integrative genetics in Ås, which aims to provide a better understanding of complex genetic characters in fish, plants and animals for scientific and commercial exploitation, The Computational Biology Unit in Bergen, which focuses on protein modelling, and The Norwegian Microarray Consortium in Trondheim, which provides microarrays and related services. There are in addition semi-public stimulation programs more narrowly focused on generating funding, or facilitating connections between potential investors and start-up firms (e.g. START, Argentum, Teknoinvest, and Neomed). Note, however, that such programs are targeted at a wider range of innovative activities than just biopharmaceutical research; so medical start-up firms will have to compete not only with each other but also with firms from other sectors.

The business environment could also be said to include public, semi-public and private facilitating initiatives aimed at generating commercialisation of research conducted within the public sphere. A few of the specialised hospitals are in the forefront of developing such initiatives. There are also some science parks, which try to capitalize on the close geographic proximity between different types of milieu, could be put into this category as well. These include Sarsia Innovation, Bergen, Bioparken AS, Ås, The Biotecnology Centre of Oslo, Leiv Eirikson Nyfotek Ltd., Trondheim, Oslo Research Park Ltd., Tromsø Science Park Ltd., and the Trondheim Innovation Centre Ltd. One type of activity that could also be included in this category is the existence of private incubator facilities. These activities consist of the setting-up of infrastructure for smaller start-up firms with the help of investments from larger firms, with the prospects of entering into potential partnerships when and if product candidates develop. GlaxoSmithKline and AstraZeneca have provided ‘incubator’ offices to some of the Norwegian dedicated biotechnology firms.

Lobbies and trade councils

Another type of supporting actor operates more on the general level in the form of lobbying activities and facilitating knowledge exchange. The foremost actor of this type is the relatively recently formed Norwegian BioIndustry Association. Finally, there has in recent years been a notable increase in exploring the possibilities for international collaboration. The Trade Council of Norway (from 2004 included in the larger organisation Innovation Norway, cf. Ch. 2) has for a number of years been the main actor in this respect. More recently, there

have also been more systematic and geographically targeted initiatives such as MedCoast and Scanbalt.

3.2. Business system

Since biotechnology is a technological activity that transcends across the manufacturing and service industries, it is not easy to identify the structure and performance of the system. The best official data comes from the 2001 *R&D and Innovation survey* carried out by Statistics Norway. This survey, which was compulsory for all enterprises with at least 10 employees, reported 15 pharmaceutical firms in Norway, of which 5 reported that a majority of their R&D activities were using biotechnology and that 28 firms in other industries were using biotechnology in at least 10 per cent of their R&D activity. To complement this survey, we carried out a *Biotechnology Use and Development Survey* of Norwegian firms in the biopharmaceutical and biopharmaceutical industries in 2003 (see appendix 1 for the questionnaire). We used the model survey under discussion at the OECD (2003) and augmented it with a more elaborate set of questions about the co-operation patterns of the biotech firms. These sources are further complemented with patent and bibliometric data from the biopharmaceutical and biopharmaceutical system.

The pharmaceutical industry in Norway

The pharmaceutical industry made up less than one percent of total manufacturing output and employment in Norway in the late 1990s (See table 1-1). The total number of firms in the pharmaceutical industry is very small in Norway as it appears in the official data. Table 3-2 shows that the number of firms in the pharmaceutical industry is about 15 on average from 1996 to 2000.[9] However, because coverage of the micro firms is not complete, many of the small, dedicated biopharmaceutical firms will not appear in statistics or they were not classified as pharmaceutical. Firm level surveys classify enterprises according to their main activity, which in some cases may be chemicals or some related activity. Finally, firms that produce diagnostic equipment or carry out other health related activities might appear in the manufacture of medical instruments or human health activities.[10] Nevertheless, Norway appears to have very few micro enterprises compared with the other Scandinavian countries. As figure 3-2 shows, Sweden, Denmark and Finland have many more micro enterprises in the pharmaceutical industry, many of which are engaged in biotech activities. This partly confirms that enterprises that use biotechnologies in Norway are likely to be classified in other industries because they do not produce pharmaceuticals as their main activity.

[9] The pharmaceutical industry appears in the *International Standard Industrial Classification, revision 3* (ISIC, rev. 3) as 2423 and includes the manufacture of pharmaceuticals, medicinal chemicals and botanical products. This definition of the industry appears in the *Nomenclature statistique des Activités économiques dans la Communauté Européenne, Revision 1* (NACE, Rev. 1) as 244, but is divided into two further categories; basic pharmaceutical products (2441) and pharmaceutical preparations (2442).

[10] Some of the small biotech firms related to pharmaceuticals may appear in the Manufacture of medical and surgical equipment and orthopaedic appliances (NACE 331), Hospital activities (NACE 8511), and Medical practice activities (NACE 8512).

Both price and non-price factors play an important role in the competitiveness of the pharmaceutical industry. Measures of price competitiveness measure relative costs for a given product quality whereas measures of non-price competitiveness consider product quality and

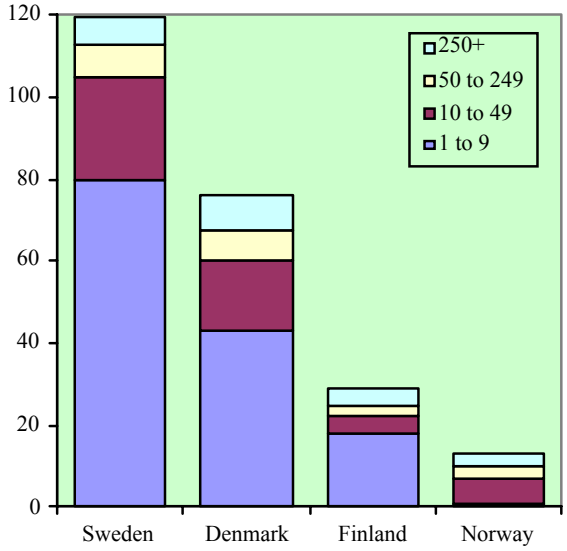
Table 3-2: Size breakdown of the pharmaceutical industry in Norway, 1996-2000

	Number of employees	Number of enterprises				
		1996	1997	1998	1999	2000
	Total	15	16	16	15	13
Micro	1 to 9	5	4	4	2	1
Small	10 to 49	5	6	6	8	6
Medium	50 to 249	1	2	2	2	3
Large	250+	4	4	4	3	3

Source: Eurostat NewCronos Database, August 2003.

technology embodied in the product. The most common measure of price competitiveness is unit labour cost. Unit labour costs are defined in the simple sense as the ratio of total labour costs per employee expressed in a common currency because exchange rates have an important impact on the competitiveness of an industry. The underlying assumptions are that movements in costs approximate movements in prices and that change in labour costs are representative of changes in total costs. Table 3-3 summarizes the unit labour costs of the pharmaceutical industry in various European economies in terms of the Euro. As the table shows, unit labour costs rose sharply in the Norwegian pharmaceutical industry during the last half of the 1990s to become the most expensive country in Europe. Indeed, except for Finland, all of Scandinavia and the UK had relatively higher growth in labour costs than in the rest of Europe. The ratio of costs between Norway and Portugal, for example, was slightly more than 2 to 1 in 1996 and increased to 4 to 1 in 2000.

Fig. 3-1: Size breakdown of the pharmaceutical industry in the Nordic countries, 2000



Source: Eurostat NewCronos Database, August 2003.

Table 3-3: Unit labour costs in the European pharmaceutical industry in terms of the Euro, 1995 to 2000.

	2000	1999	1998	1997	1996	1995
Norway	89.4	75.5	46.6	45.3	41.4	..
Belgium	59.5	57.9	56.8	56.1	56.5	56.2
Denmark	51.6	46.4	44.0	..	40.8	37.4
Germany	55.1	..	..	..	..	..
Spain	36.9	36.1	30.0	30.0	30.0	30.0
France	51.3	49.3	48.6	47.3	46.4	..
Ireland	..	36.5	35.1	35.0	31.7	30.5
Italy	44.0	..	40.0	40.0	40.0	40.0
Luxembourg	42.5	..	36.9	37.5	35.8	34.6
Netherlands	49.1	47.0	46.6	47.9	48.2	44.5
Austria	50.1	47.6	46.7	45.5	..	44.6
Portugal	23.2	21.9	21.4	20.6	19.8	..
Finland	39.9	38.0	36.0	35.7	34.3	34.9
Sweden	53.3	..	46.8	46.2	44.3	37.5
United Kingdom	50.5	45.6	38.5	37.0	30.5	..

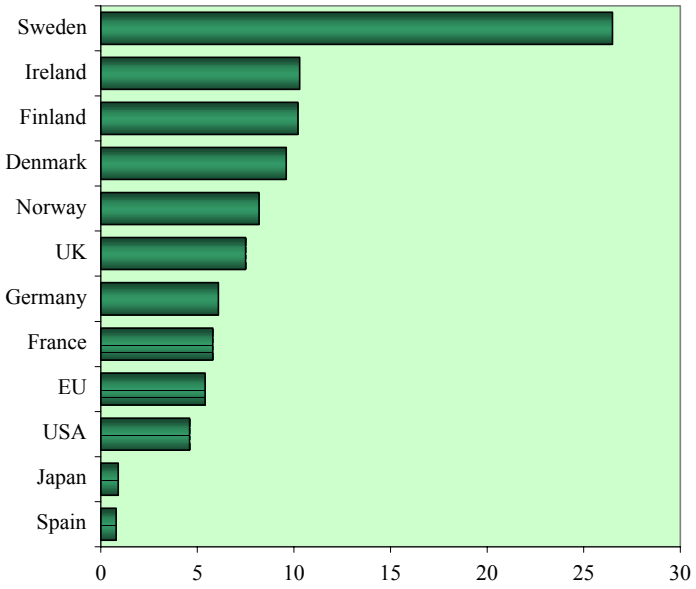
Source: Eurostat NewCronos Database, May 2003.

The Biopharmaceutical Industry in Norway

Enterprises that produce or are developing one or more products, or are carrying out R&D activities using at least one of the five biotechnologies or processes are considered to be in the biopharmaceutical and biopharmaceutical sub-sectors (see introduction). These sub-sectors are primarily made up of small, dedicated biotech firms, which actively use of biotechnology their R&D activity and in developing new products and processes, and diversified biotech firms, which integrate biotechnologies in their existing R&D and innovative activities. The European commission estimates that there were 8.2 dedicated biotechnology firms per million inhabitants in Norway in 2000, which was much higher than the EU average, but lower than in the Scandinavian countries (see figure 3-2). Sweden had the most dedicated biotechnology firms per million inhabitants, but Norway did well when compared with the larger European countries and the United States. Our *Biotechnology Use and Development Survey* that the average dedicated biotech firm in Norway had little more than 10 employees on average while the average diversified biotech company employed more than a 300 people at the turn of the century.[11] Being dedicated to biotechnology, these firms used biotechnology in about 68 per cent of their R&D activity, whereas the diversified firms used biotechnology in about 31 per cent of their R&D activity. By contrast, the pharmaceutical firms appear much smaller than the diversified firms because they are foreign subsidiaries of a large global multinational enterprise. These firms also rarely use biotechnology in their R&D activities in Norway.

[11] According to the Norwegian Bioindustry Association (NBA), about 1000 people were employed in biotech companies and organizations. Cf. also Appendix 2 of this report.

Figure 3-2: Number of dedicated biotechnology firms per million, 2000



Source: EC, The Biotechnology Innovation Scoreboard, 2002.

While the international attention in biopharmaceuticals tends to focus on therapeutics, the majority of Norwegian firms focus on marine biotechnology and medical diagnostics (Cf. Appendix 2). There are two reasons for this: firstly, developing human medicine requires a lot more time and financial resources than development of diagnostic tools, therefore it might be more realistic and less risky to put efforts on entering the diagnostics market for Norwegian companies. Secondly, the technology solves an existing problem without involving the human body, while DNA based human medicines, interacting with physiological processes in the body, may involve a number of risks that must be considered in each case.

Table 3-4: Size and structure of the biopharmaceutical sector

	1999	2001	2002
Dedicated biotech firms			
Employees	10.8	10.7	14.5
% R&D in biotech	73.6	68.3	61.9
Diversified biotech firms			
Employees	331.7	322.0	349.5
% R&D in biotech	37.0	27.0	29.2
Pharmaceutical firms			
Employees	107.7	119.7	131.7
% R&D in biotech	2.0	6.0	6.7

Source: Own calculations based on our biotechnology use survey 2003.

The most important biopharmaceutical companies that focus on diagnostics are Amersham, Axis Shield, Dynal Biotech, PhotoCure, Affitech, Genpoint, GenoVision and Biosense. The first four companies are diversified, whereas the others are small dedicated firms with fewer than 20 employees.

Amersham Health is focused on the development of molecular diagnostics, targeted towards major diseases such as cancer, Alzheimer´s disease, and heart disease. The new molecular diagnostics improve the way medicine is delivered. As knowledge about genetic variation increases, the company wishes to develop diagnostics that can identify individuals at high risk for disease or side effects of given drugs. The company's four major brands are: Ominpaque, Visipaque, Ominscan and Myoview. Visipaque is an X-ray product used in cardiac angiogrpahy, Myoview is now approved for use in breast tumour imaging and the magnetic resonance agent Omniscan is being developed for the diagnosis of cardiovascular disease.

Axis-Shield is focused on in vitro diagnostic tests based on DNA technology. The company has 440 employees, thereof 131 in UK and 309 in Norway. 65 staff is directly employed in R&D. Axis- Shield was created in May 1999 by the merger of two companies – Norwegian based Axis Biochemicals, founded in 1985 and UK based Shield Diagnostics, founded in 1982. Further growth was achieved by the acquisition of the diagnostics business of Nycomed Pharma in February 2000, which has given the group a focus in Point –of -Care (PoC) testing, as well as direct distribution in Scandinavian countries. The combined group now consists of laboratory and PoC business, backed by a strong R&D division. The company holds 300 patents and claims to be an important global force in diagnostic innovation. It is listed on the London and Oslo Stock Exchanges (Axis-Shield 2001). 2001 was the first year since creation of Axis-Shield that the company was able to generate, from its own resources, the cash necessary to fund its R&D activity aimed at future products and new technologies. This milestone was achieved even though Axis-Shield increased R&D spending significantly in 2001.

Dynal Biotech is focusing on magnetic and non-magnetic micro particles (Uglestad beads) (Dynal Biotech 2001). In 2001 the company had 242 employees in total. Dynal Biotech has been the pioneer of biomagnetic separation technology since the start in 1986. Dynabeads®, first invented by John Ugelstad in 1979, are uniquely monodisperse and superparamagnetic particles which are used in separation and analysis of biological material such as nucleic acid, cells, proteins and micro-organisms, which are utilised in research, diagnosis and therapy. Dynal Biotech is owned by the Swedish equity firm Nordic Capital. The Dynal Biotech head office is situated in Oslo, Norway with subsidiaries in US, UK, France, Germany, Australia and Japan. The production facilities are based in Norway and UK. Dynal Biotech consists of four units: Molecular Systems, Immunsystems, HLA diagnostics and Dynal Particles. *Molecular Systems* develop products for separation, handling and analysis of nucleic acid and proteins for use in genomics, proteomics and in-vitro diagnostics. The number one customer by 2001 was Roche Diagnostics and a new cooperation with Bayer Diagnostics was established. *Immunosystems* unit provides solutions in the fields of immunology and microbiology. In both fields Dynal Biotech is a recognised supplier of products for biomagnetic separation technology. Dynabeads products are used to separate and modify human cells from blood and bone marrow to enable basic and clinical research.

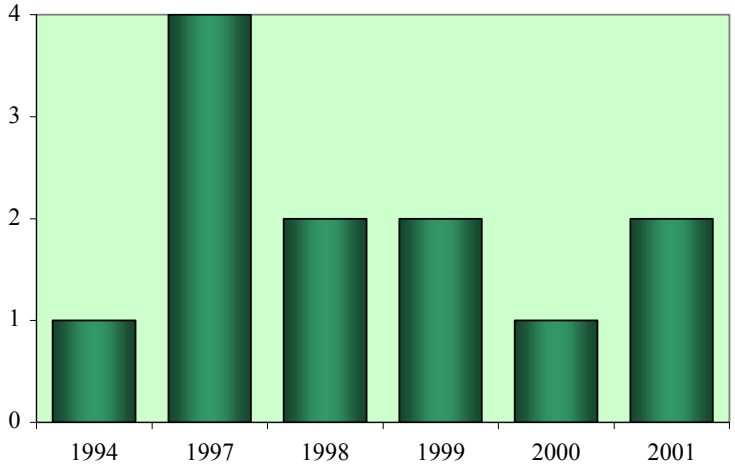
Dynabeads also form a key technology for a new immunotherapy treatment as patented by Xcyte Therapies. The treatment is undergoing clinical trials in kidney cancer and prostate cancer with encouraging results. *HLA Diagnostics* unit is located near Liverpool, UK, is the leader in the manufacture and sales of diagnostic products related to the genetic typing of donors and recipients of solid organs and bone marrow. *Dynal Particles* is a subsidiary of Dynal Biotech ASA, develops and produces non-magnetic beads for among others analytical chromatography and industrial separation. The main customer is Amersham Biosciences and the production site is in Lillestrøm, Norway.

Entry and exit, including mergers and acquisitions

A vast majority of the dedicated biopharmaceutical firms were established in the late 1990s, mainly because of the result of the merger between Nycomed and Amersham. Of the dedicated biopharmaceutical firms that answered the *Biotechnology Use and Development Survey*, all but two of them were founded after 1996 and these two were established only a few years earlier. The diversified firms were established in the mid 1980s, except for one that was established in the late 1990s. Figure 3-3 shows the number of start-ups doing biotechnology research from 1994 to 2001 who responded to our survey.

The structure of the biopharmaceutical industry has undergone major changes in recent years. Several biopharmaceutical companies had been bought up by the pharmaceutical industry, paralleling the mergers and acquisitions within the pharmaceutical sector. High sunk costs created by high R&D and marketing costs, can be an import barrier to entry into the industry. The high sunk costs also may encourage the sale of the small dedicated biotech companies to the larger pharmaceutical firms. Discovering new drugs or knowledge about biotechnology processes is an important motivation for the large pharmaceutical firms to buy or form alliances with small, dedicated biotech firms. It also provides an important avenue for the small firm to finance its R&D activities. Other exit possibilities include an initial public offering (IPO), different types of alliances and co-operation with various partners.

Figure 3-3: Entry of new dedicated biotech firms in Norway



Source: Own calculations based on our biotechnology use survey 2003.

In a qualitative market survey conducted by Ernst & Young (1999), the vast majority of Norwegian biopharmaceutical companies indicated that alliance with foreign biotech companies or academic researchers will be most probable within the next 3 years. Our interviews conducted with biotech companies in spring 2003 indicate that the trend to be bought up by foreign pharmaceutical companies persists. Some of the examples are the cases of Amersham, Axis-Shield and Dynal Biotech, the largest biopharmaceutical companies with Norwegian ownership. Moreover, it was stated that the exit possibilities for investors in Norwegian biotech firms is either IPO or to be bought up by a pharmaceutical firm. IPO is rather seldom particularly in the current financial climate, so the most usual exit for early exit is the latter. Due to the fact that big pharmaceutical industry in Norway consists of multinational firms that do not conduct basic research in Norway, the acquisitions of start-ups may mean that the research activities may be moved out from the country. However, most of the researchers stay here and search jobs either at universities or in other firms. This, again, leads to accumulation of specific skills and knowledge in the scientific society in general.

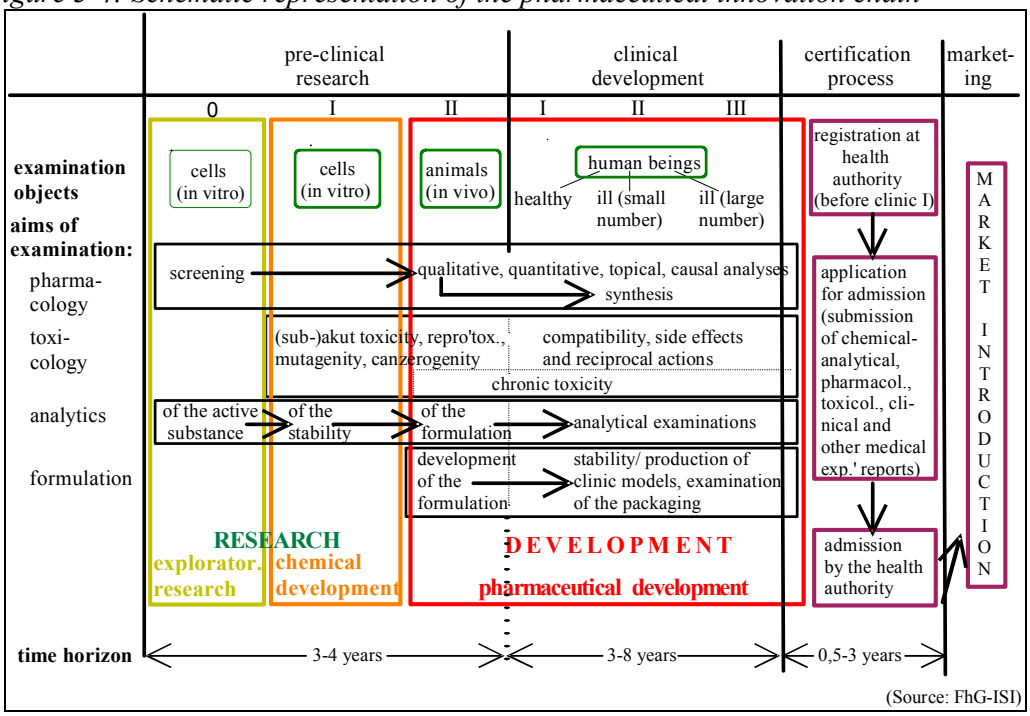
One of the important country-specific elements that might have contributed to focusing on diagnostics is the acquisition of Nycomed by Amersham in 1996. The acquisition had a significant spin off effects, and researchers who left Nycomed after the acquisition established several biotech companies. PhotoCure, one of the most successful Norwegian pharmaceutical companies in the latest years is such example, Clavis Pharma (dealing with cancer therapy) is another. A number of former Nycomed researchers are employed in the diagnostics companies Axis-Shield, Dynal and in Medinnova, the Technology Transfer Office at the National Hospital (Rikshospitalet).

Another significant effect of the merger between Nycomed and Amersham was creation of new jobs. According to figures from the Norwegian Association of Pharmaceutical Manufacturers, 4,600 were employed in the industry in 2002, of which 25 per cent were employed with Amersham Health (LMI 2003). At the time of the acquisition Nycomed had 770 employees, and in 2003 the number of employees increased to 1,180.

Research and Development

The pharmaceutical industry is a high-tech industry that tends to have a very high R&D intensity (measured R&D expenditures as a percentage of value added). Sutton (1998: 205) argues that this mainly because the cost of developing each chemical increased by more than10 times between 1962 and 1972. Most of this cost is attributed to stricter regulations that required more extensive clinical trials and a much longer time from discovery of the chemical to marketing the new product. Figure 3-4 shows the different stages of R&D activity. The development of a chemical starts from exploratory research and chemical development, which often occurs in public laboratories and universities, but shifts to the private pharmaceutical and dedicated biotech firms in the later stages. Once a product has been identified, the drug is clinically tested on a select group of people over several years. This clinical development generally requires permission by the national health authorities, and is carried out by a firm planning to market the product with the support of doctors, clinics and/or hospitals. Successful clinical development of a product requires registration and certification by the health authorities. After approval the drug can by marketed, subject to further surveillance.

Figure 3-4: Schematic representation of the pharmaceutical innovation chain



Source: Jungmittag et al (2000).

Norwegian businesses spent little more than €52.9 million ($50 million (in PPPs)) on the development of new pharmaceutical products in 1999 (see table 3-5. This represented about 9.5 per cent of total R&D spending by businesses in manufacturing. In the Nordic countries, Denmark has the highest share of R&D activity and Finland the lowest in this industry. Norway is between Sweden and Finland. The R&D intensity is relatively similar across countries, which confirms that the distribution of business R&D intensities differs more across industries than across countries within an industry.

The pharmaceutical firms locate most of their research activities abroad, but conduct some of their clinical development, especially the clinical trials, in Norway. Despite declining competitiveness (high unit labour costs) Norway is still attractive to the pharmaceutical firms because it is relatively easier to find a cohort to participate in a trial and the freedom of information laws in Norway make it easier to trace the movement of the cohort. In 1999, only about 36 per cent of R&D activity in the pharmaceutical firms is in pre-clinical research, with about 29 per cent in clinical trials and the remaining in other activities (LMI 2003, p. 78). By contrast, the dedicated biotech firms are doing mostly research and product development. Many of these firms have close connections to universities and hence basic research.

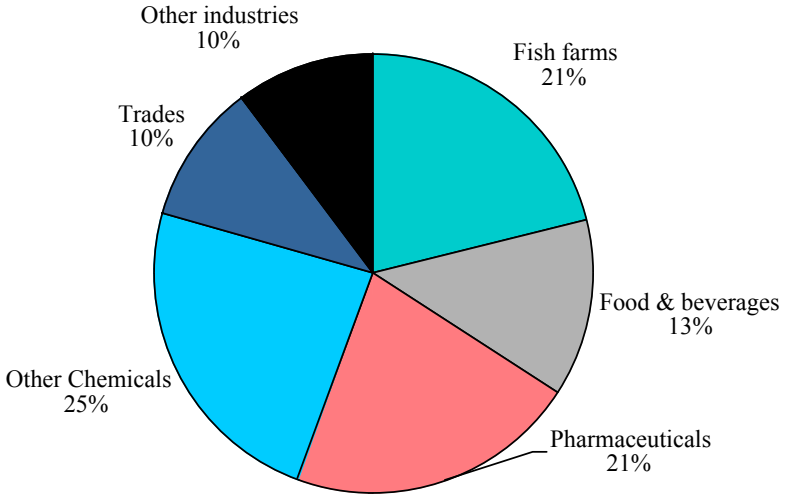
Table 3-5: Business enterprise R&D in the Pharmaceutical industry, Average 1994 to 1999.

	Millions of current PPP dollars	share of BERD in manufacturing	R&D intensity
USA	11,082	9.6	22.7
Japan	3,933	6.9	42.5
Sweden	757	17.4	45.7
Denmark	332	32.4	31.6
Finland	76	5.0	28.1
Netherlands	324	10.6	23.0
Finland	76	5.0	28.1
Norway	52	9.3	22.7

Note: Norway is 1994 to 1998 instead of 1994 to 1999.
Source: Own calculation based on OECD ANBERD database, 2002.

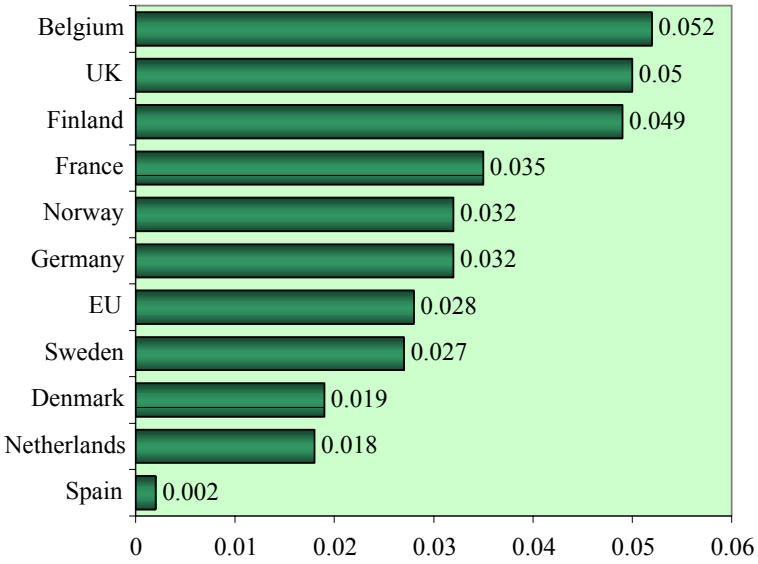
Biotechnology is a technology that is used in many different industries, including pharmaceuticals. Measuring R&D activity in biotechnology is thus difficult because it does not fit into any of the accepted methods of income accounting. In the 1999 and 2001 *R&D and Innovation surveys* firms where asked whether they engaged in any R&D activity in biotechnology and the percentage of that activity. From this information it is possible to calculate the total amount of R&D expenditure in biotechnology. As figure 3-5 shows, pharmaceuticals only make up 21 per cent of the Norwegian biotechnology R&D in 2001. Aquaculture makes up another 21 per cent and other chemicals make up another 25 per cent. Together they make up about two-thirds of the R&D activity in biotechnology, but it is also clear from the responses that a majority of the firms in these industries do not engage in any biotechnology activities. Some R&D activity appears in medical instruments, but the share is too small to include in Fig. 3-5.

Figure 3-5: Intramural R&D expenditure in biotechnology, 2001



Source: Community Innovation Survey 1999-2001, Statistics Norway

Figure 3-6: Government Biotechnology R&D expenditures as a percentage of GDP, 1994-1998

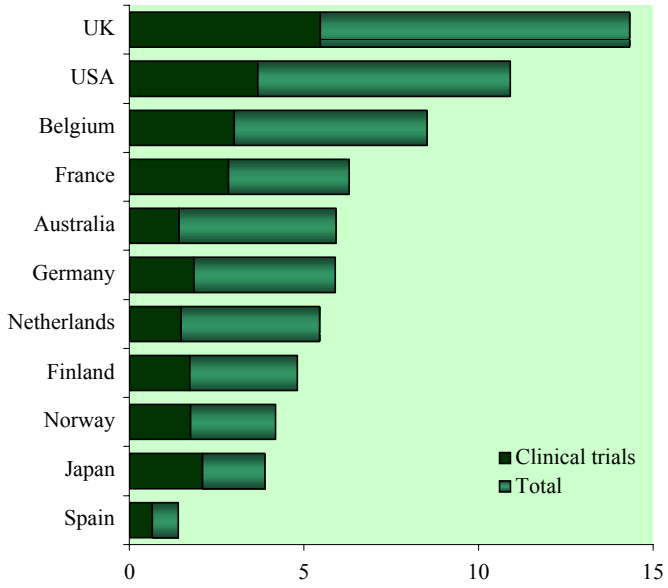


Source: EC, The Biotechnology Innovation Scoreboard, 2002

Since bringing successful products to market is a long-term and risky process in biotechnology, government finance for R&D activity can facilitate this process. Figure 3-6 shows that Norway was slightly above the EU average in government biotechnology R&D expenditures as a percentage of GDP in the period between 1994 and 1998. During this period the government spent 0.032 per cent of GDP on biotechnology R&D activities, which compares favourably with Denmark and Sweden, but is well below Belgium, UK and Finland.

Clinical trials provide some indication of national capabilities in biopharmaceutical research. According to the IMS Health (as cited in LMI 2003), Norway had 11 new drugs in the pre-clinical stage, five in stage 1 and 3 in stage 2 during 2002. Figure 3-7 shows that the number of drugs in the pipeline was significantly lower then most of the other European countries when placed in the context of the number of inhabitants. Our *Biotechnology Use and Development Survey* revealed that 58 per cent of the dedicated and diversified firms claimed to have products on the market by 2001. Figure 3-8 provides a breakdown of products under development by biopharmaceutical firms residing in Norway. This figure shows that a very high proportion of products are in the pre-clinical research stage and there are about an equal number of products in clinical development, at the certification stage and already in production. At the end of 2002, the firms that had products in the pipeline spent well over 60 per cent of their income on R&D activity, which indicates that they have too few products on the market, or that they are not spending enough money on marketing their products. This relates market organization and strategy with R&D activity. Firms in the biopharmaceutical industry must understand the markets within which they operate since competition is based not only on successful R&D activity, but also costs, advertising and product positioning.

Figure 3-7: Drugs under development in selected countries, 2002



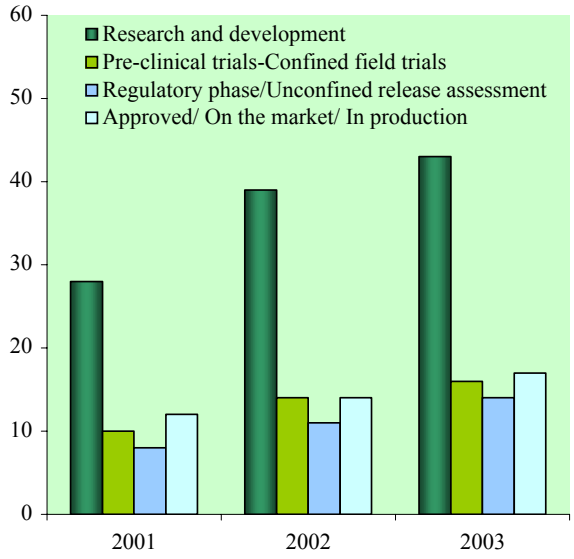
Source: R&D Focus, IMS Health Incorporated, 2002

R&D co-operation

R&D co-operation with other enterprises and organizations is essential for achieving success in using biotechnology, and especially in innovation in the biopharmaceutical and biopharmaceutical industries. Co-operative agreements allow firms to diversify their risks, increase their ability to learn, and augment their sources of information for future strategic use. Our 2003 Biotechnology Use and Development Survey contained a question to gather information about the co-operative patterns of dedicated and diversified biotech enterprises. It asked not only what kind of enterprise or organization it was involved with, but also whether it was a joint venture, joint R&D project, R&D contract, Licensing, R&D outsourcing, exchange of employees or other type. Finally it asked what where the reasons for the enterprise to be involved in different R&D and strategic partnerships. These included scientific research, development of products, development of processes, development of techniques, or marketing and other sales related activities.

The results of the co-operation survey shows that 94 per cent of companies co-operate and the most preferred type of co-operation is R&D co-operation, either with research organizations or with small and medium enterprises (SMEs). The most preferred countries where the co-operation partners are resident are Norway, USA, Germany UK and France. The preference of co-operation with Nordic countries is low.

Figure 3-8: Biopharmaceutical products in the pipeline, 2001-2003

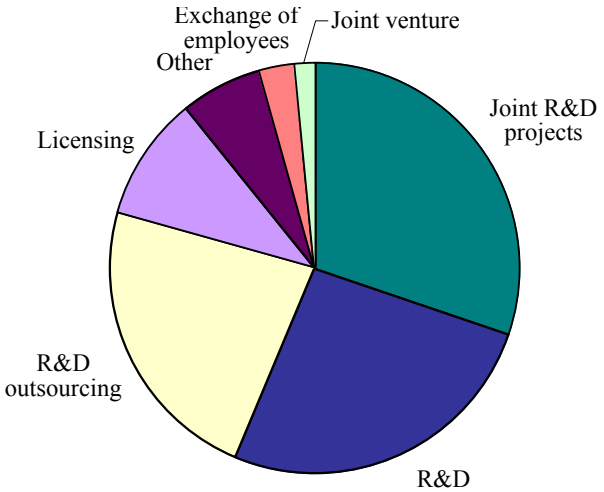


Source: Own calculation based on the 2003 Biotechnology Use Survey.

Figure 3-9 illustrates which type of co-operation firms choose. Out of the 16 responding firms, fifteen indicated at least one type of co-operation. These 15 firms were involved in 114 different co-operation projects, meaning that the majority of firms co-operate with several partners. The three most preferred types of co-operation were joint R&D projects (30 per cent), R&D contracts (26 per cent) and R&D outsourcing (23 per cent). Joint venture, licensing, exchange of employees and other types of co-operation are less than 10 per cent.

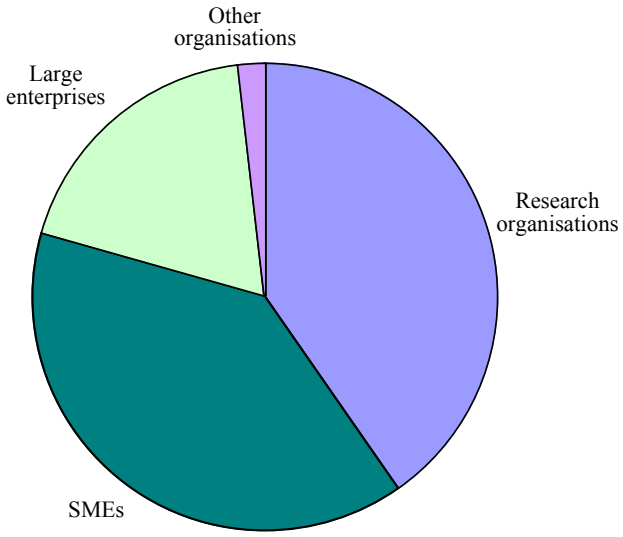
Figure 3-10 shows which types of partners are preferred in co-operation projects. Of the 114 projects carried out by the 15 firms, 40 per cent were with research organisations and 39 per cent with SMEs. Large enterprises and other organisations represent 21 per cent together.

Fig 3-9: Co-operation projects by type of partner



Source: Own calculation based on the 2003 Biotechnology Use Survey.

Fig 3-10: Co-operation projects by organisation



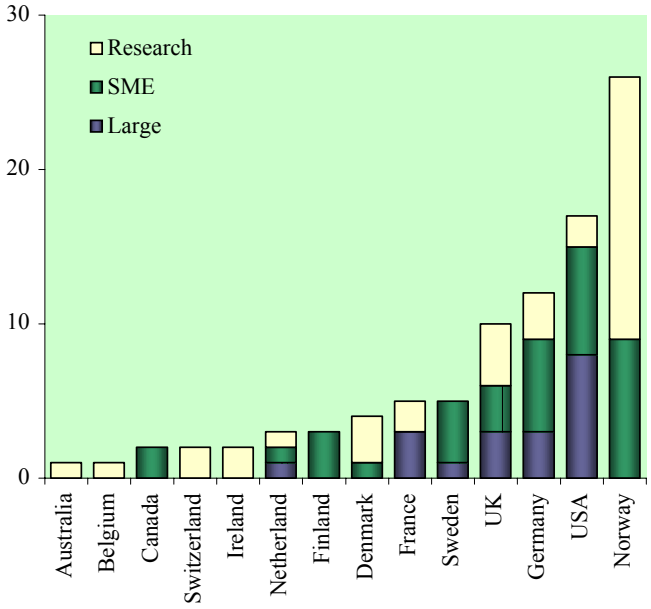
Source: Own calculation based on the 2003 Biotechnology Use Survey.

Figure 3-11 illustrates the extent of co-operation by size of partner and country. Nine out of 16 firms indicated that they had a project with a large firm. There were a total number of projects of 19, of which 42 per cent of the partners were located in the United States, and Germany, France and United Kingdom each represented 16 per cent of the partnerships. No Norwegian enterprises were partners of this type. Although the number of projects is rather low, it provides an indication of future trends. The figure also shows co-operation with SMEs. Twelve firms had a co-operation project with SME, with 40 projects in total. Almost one third of the SMEs are located in Norway. Other important partners included the United States (17 per cent), Germany (14 per cent), United Kingdom (13 per cent) and Sweden (10 per cent). The co-operation with SMEs seems to be less preferred then co-operation with research organisations, but more preferred then with large enterprises.

This figure also shows the distribution of co-operation projects with research organisations is shown by country. Fifteen companies co-operate with research organisations, and the total number of co-operation projects is 41. The majority of co-operation projects (47 per cent) are conducted with Norwegian organisations, and the rest is divided between 11 various countries, ranging from 8 per cent with Germany and Switzerland to 2 per cent with Netherlands, Belgium, Scotland, Australia. Although several efforts have been made to increase the co-operation with the Nordic countries recently, neither Sweden nor Finland is among the indicated partners. Nevertheless, it seems that this type of co-operation is a common element in all firms that co-operate.

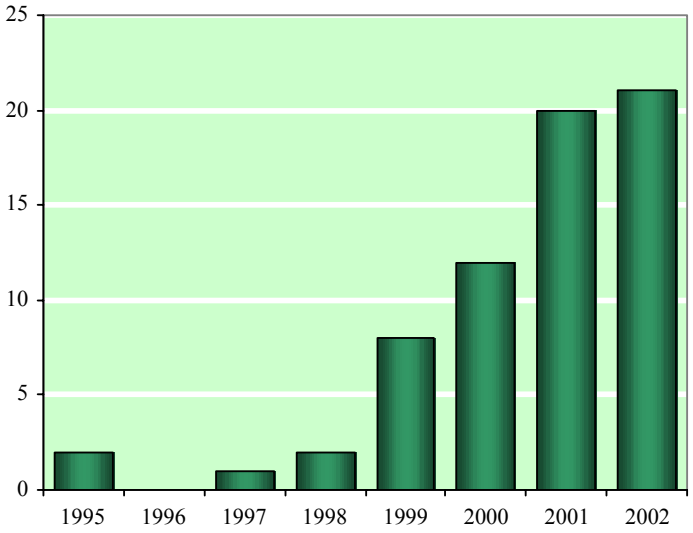
Figure 3-12 provides a distribution of the starting year for each project. Of the 114 partnerships, we obtained the starting date in 88 cases. The number of partnerships increased dramatically with the entry of new, dedicated biotech firms after 1997, which began to noticeably show in the period 1999- 2002 the number almost doubled.

Fig 3-11: Co-operation projects by organisation and country



Source: Own calculation based on the 2003 Biotechnology Use Survey

Fig 3-12: Start of co-operation projects

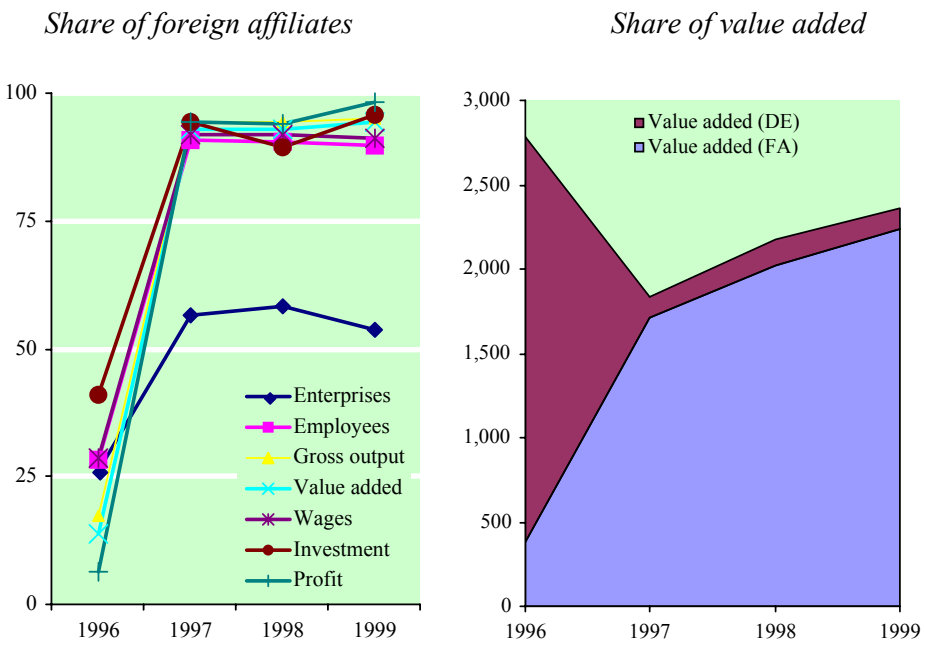


Source: Own calculation based on the 2003 Biotechnology Use Survey.

Internationalisation of the Norwegian pharmaceutical industry

The rapid trend toward globalization of the pharmaceutical industrial in the late 1990s had an important impact on the industry in Norway.[12] The share of firms under foreign control depends on several factors, including the size and attractiveness of the markets, the complementarity of strategic assets and capabilities, and the institutional environment. In Norway the share of output from manufacturing enterprises increased from slightly over 10 per cent in 1991 to over 24 per cent in 1998. This was not unusual for the OECD countries (OECD, 2002), but as Fig. 3-13 shows, the share of output in the pharmaceutical that came from foreign controlled enterprises creased from nothing in 1993 to about 95 per cent in 1997. Statistics Norway reported 14 pharmaceutical firms in 1994, of which 3 were foreign controlled, and reported 24 pharmaceutical firms in 1999, of which 12 were foreign controlled. The figure also shows that FDI coming into the pharmaceutical industry was mainly in the form of global acquisitions of Norwegian firms in 1996. In the first year after the wave of acquisitions, value added fell by about one-third (seen by the rapid decline in value added in domestic enterprises (DE)), but then began to recover over the next two years as the foreign affiliates (FA) began to invest. But a sharp rise in investment of almost 40 per cent in 1997 indicates that some of the industry shifting its focus from production to marketing and distribution. The relatively rapid rise in imports following the mergers and acquisitions confirm this trend.

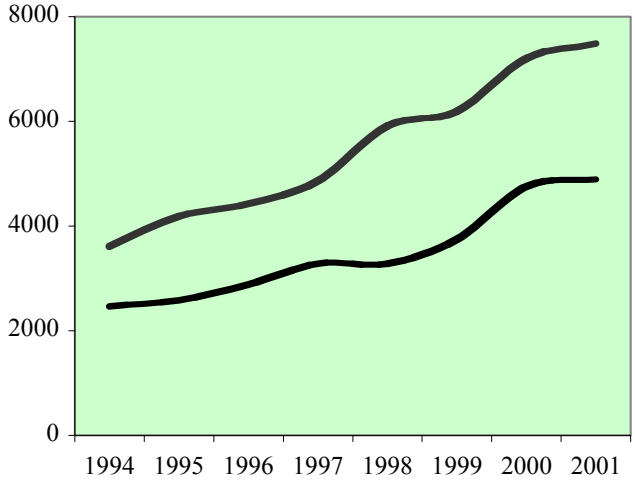
Figure 3-13: Foreign affiliates in the pharmaceutical industry, 1996 to 1999



Source: OECD AFA database, 2003

[12] Indicators on the activities of firms under foreign control describe the global dimension of the innovation system by providing the means to analyze the performance of these firms and their contribution to the Norwegian economy. Foreign affiliates do not necessarily require majority ownership to have influence over the management of the firm – most often ten per cent of a firms voting share are enough to have a voice.

Figure 3-14: Imports and Exports of Pharmaceuticals in Norway (millions of NOK)



Source: OECD Stan database, 2002.

If we only focus on the dedicated biotechnology enterprises within the pharmaceutical industry, we find a very different pattern. Of the 12 dedicated biotech enterprises that answered the *2003 Biotechnology Use and Development Survey*, one has a Swiss parent and a Swedish equity firm owned another. Both firms had an above average number of employees. By contrast all three diversified biotech firms that answered the questionnaire were foreign controlled.

The increase in labour costs partly explains why net imports of pharmaceuticals had increased from 1994 to 2001. Figure 3-14 shows that imports of pharmaceuticals increased faster than the exports during this period. However, the sharp change net imports from 1997 and 1998 is mainly explained by the acquisition of several domestic pharmaceutical firms by foreign multinationals and the consequent shift in production out of Norway that occurred during this time.

3.3 Performance

This section provides an overview of the scientific and innovative performance of Norwegian biotechnology, particularly in the pharmaceutical and medical industries. It looks first at the scientific and innovative activities, as measured by the scientific publications in pharmaceutical biotechnology and patent data. Second, it examines the innovative performance of enterprises, as measured by our biotechnology use survey and the Third Community Innovation Survey.

3.3.1 Bibliometric analysis.

Bibliometric analysis use data on numbers and authors of scientific publications and on articles and the citations therein (and in patents) to measure the "output" of individuals/research teams, institutions, and countries, to identify national and international networks, and to map the development of new (multi-disciplinary) fields of science and

Table 3-6: Number of biopharmaceutical publications, 1994 and 2001

	1994	2001	Total: 1994 to 2001	growth rate	Share of world total in 2001	Publications per million inhabitants in 2001
World	20,282	33,273	217,845	7.3	100.0	5
OECD	19,190	30,733	203,653	7.0	92.4	34
United States	8,658	13,192	88,662	6.2	39.6	46
EU	7,986	13,024	86,657	7.2	39.1	34
Japan	2,143	3,733	24,008	8.3	11.2	29
Germany	1,588	3,160	19,281	10.3	9.5	38
United Kingdom	1,910	2,970	20,043	6.5	8.9	51
Canada	889	1,453	9,636	7.3	4.4	47
Netherlands	651	1,001	6,797	6.3	3.0	62
Spain	438	936	5,652	11.5	2.8	23
Belgium	314	596	3,603	9.6	1.8	58
Finland	262	392	2,642	5.9	1.2	76
Norway	114	217	1,274	9.6	0.7	48

Source: Own calculations based on SCI via STN, Searches and calculations by Fraunhofer ISI and World Bank, World Development Indicators, 2003.

technology (OECD 2002b: 203). Like patent data, this indicator is useful for identifying basic research in biotechnology and biopharmaceuticals and it can be used to measure the 'productivity' of researchers or research quality.

Table 3-6 shows the total number of biopharmaceutical publications from 1994 to 2001 for selected countries and the world. Although Norway's share of biopharmaceutical publications in the world total is less than one per cent during the period, its publications increased from 114 in 1994 to 217 in 2001, representing an average annual growth rate of almost 10 per cent. The average annual growth rate is 2.6 percentage points higher than the OECD average growth rate and 3.4 percentage points higher than the United States, suggesting that Norway was catching-up with the leading countries in terms of publications per million inhabitants. This growth rate also parallels the high growth of new firms in the pharmaceutical and medical industries In 2001 Norwegian researchers had 48 publications per million inhabitants, which compares favourably with the United States. However, the Norwegian performance does appear to be doing so well when relative figures are used. Table 3-7 shows the biopharmaceutical publications per thousand researchers and the share of biopharmaceutical publications in total publications. With 16 biopharmaceutical publications per thousand researcher in the mid 1990s and 22 at the end of the 1990s, Norway compares favourably with the United States and Germany, but is well below the EU average. This suggests that the quality of Norwegian research is similar to research carried out in Germany and the United States. The share of biopharmaceutical publications in total publications also appeared low in Norway, but the variation across countries was not very large.

Table 3-7: Biopharmaceutical publications, 1994/95 and 1999/00

	per thousand researchers		per cent of total publications	
	1994/95	1999/00	1994/95	1999/00
Netherlands	40	49	4.2	5.3
Belgium	29	38	4.1	5.7
United Kingdom	28	37	3.3	4.2
Finland	33	30	4.7	5.2
EU	21	28	3.5	4.6
Spain	20	27	2.9	4.0
Germany	15	24	3.2	4.6
United States	18	23	3.8	5.4
Norway	16	22	3.1	4.1
OECD	15	19	3.5	4.7
Japan	7	12	3.7	5.0

Source: SCI via STN, Searches and calculations by Fraunhofer ISI, and OECD MSTI database, 2002/2

We can determine whether Norwegian research in biopharmaceutical is above or below average *relative* to the overall publication activities of other countries by computing the revealed literature advantage (RLA) for different countries.[13] Table 3-8 shows the RLA for several countries as well as the EU and OECD average. In this table 0 indicates average and +/- 100 indicates the maximum and minimum, respectively. Norway appears to be the lowest among the countries represented here and is also below the EU and OECD average. But since this indicator has a fault tolerance of between +/- 15, Norway would clearly appear to have average specialization. All of the bibliometric evidence indicates that Norway is somewhat behind, but this may only be a reflection of being a relative latecomer to the use of biotechnology in the pharmaceutical and medical fields.

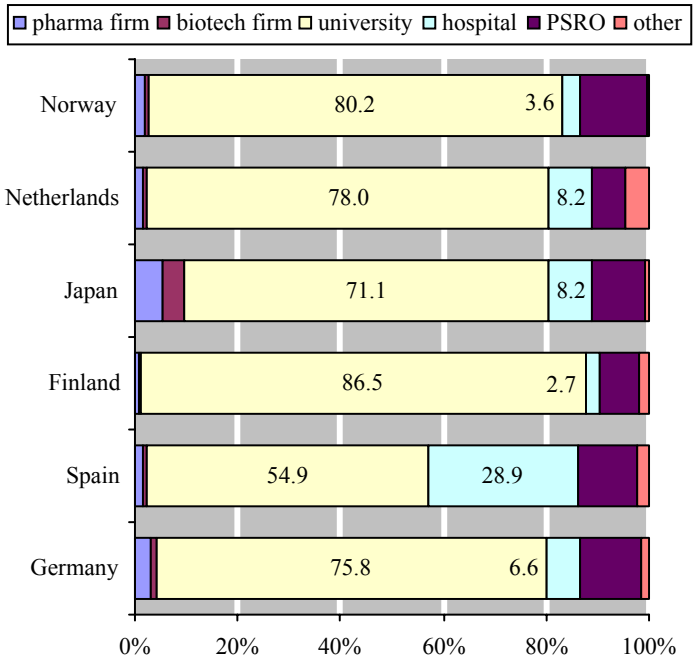
Table 3-8: Revealed Literature advantage (RLA), 1994/95 and 1999/00

	1994/95	1999/00
United States	21	24
Netherlands	30	23
Finland	41	20
OECD	13	11
Germany	4	8
EU	14	8
Norway	1	-3

Source: SCI via STN, Searches and calculations by Fraunhofer ISI

[13] The specialization indicator is defined as RLA = 100tanh ln$[(P_{ij}/\sum_j P_{ij})/(\sum_i P_{ij}/\sum_{ij} P_{ij})]$, where P denotes the number of patents in country i and subfield j. If the value of the indicator for a subfield j equal 0, the activity is graded internationally average, negative values are indicating below-average activities, positive values reflect above-average publication activities. The main relationship, which is enclosed in square brackets is also called 'activity index'. The activity index has asymmetrical properties, bound to one side (min.: 0; neutral: 1, max.: towards infinity), which would distort negative and positive specialization and hence be particularly unsuitable for calculating variance. The indicator is made symmetrical logarithmically and bound by the tangent hyperbolicus to the index value 100.

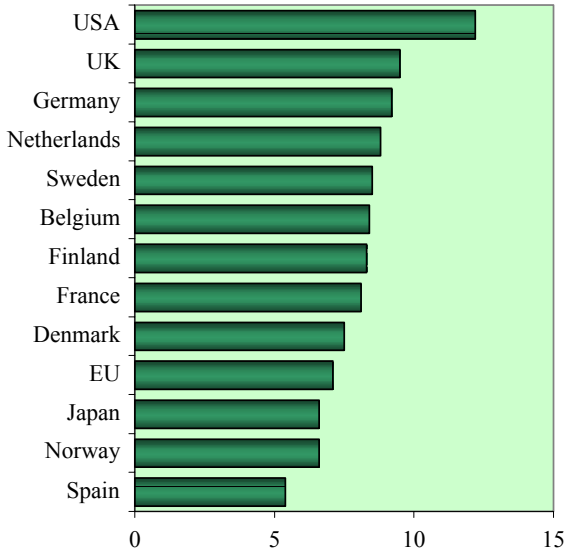
Fig. 3-15: Contribution of different author types to biopharmaceutical publications, average from 1994 to 1999.



Source: SCI via STN, Searches and calculations by Fraunhofer ISI,

Most of the Norwegian biotechnology publications were a result of basic and applied research. Figure 3-15 shows that over 80 per cent of the contributions to biopharmaceutical publications come from either universities or hospitals. Pharmaceutical firms and dedicated biotech firms contribute only a very small percentage of total publications. In Norway

Figure 3-16: Citations per publication in biotechnology, 1996-2000.



Source: EC, The Biotechnology Innovation Scoreboard, 2002

publications by these firms averaged less than 3 per cent of the total and there was only a negligible increase in the share of publications by dedicated biotech firms over the period. This suggests that public funding and public organisations play will continue to play an important role in the development of biotechnology.

The number of citations per publications captures the quality of biotechnology research. Although there is not suitable data on biopharmaceuticals, the *European Trend Chart on Innovation in Biotechnology* provides data on the mean number of citations per publication in biotechnology. An average is used because the number of citations received by publications increases over time. As figure 3-16 shows, Norway is below the EU average, but the average number of citations does not vary much across countries. This may reflect the degree of cooperation across national boarders as well as the research climate and education system.

3.3.2 Science and education in Norway

Most of the scientists and researchers in the biopharmaceuticals are educated the life sciences and in various health programs. Both programs already have a high degree of internationalization because they use a common language to communicate with each other. Participation or enrolment in these programs provides some idea as to the scope of the education system in these areas. Table 3-9 shows the participation in educational program as a share of total higher education in selected European countries. The data in the table are defined according to the International Standard Classification of Education (ISCED). ISCED97 was designed by UNESCO to serve as an instrument suitable for assembling, compiling and presenting comparable indicators and statistics of education both within individual countries and internationally. Educational programs are cross-classified by levels and fields of education, each variable being independent. The table shows that in Norway enrolment in higher education programs (ISCED 5 and 6) is below the European average in the life sciences (42), which include biology, bacteriology, microbiology, genetics, and biochemistry, whereas it is above average in health (72), which includes medical and medical services. If we include only those students enrolled in programs that lead to the award of an

Table 3-9: Participation in educational programme as a share of total higher education, Average of 1999/2000 and 2000/2001

	Life Sciences		Health	
	Tertiary	Advanced	Tertiary	Advanced
European average	2.5	7.9	9.3	14.6
Norway	1.0	5.1	13.5	18.9
Denmark	2.3	…	11.5	…
Iceland	3.2	8.8	13.3	42.6
Finland	1.5	4.7	11.0	10.7
Sweden	2.1	6.7	12.9	25.8
Germany	2.3	…	12.0	…
Netherlands	1.1	…	9.8	…
United Kingdom	4.8	13.1	15.3	12.4

Source: Eurostat, NewCronos database, August 2003.

Table 3-10: Public expenditure on education at the at the tertiary level (ISCED 5-6), 2000

	Public expenditure on education as % of GDP	Expenditure per pupil/student in EUR PPS in public institutions	Expenditure per pupil/student in public institutions compared to GDP per capita	Financial aid to pupils and students as % of public expenditure on education
Norway	1.7	12,239	37	28.6
Denmark	2.5	11,922	45	38.9
Finland	2.0	7,879	34	16.9
Netherlands	1.3	10,981	44	27.0
Sweden	2.0	13,651	57	29.5
EU-15	1.1	8,334	37	15.3

Source: Eurostat, NewCronos database, August 2003.

advanced research qualification (ISCED 6 only) these differences remain. The main reason for this tendency is the priority given by the government to social and health programs.

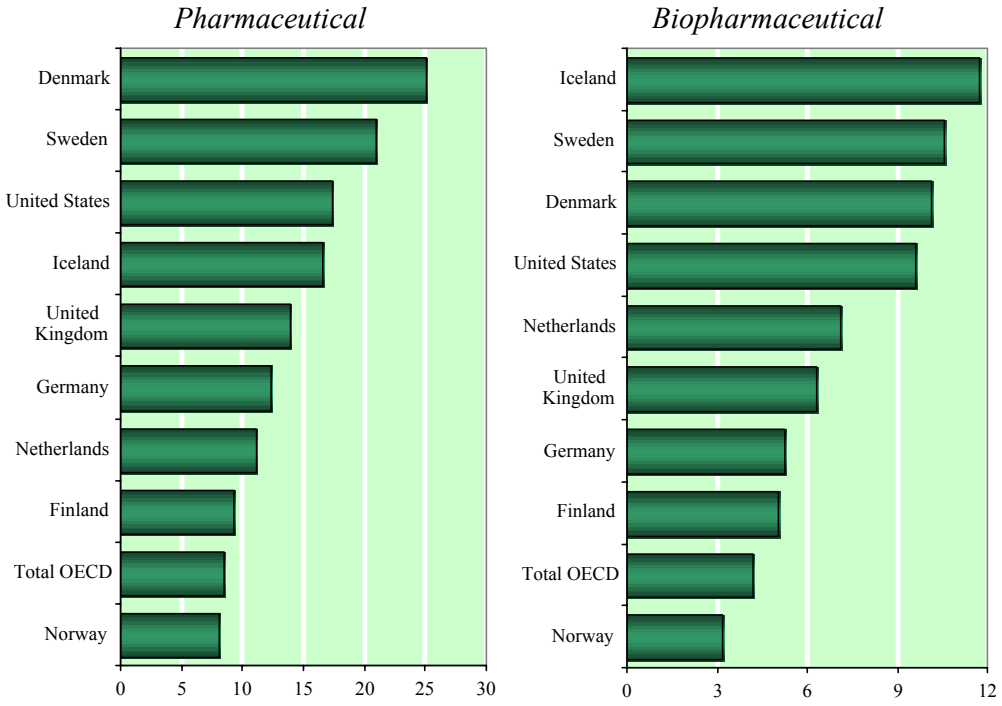
It is not possible to measure the resources invested in these programmes and their outcomes given the available statistics. But it is possible to capture the public and private investment in higher education and the educational attainment level of the workforce. Investment in human capital can be measured as the resources that each country puts into education and, in particular, its spending per student at each educational level. Table 3-10 shows the expenditure per student at the tertiary level in Scandinavia and in the EU as a whole. Norway appears very variable in this measure being almost 50 per cent higher than the EU average. In terms of per capita income, Norway appears average. But terms of financial aid per student it again appears considerably above average.

3.3.3 Patenting activity

Measuring the performance of the biopharmaceutical innovation system requires indicators that capture the outputs of the R&D system. At the industry level these may include patent statistics, bibliometrics and innovation statistics. Patents measure the output of R&D activity and as such measure the competitiveness of technological accumulation. They are suitable for measuring biotechnology because they are a property right granted for inventions in a particular field, rather than an industry. Data are available from the European Patent Organisation (EPO) and the United States Patent and Trademark Office (USPTO). Norway is a not a member of either organization, so the choice of which data are used would depend on the analysis being carried out. Data from the USPTO refer to patents granted, whereas data from the EPO refer to patent applications. Moreover an EPO patent costs six times greater than a USPTO patent and can almost twice as long as the US average of three years to be processed.

Norway performs about the EU average in terms of USPTO patents granted and below average in terms of the EPO patent applications. The Biotechnology Innovation Scoreboard 2003 identifies the number of patents applications to the EPO for the use of biotechnology as a major relative weakness. Figure 3-17 shows this weakness in both pharmaceuticals and biopharmaceuticals in terms of the average number of patents over the period 1994 to 2000.

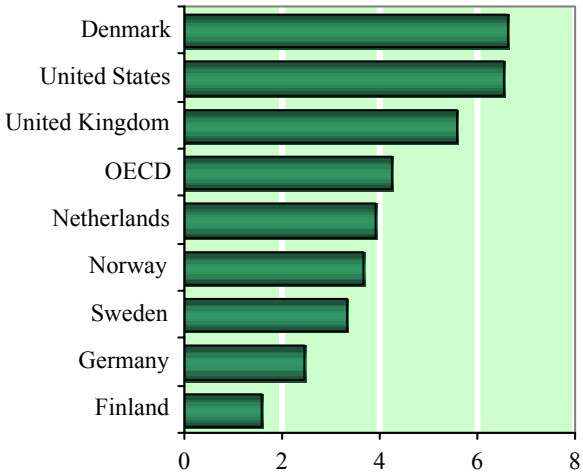
Fig. 3-17: Average number of patents granted by the EPO by inventor per million population, 1994-2000



Source: Own calculation based on OECD patent database

Figure 3-18 show biopharmaceutical patents as a percentage of total national patents filed at the EPO in 1999 and 2000. This table shows that Norway is below the OECD average but above Germany and Sweden. If we consider the average number of patent applications by inventor per million population as shown in the figure, then Norway appears even more

Figure 3-18: Biopharmaceutical patents as a percentage of total national patents filed at the EPO, for priority years 1999-2000.



Source: OECD Patent Database

behind the OECD average. A similar trend appears in the pharmaceutical industry, but Norway does not appear to be much closer to the OECD average. Nevertheless, in both cases Norway appears to be considerably behind the other countries in Scandinavia.

Table 3-11 shows the number of patents in biotechnology taken out by Norwegian inventors from 1994 to 2002.[14] The inventor's country of residence is the most relevant for measuring the technological innovativeness of researchers and laboratories located in a given country. Since there can be more than one inventor on the application, a percentage is assigned to each of the home countries. Patents are shown according to their priority date, that is the year of first filing worldwide and therefore closest to the invention, application and year granted. Between 1994 and 2000, Norwegian inventors made up 0.3 per cent of the applications for biotechnology to the EPO and 0.2 per cent of the patents granted for biotechnology by the USPTO.

The small share of patents in the total number of biotechnology patents in the OECD does not suggest that biotechnology is unimportant in Norway. To adjust for the *relative* patenting activity in Norway, and to evaluate the relative strength or weakness of Norway, the revealed technological advantage (RTA) was computed for different countries. The RTA describes the specialization of a country in biotechnology and is calculated by taking each country's share of all patenting activity in biotechnology relative to its total patenting activity over the OECD share of biotechnology patenting activity over its total patenting activity (Patell and Pavitt 1987 and Soete, 1987).[15] The RTA index varies around unity, such that values greater than one indicate that the country is relatively strong in biotechnology as compared to other, while values less than one indicate a relative weakness.

Table 3-11: Number of patents in biotechnology by inventor in Norway, 1994-2002.

	1994	1995	1996	1997	1998	1999	2000	2001	2002	1994 to 2000
EPO										
Priority date	7.7	10.3	6.6	10.9	10.9	20.1	8.1	.	.	74.6
Application date	7.5	7.7	10.3	6.6	10.9	11.2	19.8	8.1	.	74.0
Date of grant	5.5	5.7	3.0	3.0	1.5	2.2	2.0	1.3	4.0	22.9
USPTO										
Priority date	6.7	5.3	5.2	4.0	.	.	.	.	.	.
Application date	6.9	12.3	8.1	6.3	3.2	6.5	2.5	.	.	45.8
Date of grant	3.0	3.6	7.5	5.5	7.8	7.5	11.6	8.0	3.1	46.4

Source: OECD patent database, May 2003

[14] Biotechnology patents include patents from the following International Patent Classification technology classes: C12M (Apparatus for enzymology or microbiology); C12N (Micro-organisms or enzymes; propagating, preserving, of maintaining micro-organisms; mutation or genetic engineering; culture media); C12P (Fermentation or enzyme-using processes to synthesize a desired chemical compound or composition or to separate optical isomers from a racemic mixture); C12Q (Measuring or testing processes involving enzymes or micro-organisms; compositions or test papers therefore; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes); C12S (Processes using enzymes or micro-organisms to liberate, separate or purify a pre-existing compound or composition; processes using enzymes or micro-organisms to treat textiles or to clean solid surfaces of materials).

[15] The index is defined as $(P_{ij}/\sum_j P_{ij})/(\sum_i P_{ij}/\sum_{ij} P_{ij})$, where P denotes the number of patents in country i and technology j.

Table 3-12: Revealed technical advantages for Norway and selected countries in biotechnology, 1986 to 2001.

	EPO patent applications		USPTO patent grants	
	1986 to 1993	1994 to 2001	1986 to 1993	1994 to 2001
Norway	0.84	0.95	1.35	1.36
Denmark	2.71	2.43	3.03	5.38
Finland	0.98	0.54	1.36	1.13
Sweden	0.78	0.56	0.97	0.80
Finland	0.98	0.54	1.36	1.13
Netherlands	0.85	1.03	1.08	1.68
Germany	0.16	0.50	0.62	0.62
United Kingdom	1.08	1.34	1.09	1.50
United States	1.73	1.73	1.21	1.22
Japan	0.75	0.57	0.69	0.38

Source: Own calculations based on OECD patent database

Table 3-12 provides a RTA for both patent applications to the EPO and patents granted by the USPTO. Norway appears just below average in the OECD, but is surprisingly above Germany Finland and Sweden in the patent applications to the EPO. As expected, the US has a stronger specialization in biotechnology with a RTA of 1.73 in both periods, but both Denmark and the United Kingdom were strong in the technology. There is also a noticeable improvement from the eight years prior to 1994 to the period from 1994 to 2001. Norway appears even stronger when viewed in terms of the patents granted at the USPTO. Here Norway appears above the OECD average and has a RTA higher than the United States. The relatively high cost of patenting at the EPO might explain why Norway has a relatively lower RTA when viewed in terms of EPO applications.

The RTA index is also calculated for pharmaceuticals and biopharmaceuticals in Table 3-13. This table shows that the RTA for patent applications to the EPO in biopharmaceutical is below the pharmaceutical industry as a whole in the mid 1990s, but above some countries such as Germany and Finland. But there is some improvement from the mid 1990s to the end of the 1990s, when Norway appears above Sweden, Finland and Germany. This improvement parallels the entry of several new dedicated biotechnology firms in the last half of the 1990s, which indicates that at least some of these firms are at the technological frontier.

Table 3-13: Revealed technical advantages for Norway and selected countries in pharmaceuticals and biopharmaceuticals, 1994/95 and 1999/00.

	Pharmaceuticals		Biopharmaceuticals	
	1994/95	1999/00	1994/95	1999/00
Norway	0.81	0.73	0.67	0.81
Denmark	1.55	1.63	1.19	1.46
Finland	0.46	0.34	0.60	0.35
Sweden	0.73	0.82	0.90	0.74
Germany	0.58	0.61	0.46	0.54
Netherlands	0.57	0.71	0.83	0.87
United Kingdom	1.26	1.45	1.12	1.23
United States	1.48	1.38	1.69	1.44
Japan	0.78	0.72	0.58	0.61

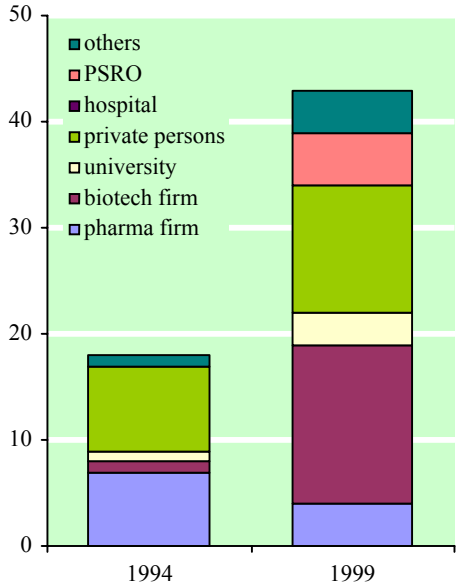
Source: Own calculations based on OECD patent database.

This is important because competition in this industry is generally based around R&D races to patent new drugs. In this context the relatively low number of patents per million suggests that Norwegian entrepreneurs do not patent as often as they should, and this may be due to a lack of finance or information on how to patent.

Figure 3-19 provides a breakdown of the patenting activity by actor type. This shows that the individuals appear as the most important actor, but in reality they are associated with either the university or public research institute. The individual who is a member of a research institute often takes out a patent. At the moment there is a lively debate over who can claim the property rights of an invention when an individual is a member of an institute. The most interesting pattern that appears in the figure is that the dedicated biotech firm has become an important actor in terms of patenting activity. This parallels the entry of several firms in the mid to late 1990s.

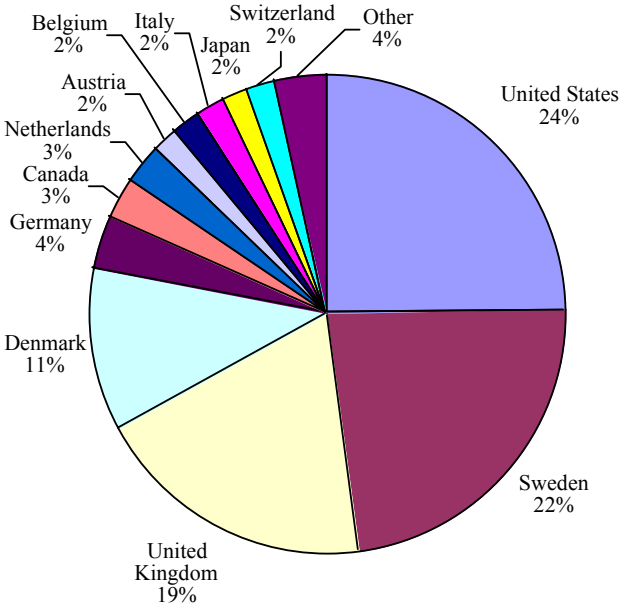
Patent data also provides important information about global R&D and strategic partnerships. Since patent applications may include multiple inventors from different countries, it is possible to measure the degree of partnerships in the EPO data. Figure 3-20 illustrates the distribution of co-inventions across countries. Of the 109 co-inventors, more than three-quarters of them reside either in the United States, Sweden, United Kingdom or Denmark. This shows a very strong relationship with the technological leaders in the pharmaceutical industry. If we narrow the patent applications to those inventors using biotechnology in pharmaceutical products, Sweden appears as the most important partner in 39 patents. As figure 3-21 shows, inventors are just as likely to have a partner in Sweden as in the United States and United Kingdom combined.

Fig. 3-19: Average number of patents by inventor granted by the EPO in Pharmaceuticals per million population, 1994-2000



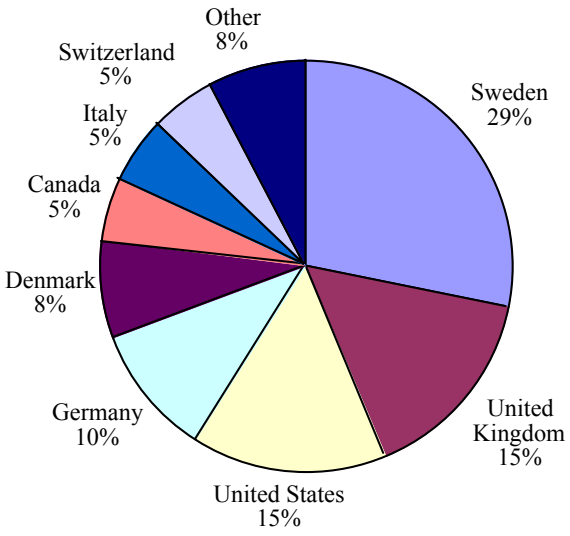
Source: SCI via STN, Searches and calculations by Fraunhofer ISI,

Figure 3-20: Co-inventions with Norwegians in the pharmaceutical industry, 1994-2000



Source: OECD patent database, June 2003

Figure 3-21: Co-inventions with Norwegians in the biopharmaceutical industry, 1994-2000



Source: OECD patent database, June 2003

3.3.4 Innovation activity in biotechnology and pharmaceuticals.

The share of firms that have introduced at least one new or improved product or process in the market over a given period of time is an indicator of the output of innovative activities and competitiveness. Three such surveys have been carried out in Norway, with the most recent one carried out for the period 1999 to 2001. In the most recent survey Norwegian enterprises were not very innovative as a whole, with only 29 per cent of them introducing new or significantly improved products or processes between 1999 and 2001, and only 12 percent of them introduced a product new to the market (Statistics Norway). When all such innovative activities are taken into consideration, Norway had an innovation rate of 36 per cent, which was very low when compared with other European economies according to Eurostat. Only Spain and Greece were less innovative, and the rate of innovativeness was noticeably below that Scandinavian, which ranged from 44 per cent in Denmark to 47 per cent in Sweden and 55 per cent in Iceland. Nevertheless, the pharmaceutical industry is generally viewed as a high-tech industry, so it is expected to have a much higher rate of innovativeness.

Measuring innovation in the biopharmaceutical sub-sector presents certain problems because the technology is the defining characteristic of this industry. As table 3-14 reveals, 80 per cent of pharmaceuticals introducing either a product or process innovation from 1999 to 2001.The questionnaire that was sent out in 2002 to all firms with at least 10 employees asked what percentage of their R&D expenditures was using biotechnology. Five firms directly connected to the pharmaceutical industry reported using biotechnology in at least 60 per cent of their R&D activity and 33 firms had reported using biotechnology in at least 5 per cent of their R&D activities. Almost all of the firms using less than 50 per cent biotechnologies were in industries not related to the pharmaceutical industry. Nevertheless, the table reveals that the biopharmaceutical industry, as well as the biotechnology industry was highly innovative, actively introducing new products to the market implementing process innovation.

The enterprises' cost of the innovation activity amounted to € 2.8 billion (NOK 23 billion) in 2001, equal to 1.5 per cent of the total turnover. More than half of the innovation expenditure is for R&D activities, but the survey also indicates that more than 40 per cent of the innovating enterprises developed new products or processes without the use of R&D. Other types of costs include design, training, market introduction and acquisition of external knowledge. The pharmaceutical industry made up 2.4 per cent of the total innovation

Table 3-14: Innovative activity in pharmaceuticals and biotechnology, 1999 to 2001

	Pharmaceuticals	Pharmaceuticals with biotech	All firms using biotechnology
Firms in Sample	15	…	…
Firms with innovation	12	5	33
Percentage share:			
Product innovations	80	100	100
Product new for the market	33	80	55
Process innovations	51	80	85

Source: CIS3, Statistics Norway

Table 3-15: Innovative expenditure in innovative firms, 2001

	Pharmaceuticals	Pharmaceuticals with biotech	All firms using biotechnology
Turnover in million NOK	5,173	423	65,000
Percentage of turnover used for innovative activities	10.8	33.0	1.6
Percentage of turnover from new products	…	13.7	10.7

Source: CIS3, Statistics Norway

expenditure in the Norwegian economy. Table 3-15 shows that the amount of turnover and the percentage of turnover used for innovative activities were very high (33 per cent of turnover) among the firms using biotechnology in the pharmaceutical industry, but very low for those firms using biotechnology. This is partly reflects the much lower percentage share of R&D activity using biotechnology in other industries such as food and beverages. Nevertheless the percentage of turnover derived from the sale of new products in the pharmaceutical firms using biotechnology is not significantly different from the entire group of firms using biotechnology.

Since the *2002 R&D and Innovation Survey* would not have covered most of the dedicated biotechnology firms, similar questions were asked on the *2003 Biotechnology Use Survey*. As table 3-16 reveals, only about 58 of these firms had biotechnology products or processes on the market from 1999 to 2001. The same percentage was developing new products and about two-thirds said they were developing new processes. Very little improvement took place during the period following the *2002 R&D and Innovation Survey*, but 90 per cent of the firms covered by the *2003 Biotechnology Use Survey* claimed that biotechnology was central to the firm's activities in the future.

The *2002 R&D and Innovation Survey* also asked what the effects of innovation where during 1999 to 2001. Table 3-17 reveals that the pharmaceutical firms using biotechnology found improved product quality to be the most important effect, whereas the entire group of firms using biotechnology emphasized the expanded range of products. Labour costs and regulatory measures were the least important effects, which indicate that product quality is driving competitive behaviour in the Norwegian biopharmaceutical industry.

Table 3-16: Innovative activity in dedicated biotech firms

	1999-2001	2002-2003	Plans
Already have biotechnology products/processes on the market.	58	60	67
Developing new products that require the use of biotechnologies.	58	55	78
Developing new processes that require the use of biotechnologies.	67	73	78
Is biotechnology central to your firm's activities or strategies?	83	82	90

Source: Own calculation based on the Biotechnology use Survey carried out in spring 2003.

Table 3-17: Effects of innovation in biotechnology during 1999-2001. (Per cent of innovating firms)

	Pharmaceuticals with biotech	All firms using biotechnology
Increased range of products	40	52
Increased market or market share	40	36
Improved quality of products	60	48
Improved production flexibility	20	24
Increased production capacity	40	39
Reduced labour costs per produced unit	20	21
Met regulations or standards	20	24

Source: CIS3, Statistics Norway

Chapter 4: Innovation barriers /drivers – Framework conditions

Innovative activities of firms and research organisations are to a large extent determined or influenced by so-called framework conditions. These include regulations, the general entrepreneurial climate, the availability and quality of specialised knowledge. They can give rise to important barriers to innovation or create driving forces that stimulate the innovation process. In this chapter, we will discuss those framework conditions that are of particular relevance to newly emerging biopharmaceutical industry: the sources of knowledge, the availability of human resources, access to financial means, the presence of an entrepreneurship and the regulatory framework. Our main finding is that the migration of researchers after the merger between foreign based (Amersham) and domestic based (Nycomed) pharmaceutical firms was the most important driving force in the start-up and subsequent growth of small, dedicated biotechnology firms in Norway. At the same time the lack of available skilled labour and finance appear as important barriers to the development of the biopharmaceutical industry.

4.1 Knowledge sources

Innovation originates from knowledge sources both within and outside the firm. The main sources within the firm include R&D activities, as well as other sources used together with these activities, such as management, marketing, etc. Laboratories provide the main source of fundamental research, but R&D activity within the firm can play an important role in creating capability to absorb technology from external sources. In biotechnology universities play a central role in performing fundamental research and firms focus on adapting, and improving existing ideas. Cohen and Leventhal (1990) pointed to the importance of these two sides of R&D activity. As Table 4-1 shows, R&D activity within the firm is by far the most important knowledge source within the firm, with all of the biopharmaceutical firms giving it high importance. About 73 per cent of all Norwegian firms using biotechnology gave it high importance. Of the total R&D expenditures by biopharmaceutical firms in Norway, more than 80 per cent of the activities were performed within the firm.

External networks are also essential to the innovation process by complementing internal R&D activities. Many external sources of knowledge are available to the innovative firm, such as government R&D institutes, university research labs, private research labs and consultants. Other external sources include suppliers, customers, competitors, professional conferences and exhibitions. Table 4-1 shows that the six most important external sources of information in the biopharmaceutical industry were: professional meetings (60%), universities (40%), customers (40%), customers (20%), suppliers (20%) and other enterprises within the enterprise group (20%). A similar pattern was observed in all firms using biotechnology, but that the universities and other institutions of higher education where given much less importance.

Table 4-1: Sources of information and co-operative projects, 1999-2001. (percentage given to high importance)

	Source of information		Co-operative projects	
	Pharmaceuticals with biotech	All firms using biotechnology	Pharmaceuticals with biotech	All firms using biotechnology
Innovating firms	5	33	5	25
Within the enterprise	100	73	..	..
Other enterprises within the enterprise group	20	21	60	60
Suppliers of equipment	20	15	60	44
Customers	40	39	60	68
Competitors	0	12	20	64
Consultants	20	9	0	8
Commercial laboratories or R&D labs	0	6	40	56
Higher education	40	12	80	64
Government or private non-profit research institutes	0	12	60	68
Professional conferences, meeting, journals	60	30	..	..
Fairs, exhibitions	0	12	..	..

Source: CIS3, Statistics Norway

The table also confirms that the biopharmaceutical is most interested in joining co-operative projects with universities and other institutions of higher education (80%), but they also give considerable importance to other enterprises doing similar research (60%), upstream suppliers (60%), downstream customers (60%), and other private or government research institutes (40%). Consultants and professional conferences appear not to be important within co-operative projects. With whom they have co-operative arrangements is also important. All five of the pharmaceutical firms using biotech in table five have co-operative projects within Norway and the European Union. Three have projects with a partner in the United States, two with other Nordic partners and one with a partner in Japan.

4.2 Human resources

Biotechnology is one the most knowledge intensive activities within industry. This requires an educated labour force with the kinds of skills that can contribution to the creation of new knowledge in the life sciences. In the previous chapter, it was shown that enrolment in the life sciences, namely biology, bacteriology, microbiology, genetics, and biochemistry, was well below the European average, enrolment in the health sciences were well above the average (see table 3-9). This difference reflects the strong emphasis placed on health care in Norway.

Table 4-2: Obstacles to Commercialisation of biotechnology faced by dedicated biotech firms in Norway, 1999 and 2003

	2003	1999	Percent change
Inputs			
Access to capital	3.79	3.00	-21
Access to information	2.43	2.25	-7
Human resources	3.36	3.00	-11
Markets			
Domestic market too small	2.71	2.55	-6
Access to international Markets	2.00	2.10	5
Distribution channels	2.54	2.50	-2
Constraints			
Perceptions	2.13	2.33	9
Regulations	2.80	2.92	4
Time/cost	3.20	3.00	-6
Patent rights	2.53	2.25	-11
Lack of Patent protection	1.80	1.58	-12
Source of finance	3.47	3.00	-13
Economic Risk	3.73	3.25	-13

Note: The number represents an average between one and 5 with one being unimportant and 5 being most important.

Source: Own calculation based on the 2003 Biotechnology Use Survey

The availability of and access to qualified human resources appears to be bottleneck in the biopharmaceutical industry in Norway. In 2000, this percentage was one of the lowest in Europe and will likely become a significant obstacle if the industry should expand. Even now the respondents to our Biotechnology Use and Development Survey indicated that According to our *2003 Biotechnology Use Survey*, the dedicated biotechnology firms considered human resources as one of the most important obstacles between 1999 and 2001, and it became worse in recent years (see table 4-2). The small, dedicated biotechnology firms are having more difficulty recruiting than the larger diversified and pharmaceutical firms.

By contrast, in 1996 the merger between Nycomed by Amersham created a surplus of well education scientists, which also because a driving force in the formation of the dedicated biotech firms in the late 1990s. These scientists chose to remain in Norway rather than pursuing R&D careers abroad, were behind several new start-ups since 1997. the migration of scientists from one research lab to another became one of the most important sources of knowledge acquisition in Norwegian biopharmaceutical industry. PhotoCure and Clavis Pharma are two examples of new firms that were established by scientists who left Nycomed. Several other researchers left for already established firms such as Axis-Shield, Dynal, Medinnova, and the technology transfer office at the National Hospital (Rikshospitalet).

The institutional arrangements of the educational system and the level of effectiveness of education policies can also constrain the availability of skilled labour in the life sciences. Education is an investment in human skills and competences that, over time, become part of the human capital stock, or social capabilities, of a country. The FUGE programme may speed of the restructuring of life science studies by providing funding to the universities for new research programmes This would require the universities to encourage greater

participation in the life sciences and to create new and relevant programmes that attract more students to the area. A short-term solution would be to attract qualified researchers from abroad, but the skills shortage is also a problem in many of the leading countries doing biotechnology research.

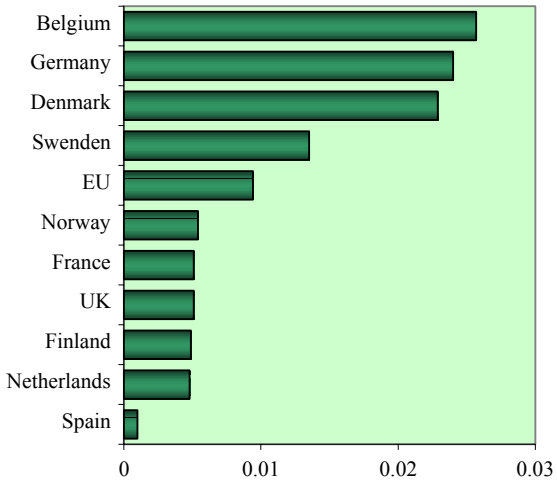
4. 3 Private finance and venture capital

The long-run viability of biotechnology depends on the availability of venture capital. Figure 4-1 shows that Norway raises about half of the amount of venture capital than the EU average, and it is well below the other Scandinavian countries. The 2002 European Innovation Scoreboard considered the inability to raise venture capital to one of two most important weaknesses in the Norwegian Biotechnology innovation system. In this case of the US this was essential for the commercialisation of biotechnology. Most of the dedicated biotech firms in are still have a long way to go before becoming commercially successful.

Private Venture Capital firms in Norway were in 2001 responsible for investing €40.3 million (331 million NOK) in life sciences, thereof approximately one fourth (€10 million , i.e. 82 million NOK in biotechnology (data from European Venture Capital Association, EVCA). In Europe these investments totalled 2.5 billion euro in life sciences and 840 million euro in biotechnology (EVCA 2001). According to the European commission, Norway was below average in terms of biotechnology venture capital as a percentage of GDP. As figure 4.1 shows, 0.0054 per cent of GDP was invested in biotechnology in 2001, slightly above half of the EU average. Belgium, Germany, Denmark and Sweden were well above this average.

In the 1980s and 90s the life science companies in Norway have been financed through spin offs from established companies which had their main activities in other sectors. Financing from private persons was another important source. Lately, several Venture Capital financing companies have started to focus on early stage biotechnology firms and the financing reached its top in the years 1999-2000 Hindar (2003). Similar trends can be seen in Europe and USA where the investments has increased from 2 billion euro in 1995 to 10 billion euro in 2000. In the interviews respondents were concerned about biotechnology start-ups being able to obtain public grants in the early phase of their innovation activities, but in most cases, research in seed phase must be financed from private sources. In the last 2 years rising of venture capital has been difficult and poses an extra uncertainty in the development of the firm. One of the consequences of the uncertain financial situation between the early phase and seeding phase of innovation is loss of human resources. Skilled researchers with highly specific competence leave the start-ups and search jobs other places. This means that the competence of Norwegian researchers increases while the growth of biotech companies stops due to lack of seed money.

Figure 4-1:Biotechnology venture capital as percentage of GDP, 2001



Source: EC, The Biotechnology Innovation Scoreboard, 2002

4.4. Regulations for biotechnology

The regulation of biotechnology in Norway places the country among the most restrictive countries in Europe. The legislation is characterised by special legal standards in combination with casuistic preconditions that are basically identical with EU regulation.

There are two laws regulating biotechnology in Norway, the *Biotechnology Act* and the *Act on Gene Technology*. The Biotechnology Act came to force 1 September 1994, and included a revision that took effect on 21 December 2000. It covers in vitro fertilisation, storage of fertilised eggs, cloning of humans, pre-implantation diagnosis, foetal diagnosis, genetic testing of born individuals, use of genetic information, gene therapy and approval of institutions responsible for these tests. The responsible Ministry is the Ministry of Social Affairs and Health and it has been reviewed in 1999 and in 2001.

The law is supplied by directives from The Norwegian Board of Health, covering the following 6 areas: (1) Definition of genetic testing; (2) Gene tests in disease diagnostic; (3) Institutions to be approved; (4) Approval of tests and methods; (5) Test for Følling syndrom; and (6) Ultrasound diagnostic. The Norwegian Board of Health (Norwegian: Statens helsetilsyn) is part of the central health administration, and its main responsibility is the overall supervision of health services in Norway. The Board of Health is an independent technical agency, and is administratively part of the Norwegian Ministry of Health. The Board of Health provides the Ministry with technical advice and information.

The Ministry of Health of the government in power, consisting of a coalition between Christian Party (KrF), Conservative Party (H) and a Liberal Party (V) has prepared a White Paper for a new biotechnology law which will replace the Biotechnology Law of 1994, based on values compatible with their value-conservative ideology. The White Paper is now finished and the draft law is to be passed by the Parliament.

The Act on Gene Technology came to force on 1 September 1993, and was revised on 15 June 2001. The law regulates manufacturing and use of genetically modified organisms (GMOs), including micro- organisms, plants and animals used in research and industry production. The law also regulates their deliberate release and marketing of GMOs. The Norwegian law is in accordance with EU directives on contained use and on deliberate release of GMOs.[16] The Act is thus highly relevant as a potential barrier for marine sciences, but does not have such a great impact on the types of research currently being undertaken by diversified and dedicated biopharmaceutical firms and research institutes in Norway.

4.5 Entrepreneurship.

Rapid growth of dedicated biopharmaceutical firms in Norway is a sign of that entrepreneurship is flourishing in the industry. However, Norway is often characterised as a country without entrepreneurial spirit. Academic scientists generally prefer to remain at the university even when they establish a new biotech firm. Interviews suggest that some remain at the university and let the researchers run the company. Perhaps more importantly, the new dedicated biotech firms often lack knowledge about management and marketing, including advertising and product positioning. These are all important internal sources of knowledge that are often overlooked by new scientific based firms. In the pharmaceutical industry, the costs of marketing, or sunk costs as economists often describe it, generally equal the cost of R&D activity in that industry. These sunk costs can be very substantial and can create significant barriers to entry. At the end of 2002, Norwegian firms with products in the pipeline spent well over 60 per cent of their income on R&D activity, which indicates that they have too few products on the market, or that they are not spending enough money on marketing their products.

The Norwegian government recognizes the lack of entrepreneurship as an important barrier to innovation. While there are relatively few instruments aiming at fostering an entrepreneurship culture in Norway, entrepreneurship policy is now an integrated part of the new holistic innovation policy. On the positive side, the Research Council of Norway and the Confederation of Norwegian Business and Industry offer prizes for good entrepreneurship. And in November 2000, the university in Trondheim, established START to help studies across Norway to discuss entrepreneurship and get relevant information.

4.6 Innovation barriers/drivers.

Innovation is a complicated process and enterprises may face several kinds of problems. As table 4-3 shows, a large number of enterprises in the pharmaceutical industry reported that their innovation activity was hampered by serious problems. Economic factors like innovation costs too high, excessive perceived risk and lack of appropriate source of finance are the most decisive ones. Other factors like lack of qualified personnel or lack of technological information were of minor importance. Inflexibility of regulations or standards was also cited as an important obstacle in the pharmaceutical industry.

[16] Other relevant acts are: The Act relating to transplantation, hospital autopsies and the donation of bodies etc; The Act concerning Termination of Pregnancy; The Act on personal health data filing systems and the processing of personal health data; The Act relating to the processing of personal data; The Patents Act.

Table 4-3: Factors Hampering Innovative Activity in firms with innovation, 1999 to 2001 (percentage distribution)

	All	Pharma-ceutical	Bio Pharma-centical	All biotech firms
Economic Factors				
Excessive perceived economic risks	15	46	60	39
Innovation costs too high	17	46	60	33
Lack of appropriate sources of finance	15	30	20	24
Internal Factors				
Organisational rigidities within the firm	5	-	-	6
Problems to keep or recruit qualified personnel	5	-	20	3
Lack of information on technology	3	8	20	3
Lack of information on markets	4	-	-	3
Other Factors				
Insufficient flexibility of regulations or standards	4	21	20	6
Lack of customer responsiveness to new products	4	8	-	3

Note: CIS-3 covered 8,494 enterprises, of which 3,418 introduced some kind of innovation. Of these innovative firms, 12 were in pharmaceuticals.
Source: CIS3, Statistics Norway

The *2003 Biotechnology Use Survey* shows that there are considerable barriers faced by the dedicated biotech firms (see table 4-1). Access to capital appears as the most important obstacle, followed by human resources and risk. Perhaps the most important trend is that the economic obstacles appear to get worse from 1999 to 2003, whereas the public perception of biotechnology had improved over this period. This suggests that the state of the economy has an important impact on biotechnology and that the pubic is gradually getting more accustomed to the new products that might become available in the future.

Chapter 5. Demand Side Factors

Demand side factors influence the innovative capacity of firms and research organisations as well as the speed and directive of new developments in biotechnology. The market for pharmaceuticals is to a great extent shaped by the national health care system and the regulation of market. Moreover, socio-economic and ethical issues have been very controversial and have an important influence on the development of products and processes using biotechnology. In this chapter we discuss the main demand factors that influence the innovation processes in the biopharmaceutical innovation system.

5. 1 Organisation of national health care system

Historical overview

The organisation of the health care system in Norway has during the last three decades undergone three rather distinct waves of reforms, with the first consisting of the delegation of a comprehensive set of responsibilities to the municipal level and starting in the mid-1980s, the second consisting of adjustments in the early 1990s, and the third starting with the nationalisation of large hospitals etc. in the current early 2000s.

In 1984 a new Parliamentary Act on Local Authority Health Care (in reality a Primary Health Care Act) came into force. In the preceding periods of the 1960s and 1970s, the central government, the county and the local health authority each owned part of the health centre. The health workers were sometimes employed by central government, sometimes by the county, and sometimes by local authorities. In this new reform, however, many new tasks were assigned to local authorities.

Concurrently with the adoption of the new legislation, new regulations for decentralised funding of health services were introduced. Primary health care services would be the basic element of the national health services. All citizens had the right to satisfactory health care, accessible within their local community. The Act thus left a wide mandate for local health care services to take part in shaping the local social structure.

The intention behind this was to let the users and providers of primary health care to an ever-greater degree create their own services at local level. Expansion of the hospital sector had been an important reason for the large increases in health expenditures of the country. At the same time public health research demonstrated that the real health gains had come about as a result of simple measures, such as vaccinations, nutrition information and general improvement of living standards. A further expansion of these basic primary health care services might have the double benefit of improving public health and controlling resource utilisation in the health sector.[17]

[17] Cf. WHO (2000) for details on these developments.

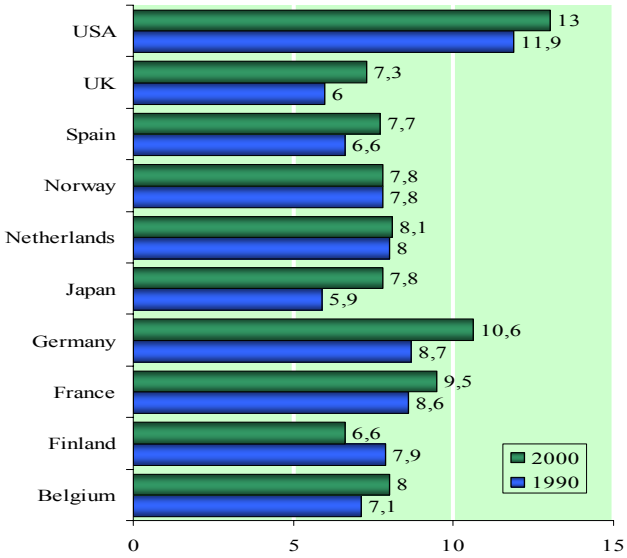
The six political priorities of the 1990s were: (1) psychiatric disorders; (2) psychosocial problems; (3) musculo-skeletal disorders; (4) accident prevention; (5) allergies; and (6) domestic violence, including sexual aggression against women and children. These latter problems had previously been uncovered and exposed through the work of voluntary organisations, and through research often undertaken on a voluntary basis. The responsibility of local health care authorities was further increased in 1991, when care of the disabled was added to their charge. Care of the mentally disabled is particularly resource demanding, and requires modes of work that are new to the health sector.[18]

Since 2000 Norway has been undergoing another major health reform consisting first of designating a local general practice doctor to each citizen ("Fastelege-ordningen"), and then in 2002 a reform consisting in shifting the ownership and responsibility of the general hospitals from the prefectural to the national level.

Current reimbursement system

Norway has traditionally endorsed a principle of equal rights to satisfactory health services, to be funded by the National Insurance Fund. A complex system financing health services and social services has evolved over time. Public health expenditures constitute about 12 per cent of total public expenditure, against 1.5 per cent for private health care expenditures. Health expenditures as a percentage of Gross Domestic Product has increased from 7.4 per cent in 1988 to about 8.2 per cent in 1994. The largest part of these expenditures is the cost of salaries. Only 2 per cent of private consumption expenditure is on health care. Of this expenditure again 40 per cent is on dental services. However, the total amount of health expenditures is, when comparing to e.g. Germany and France, not particularly large (cf. Fig. 5-1).

Fig. 5-1: Total spending on health care as a percentage of GDP at market prices.



Source: Compiled from OECD Health Data 2002.

[18] Cf. WHO (2000) for further details on these developments.

Table 5-1: Expenditures on health and pharmaceuticals 1995 and 2000, million US $, PPP

	Total health expenditures		Total expenditures on pharmaceuticals		Share of pharmaceuticals, percent	
	1995	2000	1995	2000	1995	2000
Germany	184,843	225,862	23,188	30,825	12.4	13.6
Japan	204,822	234,638	43,941	38,375	21.5	16.4
United States	973,170	1,274,113	86,342	152,997	8.9	12.0
United Kingdom	77,055	87,403	11,755	13,932	15.3	15.9
Spain	46,410	61,422	8,232	…	17.7	…
Netherlands	27,630	35,766	3,034	4,205	11.0	11.8
France	114,544	138,342	20,009	27,849	17.5	20.1
Finland	7,227	8,623	1,015	1,340	14.0	15.5
Belgium	19,257	23,255	3,142	…	16.3	…
Norway	**8,131**	**9,661**	**729**	**890**	**9.0**	**9.2**

Note: * I.e. Share of total expenditures on pharmaceuticals from total expenditures on health. ** Figures in 2000-column for Japan are 1999, for Norway and United Kingdom 1997.
Source: Compiled from OECD Health Data 2002

The expenditures on pharmaceutical products has continuously been increasing over the last decades. In addition, the growth of the pharmaceutical expenditures has been stronger than the growth of the total expenditures on health (cf. Table 5-1). The continuing high ratio of pharmaceutical spending has lead to the implementation of cost containment measures. In the case of Norway, prices are set while referring to the average of the 3 lowest prices of 9 countries (Austria, Belgium, Denmark, Finland, Germany, Ireland, Netherlands, Sweden, UK.).

5.2 Regulations

The Norwegian Medicines Agency (NoMA) is the national regulatory authority on assessment and surveillance of new and existing medicines in Norway. The Norwegian Medicines Agency reports to the Ministry of Health. Some of the main tasks for NoMA is the control of manufacturing, testing and marketing of medicinal products.

Even though Norway is not a Member State in the EU, the regulation of the medicinal market is in accordance with the Commission´s Pharmaceutical Legislation. According to the extension of the EEA-agreement, effective 2000-01-01, the EMEA and Norway has published a guidance document which describes the harmonisation of existing marketing authorisations, and the processing of new centralised applications. The current system is based on two separate procedures for the granting of marketing authorisation for a medical product:

1. The centralised procedure leads to a single marketing authorisation valid throughout the whole EU, which is based on a scientific evaluation by EMEA in London. This procedure is manadatory for certain medical products developed by means of biotechnological processes, and is optional for certain other categories, such as those which contain new active substances and those presented for entirely new indication.

2. For those medical products not eligible for the centralised procedure, or where the applicant chooses not to follow the centralised procedure, the system provides for a mutual recognition procedure. This procedure has to be used by the applicant whenever an application for marketing authorisation concerns two or more Member States.

The centralised procedure entered into force in 1995. Since its inception, the number of biotechnology-related products approved by the European Medicines Evaluation Agency (EMEA) each year has steadily increased, whilst the time the approval process takes has reduced. The procedure has proven its effectiveness for biotechnology and innovative medicinal products, although the drug approval body is continuing to look for ways to speed the time in which it approves drugs for launch into market. The main changes proposed include reduction of duration of the procedure, extension of the system of inspections, modification of definition to include new therapies, harmonisation of data protection period etc.

While EMEA tries to streamline the approval procedure, balancing the speeding up and maintaining the high quality standards, much of the time and cost saving activities lies within clinical development.

Pharmaceuticals are divided into three categories. Non-prescription medicines are fully paid for by the individual; prescriptions are either covered by the National Insurance Scheme ("blue prescriptions"), or paid for in full by the patient ("white prescriptions"). There is a co-payment on blue prescriptions that is limited to 36 per cent of the prescription fee. In 1999, there was a ceiling of €161 (NOK 1320) per year on all co-payments, including co-payments for outpatient care or primary care. Patients in hospitals do not pay anything for medication (WHO, 2000).

Some two thirds of the medicine costs are financed through the National Insurance Scheme, including blue prescriptions and medicines to hospitals and nursing homes. The remaining third is roughly evenly distributed between non-prescription drugs, patient co-payment and white prescriptions.

The pharmaceutical industry is strongly regulated by the Government. The Government, through he Norwegian Medicines Agency, determines the prices on all prescription medicines. Prices on non-prescription drugs are, however, regulated by market forces, and so are the pharmacy produced medicines and veterinary medicines (LMI, 2003).

5.3 Role of users

The three user groups described here are, firstly, selected patient groups, secondly, the role of physicians, and thirdly, a Life Sciences-related industry-group.

Patient groups: three examples.

The Norwegian Cancer Society (Kreftforeningen, NCS) is a national voluntary organization with 170.000 members. The secretariat consists of 180 persons, whereas 252 persons are employed in research. NCS has 19 local county offices. Total revenues in 1999

were € 35.3 million (290 million NOK), whereas €15.7 million (129 million NOK) was spent as contributions to R&D activities (Norwegian Cancer Society, 2003).

The main strategic goal for NCS is to make an active contribution by supporting research projects and building up competence in selected areas of basic and experimental research, in order to enhance our understanding of the nature of cancer and reduce mortality from the disease. This can be achieved only when financial conditions are secured, and therefore one of the Society's greatest challenges is to raise funds.

> The Norwegian Cancer Society has been one of the most significant contributors to medical research in Norway for many years. The Society supports clinical research on new forms of treatment, quality assurance of therapeutic results, and optimal palliative care. NCS also emphasises prevention and early diagnosis, and urges the establishment of national screening programmes. The Society gives substantial support to research on new methods of diagnosis. Other studies focus on the biology of cancer, how the disease spreads in the body, and the importance of the immune system for development and treatment (Norwegian Cancer Society, 2003).

The National Association of Heart and Lung Diseases (LHL) is with its 60.000 members one of the largest patient organisations in Norway. The Association has 300 local units and 19 county organisations. In 1993 a patient ombudsman was established. The main objective of the ombudsman office is to represent the interests and improve legal status of patients in the health care system and in the society in general. The ombudsman offers juridical advice in cases where the Social Security Agency, health care system or insurance companies are involved. In addition, through examining individual cases a number of systemic failures have been discovered and lifted to the political arena. LHL By promoting the interests of patients on a political level, LHL represents a powerful actor in the health care system, especially due to the direct contact with individuals through the ombudsman (LHL, 2003).[19]

Norwegian Asthma- and Allergy Federation (NAAF) is a patient organisation consisting of approximately 23.000 members. Due to dramatic increase in asthma and allergy in the last decade, the tasks of the Federation have been expanded. The five most important tasks are to: (1) Promote research through Research Foundation for Asthma and Allergy; (2) Obtain better diagnostic- and treatment conditions for patients; (3) Improve social conditions; (4) Combat negative effects of environment; and (5) Spread knowledge about asthma, allergy and eccema in schools, health care personnel, youth organisations and individuals (NAAF, 2003).

Physicians.

Norwegian physicians are represented by the Norwegian physicians' association (Den norske lægeforeningen) as well as smaller specialists' associations. The Norwegian

[19] LHL emerged from the Tuberculosis Aid Organisation (THO), established in 1943. The THO struggled for important socio-political issues of that time, like right to treatment, right to social security and education possibilities for disabled. The close relation of tubercolosis to heart and lung diseases resulted in increasing the range of activities and establishing an interest organisation for patients with heart and lung diseases.

physicians' association has over the years achieved a significant position in terms of direct influence on health policies in Norway.

"Life Science Norway": A sector-initiated programme.

Biotechnology stakeholders in Norway have grouped together under the banner Life Science Norway, in order to raise the profile of the country's emerging biotechnology sector (*BioWorld Today*, April 30, 2003). The move has both a domestic and an international agenda. The bodies behind the initiative are the Norwegian BioIndustry Association (NBA), the Research Council of Norway and the Norwegian Trade Council, and the aim is to attract overseas flows of capital and scientific skills to Norway. The programme also wants to make clear for the government the importance of developing a coherent national biotechnology policy plan (interview with NBA director).

5.4 Lead market features

A lead market is a market that adopts successful innovations quickly, despite the fact that the technology was not necessarily invented in this market (Beise and Rennings, 2003). Moreover, lead markets first adopt a globally dominant innovation design; and subsequently "lead the international diffusion of an innovation and set the global standard" (ibid.). Due to this perception of the nature and function of lead markets (and "lead customers"), it has been argued that lead markets are not so relevant in science-based activites:

> [W]hile some dynamic business segments can still be considered as 'science-based' e.g., biotechnology, an increasingly large share of dynamic businesses are characterized by patterns of lead market induced innovation, and by novel ways of demand articulation. …Typical examples of lead market driven innovation are consumer electronics or telecommunications (Gerybadze and Reger 1999).

However, presence in lead markets is nevertheless of importance for firms within science-based activites:

> The importance of lead markets in anchoring existing industrial R&D activities and attracting new activities has increased. The market's function as a 'lead market' is decisive for innovations which only fully mature when they come into close contact with demanding, innovative customers. In fields of technology that are strongly science-based, it is the results of scientific research that constitute a driving force in the internationalization of innovation processes. In both cases, regional proximity to external partners such as customers, competitors and scientific institutions is an advantage (Meyer-Krahmer and Reger 1999).

We delimit and clarify the lead market aspects we describe as follows. We describe the market characteristics of Norway, and conclude whether Norway may be characterised as a lead market in particular therapeutic areas, i.e. the "demand for therapeutic category" (Agrawal, 1999: 38). Methodology is predominantly interpretation of statistical material.

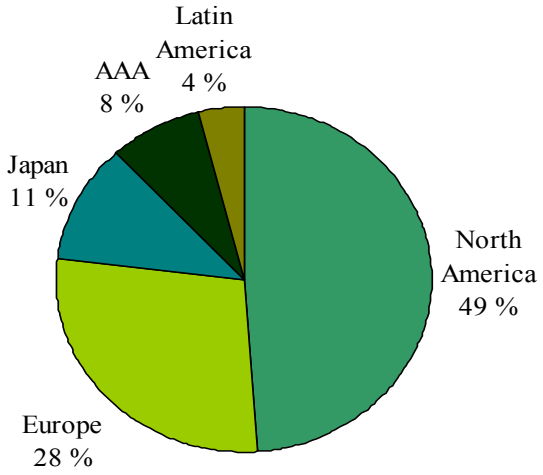
Market characteristics.

Between 1991 and 2002 the world market for pharmaceuticals more than doubled. The annual growth rates during this period were in the range between 2 % and 15 %. The market share of the US was 45 % in 2001 and close to 50 % in 2003 (Fig 5-2). The European market share dropped at the same time to about one fourth of the world market (EFPIA 2003).

Norway has a very small share of this market (approximately 0.3 percent) in absolute terms, but has a rather high per capita consumption of pharmaceuticals (Table 5-2).

The ratio of prescription drugs to over-the-counter (OTC) drugs may be an indication of the degree of competition within a particular market. There is a tendency towards a lower degree ratio with larger total market. Nevertheless, Norway, although one of the smaller European markets, has relatively high ratios of prescription drugs (Fig. 5-3).[20]

Fig. 5-2: Breakdown of world pharmaceutical market by geographical region (2003, percent of global sales).



Note: Actual sales of approximately 90% of all prescription drugs, and specific OTC drugs. "AAA" signifies Africa, Asia except Japan, and Australasia.
Source: IMS World Review 2004

The projections of age distribution in the Norwegian do, as with most other industrialised countries, indicate a sharp increase in the ratio of the population over 67 years of age, with this segment increasing from ca. 610.000 persons in 2002 to 1.249.000 persons in 2050 (LMI 2003: 97). Nevertheless, the total population of Norway, and, hence, the size of the market for pharmaceutical, is extremely limited (Table 5-2).

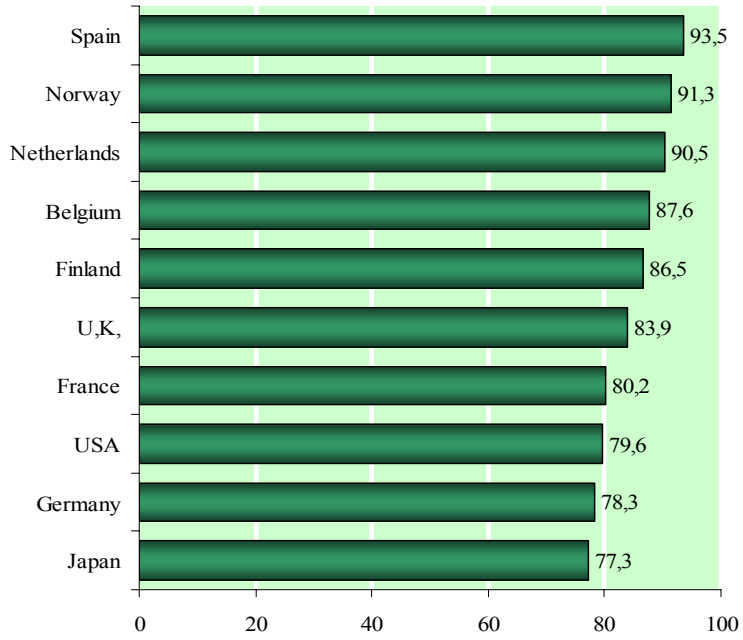
[20] The ratio of generics, i.e. out-of-patent pharmaceuticals, is an important element to the competitive situation of a particular market. The situation as of 2001 in this respect is for Norway 11 &, compared to 27% in Germany, 18& in the UK, 13% in the Netherlands, 8% in the USA and in Japan, 3% in Spain and in France, and 2% in Belgium (EC 2003: 48).

Table. 5-2: Pharmaceutical market value 2000

	Total (millions of €)		Per capita (€)
	Ex-factory prices	Retail prices	Retail prices
Belgium	2,667	3,973	387.87
Finland	1,142	1,648	318.09
France	17,263	27,698	470.32
Germany	18,375	30,624	372.81
Japan (2001)	…	42,467	335.00
Netherlands	2,555	4,035	254.11
Norway	925	1,406	313.70
Spain	7,295	10,626	264.84
UK (1999)	11,850	14,172	238.18
USA (2001)	…	119,931	420.80

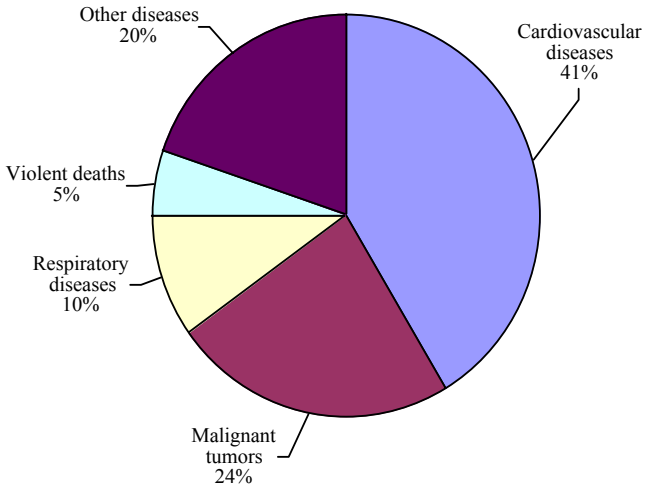
Source: Farmaindustria (2002: 92), IMS Strategy Group (Japan, USA), and own calculation (Japan, USA per capita figures).

Fig. 5-3: Approximate comparison of the ratio of prescription drugs to OTC drugs 2001.



Note: Japan figures are for 1999, USA figures are for 2000. Additional reservation, related to source see below.
Source: Compiled from IMS Health data as cited in EC (2003) calculated as reversal of OTC shares, with the addition of USA and Japan compiled from OECD Health Data 2002, 4th edition.

Fig. 5-4: Cause of death in Norway (2000). Source: Statistics Norway.

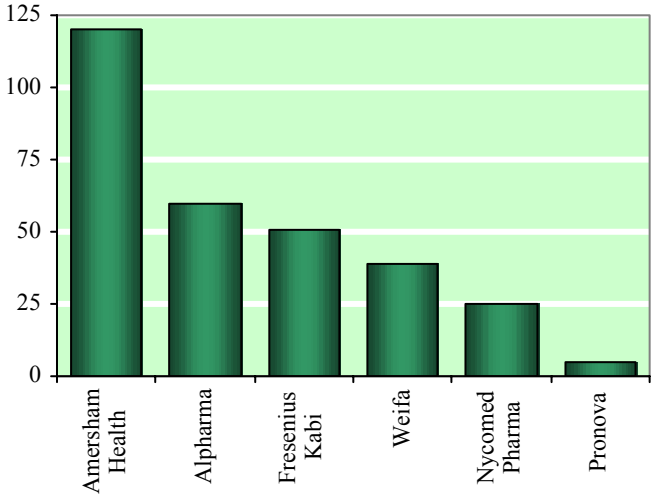


Death rates in Norway are in overall comparable to death rates elsewhere in Europe (Fig. 5-4). Cardiovascular disease, or more precisely, coronary heart disease, has persistently topped the list as the cause of deaths. However, deaths caused by cardiovascular diseases have decreased from the 1970s to the 1990s. Exceptions from the European average both in terms of lifestyle as well as cause of death are, firstly, that the average of smokers is relatively high. Among the population aged 15 years and older the general rate was 33.6 per cent in 1997 and the fifth highest in Europe. In recent years health authorities have run extensive anti-smoking campaigns (WHO, 2000: 4). Secondly, deaths caused by ischaemic heart disease are above the EU average. This is especially the case for men aged under 64, where Norway is third in Europe after Finland and the United Kingdom. In addition, cancer amongst females is slightly above EU levels (WHO, 2000: 4-5).

As shown in Chapter 3, the imports to, as well as exports from, Norway in pharmaceuticals is significant. Concerning the latter the number of countries receiving products produced in Norway is quite, especially in the case of Amersham Health (Fig. 5-5). The percentage of innovative drugs within total market was 37.4 percent in 2002, whereas generics' share of total market was 23.7 per cent in 2002 LMI (2003: 26).

We may thus conclude that the Norwegian market for ethical pharmaceuticals has two characteristics: (1) Very small in the context of world ethical pharmaceutical sales; and (2) "Reflects" to a certain extent the world market, and also to a certain degree, the lead US market, with cardiovascular diseases as one of the key therapeutic areas.

Fig. 5-5: Number of countries receiving pharmaceuticals produced in Norway for each firm, 2003.



Note: Alpharma is specialized in generics, incl. both human and animal pharmaceuticals.
Source: LMI (2003: 61).

Biopharmaceuticals.

As for biopharmaceuticals as seen separately the Norwegian market shows some particular traits, mainly by way of being represented very high in the consumption of cytostatics (together with Finland and Japan), and relatively high within the musculo-skeletal biopharmaceuticals segment in terms of consumption.

Products of the biopharmaceutical sector are expected to contribute innovative solutions to medical problems. After the first US approval of a biopharmaceutical drug in 1982, the development of new drugs has evolved rather incrementally up to ca. 2000, when there was a significant influx of new products. The annual global market sales have risen from 9.1 billion USD in 1994 via 11.6 in 1996, 22.7 in 2000, to 32,4 billion USD in 2002 (Bibby et al. 2003: 3-5). The sales figures were estimated to rise further to approximately 41 billion USD in 2003 (Research and Markets 2003).

The approximate ratio of biopharmaceuticals within the global market is, as of 2003, approximately 10 percent on a global scale, and also within the large US market, the ratio of biopharmaceuticals to non-biopharmaceutical is still ca. 9 percent as of 2002 (Bibby et al. 2003: 6). Also this ratio is predicted to change gradually, since the compound annual growth rate is considerably higher for biopharmaceuticals than conventional pharmaceuticals (28.3 percent to 14.0 percent over the last five years to 2002) (ibid.).

As indicated in Table 5-3 the types of products dominating global sales has on the one hand remained stable, with *erythropoietins* (treatment for anemia, i.e. productcs aimed for kidney and cancer patients since they stimulate the growth of red blood cells) such as Procrit/Erypo, Epogen and Neupogen dominating both in 1996 and 2002. On the other hand, *interferons* (proteins interfering with a cell's ability to produce, and serving as basis for drugs for osteoporosis, multiple sclerosis, and other diseases) are, although existing also in 1996, on

the increase . *Human growth hormones* (Humatrope) and *human insulins* (Humulin) have to a large extent left the top selling lists as individual drugs,[21] and been substituted with newly developed product types such as *monoclonal antibodies* (individual antibodies produced in the blood in order to recognize and bind to foreign invaders, singling them out for elimination by immune defences, "MAbs") such as Remicade used for Crohn's disease and rheumatoid arthritis and Rituxan/Mabthera used for a certain type of lymphoma. [22]

As of 2002 there were 119 products classified as biopharmaceuticals on sale globally, but the inter-regional ratios when it comes to 2002 sales figures were very uneven with North America leading (58 percent), followed by Europe (22 percent) and Japan (9 percent) (Bibby et al. 2003: 3). The overview of the situation for each of the case countries is not complete, nor directly comparable. We will here summarize some key points, starting with some observations as for actual sales and market shares of biopharmaceuticals to conventional pharmaceuticals, followed by two proxy measurement methods (ratio of new substances and ratio of particular therapeutic groups especially relevant to biopharmaceuticals).

In the case of Norway the sub-total market share of biopharmaceuticals is unknown. However, it is evident that it is a somewhat complex market with great regional variations. Due to high levels of rheumatoid arthritis problems in many regions, the biopharmaceutical Enbrel has been on the top-25 list of best selling drugs nationwide for several years (1.1 percent of total pharmaceutical market in 2003), and the MAb Remicade entered the list in 2003 (1.0 percent of total pharmaceutical market). For the urban Oslo region, there are in addition to Enbrel (no. 16 in sales for 2002) biopharmaceuticals with high turnover such as Recombinate and ReFacto (blood clotting agents, no. 8 and 10 respectively), and Gonal-F (recombinant fertility hormone, no. 14).

[21] In totality several drugs of this type make up together a significance presence still.

[22] See Bibby et al. (2003), PhARMA (2002), and Medical Research Council (n.d..) for a further description of biopharmaceuticals classes..

Table 5-3: Top-selling biopharmaceuticals on global market 1996 & 2002

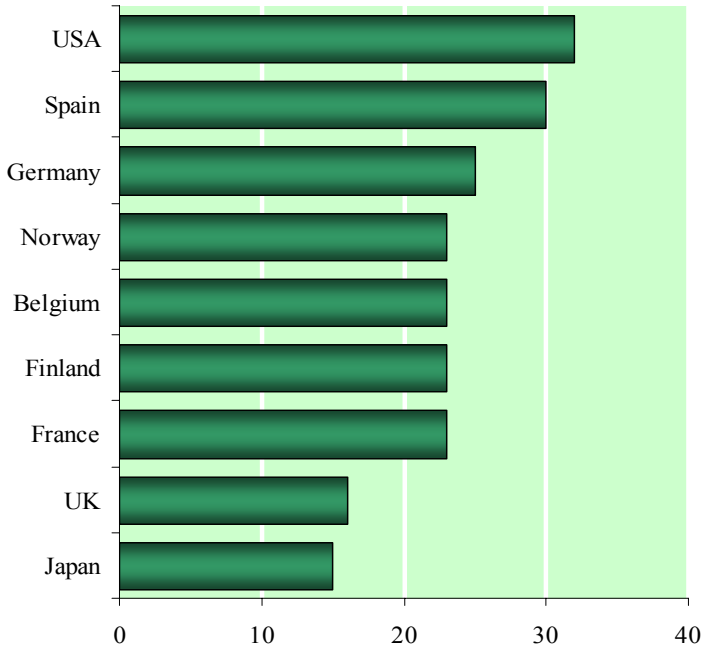
1996		2002	
Epogen (erythropoietin)	1,150	Procrit/Erypo (erythropoietin)	3,972
Neupogen (erythropoietin)	1,017	Epogen (erythropoietin)	2,840
Procrit (erythropoietin)	995	Remicade (MAb)	1,520
Humulin (human insulin)	884	Neupogen (erythropoietin)	1,503
Engerix-B (hepatitis B vaccine)	568	Rituxan/Mabthera (MAb)	1,183
Intron A (interferon for leukemia etc.)	524	Avonex (interferon for multiple sclerosis)	1,097
Betaseron (interferon for multiple sclerosis)	353	Enbrel (soluble receptor for rheumatoid arthritis	938
Epivir (n.a.)	306	Viraferon PEG (n.a.)	857
Activase (tissue plasminogen activator for infarctions etc.)	184	Betaseron * (interferon for multiple sclerosis)	682
Humatrope (human growth hormone)	268	Humalog (human insulin)	630
Sub-total	6,349	Sub-total	11,298
Total market, ca.	11,600	Total market	32,402

Notes: Explanations added (in parenthesis) based on PhARMA (2002). Betaseron is in the 2002 listing listed as Betaferon. Misprint in 1996-source corrected to "Humatrope".
Source: *Chemical Market Reporter*, June 22, 1998, p. 16, as cited in Office of Industries, U.S. International Trade Commission (1999) (1996 products and sub-total), and Bibby et al (2002) (2002 products and sub-total and 1996 & 2002 market total).

One proxy that may to a certain extent illuminate clearer the current situation is to investigate the ratio of new substances - biological and conventional - within the market (Fig. 5-6). According to this measure, the Norwegian market does not stand out as particularly innovative. The two country markets which stand out as least innovative are Japan and the UK, while the USA together with Spain and to a certain extent Germany stand out as the country markets accepting a very high ratio of innovative drugs. It would thus be expected that ratio of biopharmaceuticals would also score high in these markets. Norway positions itself approximately at the middle of this scale.

The ratio or dominance of particular therapeutic groups especially relevant to biopharmaceuticals also shows particular characteristics. Table 5-4 shows a rather short time series, and increases within this segment should be interpreted with caution. However, the overview shows that therapeutic profile groupings single out as Japan and Finland as exceptionally high consumers of blood and blood forming agents, with the other countries except the US and the UK as a second group. Knowing that the actual present day ratio of biopharmaceuticals within this segment is evident, especially in Japan, the potential for increased presence of biopharmaceuticals within the segment should therefore be evident. When it comes to cytostatics, the Nordic countries Finland and Norway stand out together with Japan, and whereas the situation evens more out when it comes to drugs aimed for the musculo-skeletal system.

Fig.5-6: Share of market within each national market for new products launched in previous five years before 2001



Note: The percentage, by value of national pharmaceuticals markets accounted for by new molecular entities launched within the last 5 years at 2001.
Source: IMS Health as cited in EC (2003); LMI (2004).

Table 5-4:Three main therapeutic groups (ATC) with particular current relevance to biopharmaceuticals, with addition of group C (cardiovascular system), 2001-2003. Percent of total turnover.

	C. Cardio-vascular system			B. Blood and blood-forming organs			L. Anti-neoplastics and immuno-modulating agents			M. Musculo-skeletal system		
	01	02	03	01	02	03	01	02	03	01	02	03
World	19.5	19.3	19.4	3.1	3.2	3.5	4.1	4.5	4.6	6.1	6.0	6.3
Germany	…	22.3	22.1	…	3.5	3.9	…	6.5	6.9	…	4.9	5.1
Japan	…	19.3	19.6	…	6.8	6.8	…	7.6	7.7	…	6.5	6.4
USA	…	18.2	17.5	…	2.2	2.6	…	3.7	3.9	…	6.0	6.3
UK	…	24.4	25.3	…	1.8	2.1	…	3.1	3.0	…	5.4	5.8
Spain	23.0	23.2	22.7	3.3	3.6	3.6	4.1	4.3	4.6	5.8	5.5	5.7
Netherlands	23.6	23.7	…	2.1	2.9	…	5.1	5.6	…	4.4	4.5	…
France	…	24.1	23.5	…	3.2	3.5	…	2.9	3.9	…	5.8	5.8
Finland	17.8	18.6	…	6.1	6.2	…	6.3	7.9	…	6.6	6.2	…
Norway	21.7	21.8	20.5	4.8	4.9	5.2	8.1	8.4	9.7	5.2	5.8	5.9

Note: Finland = 2000, (2002) & [2003].
Source: Compiled from calculations based on national pharmaceutical industry annual reports (Finland, Netherlands, Norway) and IMS Drug Monitor.

It should be noted that the US market characteristics are special in a number of respects. Firstly, it differs in the sense that drugs related to the central nervous system (ATC group N), and not cardiovasculars, top the list. Secondly, although the ATC groups assumedly most

relevant to the current and near future biopharmaceuticals do not occupy astonishing high shares of the market (with the exception of group M), it should be noted that even the modest percentage shares in this market signifies very high sales figures in international comparison. For example, even if cytostatics hold 3.7 and 3.9 percent of the US market in 2001 and 2002 respectively, the actual sales figures for this group of medicine surpasses the aggregate sales of all the European countries listed in Table 5-4 combined.

Conclusion.

We may thus conclude that market access in itself would thus hardly be a great enough incentive for business activities in Norway, although we have not been able to pursue this issue in concrete inquires to the parts of the industry which is indeed present in Norway. However, although this issue is based also on our interpretations it would be fairly safe to state that the Norwegian market could be interesting to the industry for other reasons. These reasons are based on the illness profile of the Norwegian population, and, subsequently, the causes of death as well as pharmaceutical turnover according to therapeutic groups. With some exceptions all these factors are in fact reflecting the overall trend of major overseas markets and Norway thus emerges as a microcosm for the more profitable international markets.

Norway-related firms are active in a number of overseas markets, and Norway as such is thus in overall not the lead market for Norwegian based firms- the Norwegian location does in a way function as – in its terms - a science-related inducement for location there, with its cluster of diagnostics specialised firms and access to "representative" therapeutic areas present in the population.

5. 5 Socio-economic / ethical aspects

One way of assessing the level of public support for (versus opposition to) biotechnology in general as well as for biopharmaceutical research and products is to refer to longitudinal surveys of the population.[23] Such surveys exist for a selection of the case study countries (Table 5-5).[24]

In general there is a tendency towards a very unclear divide when it comes to general public support. Taking the case of support versus opposition when it comes to genetic testing and genetically modified food, the public in Spain and the Netherlands is relatively positive towards both types of biotechnology applications. There is a tendency towards increased levels of criticism especially when it comes to genetically modified food, especially in countries like France and Norway. But support for medicinal purposes is in general high. In Germany and the Netherlands the levels of opposition have even decreased during the time period in question. Opposition towards this kind of research does thus not seem to serve as a particularly high constraint on the development, production and marketing of such products.

[23] Other approaches are to assess the debate within media, the existence of ethical committees, and so on (cf. the national reports).

[24] For results from the 2002 survey excepting Norway, see Gaskell et al. (2003).

Table 5-5: Levels of opposition to genetic testing and GM food in selected European states 1996 and 1999, percent.

	Genetic testing			GM food		
	1996	1999	Change	1996	1999	Change
Belgium	5	10	5	28	53	25
Finland	5	9	4	23	31	8
France	4	6	2	46	65	19
Germany	13	10	(3)	44	51	7
Netherlands	7	4	(3)	22	25	3
Norway	22	22	0	56	65	9
Spain	4	6	2	20	30	10
U.K.	3	4	1	33	53	20

Notes: For methodology and reservations regarding interpretation, see Gaskell et al. (2000).
Source: Based on Gaskell et al. (2000: 938).

The public discourse on political regulation of modern biotechnology in Norway has passed through three distinct and successive phases:

(1) initiation (1974-92), dominated by three independent discourses regarding risk, R&D and moral concerns;

(2) legislation (1993-94); and

(3) domination by technological development, actual applications and legal adjustments (1995-2000) (Nielsen et al, 2002).

Firstly, during the period 1974-92, moral concerns regarding experiments with human growth hormones in ”super salmon” and the use of IVF (in vitro fertilization) had been spur for the legislation. Legal standards with semi-ethical content are specific to the laws, but the prolonged legislative process ended up as a kind of ”trial and error process” from the ethically formulated concern back to legal standards of a more political nature. The first major official policy document was presented within the sphere of ”normative” philosophical ethics. It contrasted consequences with emotive arguments, ”utility” with ”duty” and it referred to classical philosophers such as Jeremy Bentham (1748-1832) and Immanuel Kant (1724-1804).

Secondly, there was a period of legislation (1993-1994) with the two major acts The Gene Technology Act and the Biotechnology Act described elsewhere in this report.

During the third period (1995-2000), several ethical and social issues were raised in the media and elsewhere in the course of the new Biotechnology Act. One of them was the concern that the availability of techniques, like genetic testing of embryos, will create a *selection society*, where the genetically “unfit” individuals will be regarded as second class citizens. The same technology would turn to a social pressure on parents.

Another issue of debate was an attempt to *define the start of human life* and the moral status of an embryo. The arguments may be similar to those in the debate on abortion, but in context of biotechnology, the question is posed as: “Is a fertilised egg a person?” And as: “Can we use a fertilised egg as an object of research?” One may obviously approach such questions from rather different angles, and there will probably always be disagreement when

it comes to such debates. This is due to the potential religious ("created by God") rather than philosophical underpinnings of particular approaches.

The main problem was, according to philosopher Øyvind Baune, that previously valid ethical theories could not be applied to the new situation. Therefore, he argues, the question remains unanswered, until the scientific society develops ethical tools suitable to examine this issue. One illustration he mentioned was the theory of Kant, saying that no persons can be used as means, i.e., each person is a goal in itself. If we wish to apply this category, we must clarify the notion of a "person". So far, in accordance with the Biotechnology Act, research on fertilised eggs is prohibited in Norway.

The arguments regarding use of gene technology, either in testing for inherited genetic disorders or in predicting disposition for disease, focus on an individual and its vulnerability. Professor Torben Hviid Nielsen argued that the problem must be examined in a wider context. Our liberalism, he says, which puts the individual to a position to choose the genetic make up of the unborn child without considering what would be right or wrong to the society, can be called a state-liberalism. We must formulate new questions, which depart not merely from the interest of the embryo but also from the perspective of *societal* transformation. What will happen to a society if the individuals are given a choice to either select away their unborn children or equip them with the best genetic make up?

Chapter 6. Synthesis and Conclusions on Research Questions

The previous chapters described the different components of the biopharmaceutical innovation system in Norway. In this chapter we consider some of the main research questions of the OECD Case Study on Biopharmaceutical Innovation Systems. Section 6.1 looks at the systemic imperfections that are responsible for a sub-optimal performance of the pharmaceutical biotechnology innovation system, especially in the business system. It then considers what elements of framework conditions and horizontal innovation policies are key to foster innovation. Section 6.2 asks whether there is a relation between the openness of a national system of innovation and its performance, and if so, how open should the system be to achieve maximum performance. Section 6.3 ponders what specific demand-side factors influence the biopharmaceutical innovation processes and what the effects on the innovation outcomes are. Finally, section 6.4 considers the extent to which innovation policies should be customised to the particular needs and features of the biopharmaceutical innovation system.

6.1 Systemic failures

The OECD (1999: 10) stresses that governments should not only address market failures caused by technological activities, but also "the systemic failures that block the functioning of innovation systems, hinder the flow of knowledge and technology and, consequently, reduce the overall efficiency of R&D efforts." The causes of systemic failure can be classified into four broad categories:

1. Missing or inappropriate functions in the system of innovation, e.g. production, diffusion and application of new knowledge, demand articulation, financing of innovation activities, education and training of skilled researchers, etc;

2. Missing or inappropriate actors in the system of innovation, e.g. firms and research organisations but also regulatory authorities, users/consumers, funding organisations, etc;

3. Missing or inappropriate institutions and framework conditions in the system of innovation, e.g. set of laws and regulations, entrepreneurship, innovative climate, public policies, etc;

4. Too much or too little interaction or co-ordination between the elements in the system of innovation.

Each of the following four sections will discuss the systemic failures of the biopharmaceutical innovation system in Norway. Table 6.1. summarizes the discussion.

Table 6.1. Systemic failures in the Norwegian biopharmaceutical innovation system.

	Absent/ inappropriate functions	**Absent/ inappropriate actors**	**Absent/inappropriate institutions and framework conditions**	**Too much/little interaction and co-ordination**
Enterprise system	-Marginal firm growth. -Lack of managerial skills: Not enough emphasis on management and marketing. -Insufficient exploitation of academic research	-Absence of significant national pharmaceutical industry. - Lack of critical mass of biopharmaceutical firms	- Need of risk capital especially between the start and seed phase. -Few public/semi-public funding programmes.	-Little coordination or promotion of patenting activities.
Public R&D system	-Not enough emphasis on basic research in biotechnology in the past. - Imbalance regarding basic research vs. applied development.			-Too little interaction between universities and industry. -Too little interaction between different government agencies.
Demand system	- Limited product market			- Despite active patient organisations patients~industry links lacking due to local non-presence of latter
Institutional rigidities			-Education system producing few graduates in life sciences. -Weak entrepreneurial climate.	-Too little interaction between ministries, no clear biotechnology policy

6.1.1 Systemic failures: Absent/inappropriate functions

There are both positive and negative aspects to the private enterprise system in the Norwegian biopharmaceutical innovation system. The first and perhaps most important positive outcome is the large number of new entrants since 1997. Most of these firms are dedicated to specific areas in human health biotechnology, especially cancer and immunology. These firms have been able to acquire specialised knowledge and scientific expertise. Second, our Biotechnology Use and Development Survey indicated that several of these firms are involved in a large number of co-operative projects with both national and international partners, which suggests that they are up to international standards.

Nevertheless, a leading biopharmaceutical industry has not emerged in Norway over the last decade. Within the enterprise system, the new entrants since 1997 have not developed into more mature and market-oriented firms. The majority of the firms remained very small and only a minority are profitable. They are severely limited in intensity and scope of their activities because of their relatively small budgets and the high-burning rates of financial capital to be spent on R&D. Moreover, the patenting intensity in the field of biotechnology appears very low in Norway, even when corrected for country-size. It was above average when the United States Patent and Trademark was taken into account, but the relatively low patenting intensity at the European Patent Office indicates that Norwegians do not have knowledge about what is patentable and/or enough support to make the application at the appropriate patent office.

Marginal firm growth.

It could be possible that these firms will get locked into a vicious circle. They lack the critical mass and managerial skills for speeding up the research process and attracting new capital, which implies that it takes a considerable longer period of time before potential products actually reach the market, which leads to an increasing investors' reluctance in providing financial means.

Lack of managerial skills

Enterprises that use biotechnology are generally science-driven. While the dedicated biopharmaceutical firms in Norway have a good international scientific reputation, they have little knowledge of management and marketing. Several of the interviews reported that these firms lack sufficient managerial skills. Although the dedicated biotechnology firms appear to be innovative and develop new products, our Biotechnology Use and Development Survey also indicated that the lack of human resources and the access to capital were two of the most important obstacles to the commercialisation of biotechnology, and that these obstacles became stronger from 1999 to 2003. Fostering greater commercialisation will not easy. It will require more active participation by venture capitalists and better linkages with downstream customers.

Insufficient exploitation of academic research

Despite the low basic research activity, an important system failure in the public R&D system is that the biopharmaceutical industry has not been able to fully exploit research done at the universities. About 80 per cent of all contributions to biopharmaceutical research came from the universities in Norway in the last half of the 1990s. One reason might be that the research results have not been sufficiently prioritised by universities and scientists. But it appears that institutional support of technology transfer activities from universities to the private sector such as establishing spin-offs or mediating licensing agreements is insufficient. This is caused to a large extent by the lack of technology transfer organisations at universities, and the need to have expertise in legal, technological and commercial issues at the universities.

Imbalance regarding basic research vs. applied development

The biopharmaceutical industry would most probably be greatly enhanced if there were more public funding of basic research. The global pharmaceutical corporations that have a presence in Norway conduct mainly clinical research. Only about 3 per cent of R&D spending by the pharmaceutical industry was on basic research in 2001. Prioritising applied and clinical research at the expenses of fundamental research could weaken the biotechnology knowledge base, making it more difficult to keep up with new scientific developments. This could have serious long-term consequences for the development and growth of the biopharmaceutical industry. The recently started FUGE programme may bring the level of the basic research disciplines underlying functional genomics up to international standards.

6.1.2 Systemic failures: Absent/inappropriate actors

The most important systemic failure with respect to the absent or inappropriate function actors is the very modest size and strength of the Norwegian pharmaceutical industry. This may be related to the size of the market; nevertheless, virtually all of the medium to large size firms in the industry are subsidiaries of foreign pharmaceutical multinationals and rely heavily on R&D activities in the parent firm. With only few exceptions, these firms do clinical research or relatively small-scale activities in Norway, such as packaging and distribution, marketing and sales.

The dedicated biotechnology firms are very small and young, depending heavily on external funding and cooperative arrangements. Geographical proximity of large pharmaceutical firms may in certain cases be important for these firms since more experienced pharmaceutical firms are often downstream customers and are thus important drivers in the innovation process (McKelvey et al. 2003). These large firms have the expertise in the managing pharmaceutical R&D processes and marketing that most of the dedicated biotechnology firms in Norway do not have.

6.1.3 Systemic failures: Absent/inappropriate institutions and framework conditions

One of the most important aspects of the institutional framework is that the regulatory environment relating to biotechnology is similar to EU legislation. The Gene Technology Act is

stricter than EU legislation, but it does not pose any serious threat to R&D activity in biopharmaceutical industry. While this act may be considered overly strict by some standards, it does not appear to be an important obstacle to the development and commercialisation of products since the firms based in Norway currently conduct research well within the regulatory framework anyway. Some of the interviews reported unclear or complicated application procedures for registering a new product, but there was no indication that it hindered the development of new products. Although the regulatory environment ranked relatively important in our Biotechnology Use and Development Survey, its importance declined since 1999, putting it well below the economic variables such the need for risk capital.

Need of risk capital; few public/semi-public funding programmes

Many dedicated biopharmaceutical firms encounter increasing difficulties in raising financial capital after the start-up phase. The slowdown in the economy has exacerbated these difficulties and may be the reason for the lack of new entrants into the industry in recent years. Both the Community Innovation Survey and the Biotechnology Use and Development Survey indicated that economic risk was a factor hindering innovation process and the commercialisation of products. The firms that answered the latter survey indicated that the risk has also increased significantly since 1999. National champions such as Norsk Oil and Norsk Hydro are not interested in providing funds to the biopharmaceutical industry. The large pharmaceutical firms do not generally provide funding, but GlaxoSmithKline and AstraZeneca have provided 'incubator' offices to some of the small firms. This means that the biopharmaceutical industry must rely on public funding or the venture capital markets. Only limited funding is available through the European Union and various national sources such as the Norwegian Research Council, and the Cancer Society. The venture capital market has also dried up as investors have become increasingly reluctant to invest in biotechnology firms that are not able yet to generate a significant turnover. As a consequence, the financial insecurity after the start-up phase will likely put the industry in jeopardy, unless the economic situation improves significantly in the near future.

Education system producing few graduates in life sciences

Although the percentage of students choosing health programmes was well above the European average, the percentage choosing the life sciences was well below the average. In 2000, this percentage was one of the lowest in Europe and will likely become a significant obstacle if the industry should expand. Even now the respondents to our Biotechnology Use and Development Survey indicated that human resources are one of the most significant impediments to the commercialisation of biotechnology, and it became worse since 1999. If the FUGE programme is successful, it will become imperative for the universities to expand their educational programmes. Some of the shortage may be due to a skills mismatch since some biotechnology researchers became unemployed because of the merger between a foreign-based Amersham and the domestic-based Nycomed pharmaceutical firm in 1997. This would require the universities and other institutions of higher education to encourage greater participation in the life sciences and to create new and relevant programmes that attract more students to the area.

A short-term solution would be to attract qualified researchers from abroad, but the skills shortage is be a problem in many of the leading countries doing biotechnology research.

Weak entrepreneurial climate

Entrepreneurial spirit is considered as an important omission in the Norwegian innovation system as a whole and the biotechnology sector more specifically. Interviews with various actors and our Biotechnology Use and Development Survey indicate that many of the dedicated biopharmaceutical enterprises cannot design a proper business plan. On the other side, investors appear unwilling to take the risks necessary to develop the industry. The FUGE programme may help the industry, but this will depend on how much funding will be available enterprises in the post start-up phase. Nevertheless, long-term growth will depend on the entrepreneurial spirit within Norway.

6.1.4 Systemic failures: Too much/little interaction and co-ordination

Inconsistencies in public policies concerning biotechnology can sometimes happen because six Norwegian ministries develop their own policies in the area without proper co-ordination among them. The government has not yet provided a joint plan to remove these consistencies.

There are also too many policy actors doing similar things, including governmental, non-governmental and other initiatives. The delay in creating the FUGE programme may have been partly caused by differences between the many policy actors. At the same time there appears to be a lack of a coordinated effort to protect their intellectual property rights. This problem may be even more important in the academic community, since the universities are relatively autonomous in developing their own policies. As a result, there are too many underdeveloped and often ineffective IPR policies in place.

6.2 System Openess

System openness is important because it contributes to the introduction of diversity and the selection of alternatives. It can act as a driver for change and innovation as well as increase the performance of the system. Two factors defined system openness in the project: (1) a national innovation system is open to or affected by international factors, such as the presence of foreign firms in the system, co-operation with foreign partners or the international regulatory frameworks governing innovation activities; and (2) actors can enter or leave the system, entry and exit dynamics are important for those actors that are directly involved in innovation activities, such as firms and research organisations.

International openness

The Norwegian biopharmaceutical innovation system has a relatively high degree of 'international openness' because the industry is dominated by foreign subsidiaries, most of which have production facilities abroad. As a result, imports exceed exports, but the trade balance only makes up a very small percentage of trade in manufactured goods. Oil and related industries drive the Norwegian economy, including the exchange rate and the cost of production for other industries. Nevertheless some of the global pharmaceutical firms carry out research, production and sales activities. Despite high labour costs, the number and extent of clinical trials conducted in Norway is significant due to other non-cost factors. The dedicated biopharmaceutical firms have started to develop an extensive international network for collaborative R&D. This helps speed up the process of knowledge transfer and builds the basis for a learning economy. Finally, being a part of the European economic area (EEA), Norway harmonized its regulations concerning pharmaceuticals with EU regulations. The major advantage of the internationalisation of regulatory frameworks is that it removes legal and regulatory differences between countries that could harm international competition and performance. However, certain international differences in national implementation may persist.

Business entry and exit

Since 1997 several new dedicated biopharmaceutical firms have entered the Norwegian biopharmaceutical innovation system. They have contributed to diversity in the system as they specialised in specific technologies and product platforms, covering different types of activities in the pharmaceutical innovation process. Some of the firms where created as spin-offs from universities, and others were created by scientists made redundant by the merger between a foreign based (Amersham) and domestic (Nycomed) pharmaceutical firm in 1997. A consequence of this is that a small cluster of dedicated firms focusing on diagnostics that use biotechnology appeared in the late 1990s. These new entrants influenced the performance of the Norwegian innovation system as a whole since they have been one of the main contributors to the growth in biopharmaceutical patent applications in the period 1995-1999.

The degree of openness in terms of firms leaving the system seems rather limited. Business exit has hardly occurred since 1997; only very few biopharmaceutical firms went bankrupt,

merged with or acquired by other firms. However, one can expect more exit dynamics in the years to come. Not all biotechnology firms that have been started over the last years are expected to survive, mainly because of the lack of public and private capital, managerial skills and entrepreneurial spirit, etc.

6.3 Role of Demand

Growing demand for health care can play an important role in the development of new products in the pharmaceutical industry. To meet the growing demand for new vaccines and other medicines that use biotechnology, the pharmaceutical industry continuously searches for new medicines that meet this demand. In 2002 more than 37 per cent of the products sold in Norway contained a new active substance, or about average for the years since the late 1990s. Three issues related to health care policy are highly relevant to the functioning of the Norwegian biopharmaceutical innovation system.

Pricing and demand in the Norwegian health care system.

In Norway, the financing and ownership of hospitals are public, and put under the control of the national government, which transformed them into quasi-independent public firms on 1 January 2002. There are also extensive regulations for development, production, marketing and sales of medicines in Norway. One of the reasons for such extensive regulations is that the high patenting intensity in the industry gives firms considerable monopolistic advantages, despite there being a large number of producers and importers of medicines in Norway. There are five important actors in the market for vaccines and other medicines besides the government authorities: (1) the pharmaceutical firms that manufacture in Norway or import from foreign sources; (2) the wholesalers; (3) pharmacies; (4) patients; and (5) doctors and hospitals. The regulations, including the prices of each medicine, then determine the interaction between these groups and the sales or turnover of each product. To overcome the monopolistic advantages and escalating health care costs, the Norwegian Medicines Agency determines the prices of prescription medicines on the basis of the prices in Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands, Sweden and the UK. Since 1 January 2001, the prices of prescription medicines in Norway must not exceed the average price of the three countries with the lowest price. Prices are adjusted at least once a year to reflect changes in the market price for the medicine and the exchange rate. Most non-prescription drugs were deregulated on 1 November 2003, making it possible to obtain basic drugs such as aspirin in any shop.

Between 1993 and the end of 2000 Norway used a reference pricing system for reimbursements of ‘blue’ prescriptions to contain costs. During this time the National Insurance Administration would only reimburse the price corresponding to the price of the least expensive medicine. The authorities expected large savings, and expanded the scheme three times. Modelled after the drug reimbursement systems in Germany, the system was severely criticized for not being able to foster more rational prescription practices costs that were greater than the savings achieved. There is also a considerable controversy over whether this method of pricing dampens innovation because the pharmaceutical firms have more difficulty recouping the costs

of R&D activity. In addition, the reimbursement system tended to reduce demand for expensive medicines, which resulted in relatively lower sales turnover than typically found in Scandinavia, and increased the risk of incorrect use of medicines.

Input of patient organisations in the innovation process

The presence of patients' organisations, which advocates the patients' interests through maintaining relations with policy-making bodies, pharmaceutical firms and research organisations, is high in Norway. They also form an essential link in the communication of the pharmaceutical industry with the patients, as the industry is not allowed to advertise directly to the consumer. These organizations can have an important influence on the biopharmaceutical innovation system by articulating their needs directly to the pharmaceutical industry. They can also communicate these needs to scientists and the authorities. In practice, however, the input provided by patient organisations to industry remains limited. This is partly caused by the heterogeneity and fragmentation of the numerous patients' organisations and their lack of critical mass. It is also caused by the reluctance of patients' organisations in maintaining intense relations with pharmaceutical firms. Their main fear is to lose neutrality and independence vis-à-vis the pharmaceutical industry.

Public acceptance of biotechnology

Public acceptance of biotechnology can be an important influence on the growth of demand. The average Norwegian knows more about biotechnology than the average European. There is a tendency towards increasing levels of criticism especially when it comes to genetically modified food, but support for medicinal purposes is high (Gaskell et al. (2000: 938).. However, Norwegians tend to expect less from the technology. This may be because of a lack of trust in pharmaceutical industry as a source of information. Norwegians much rather prefer to obtain their information from patient organizations, the medical profession and universities (Nielsen et al. 2002). Nevertheless, the approval of biopharmaceuticals has increased steadily from 1993 to 2002, and our Biotechnology Use and Development Survey indicated that the dedicated biopharmaceutical firms ranked this obstacle to commercialisation not very high, and confirm that it has diminished over time.

6.4 Policy implications

One of the main goals of the OECD Case Studies in Innovation project is to formulate policy implications resulting from the analysis of national biopharmaceutical innovation systems. The purpose is to draw attention to the so-called systemic instruments in innovation policies that enable policy makers to address all relevant aspects of national innovation systems.

Table 6.2. lists, on a preliminary and general basis, the systemic failures. For each failure we formulate conclusions regarding policy implications. However, it is not always evident that national public policies are the correct address for the identified imperfections, given the differing but sometimes overlapping responsibilities of the various actors in the system,. In many

cases it is not evident who the actors most involved in the failure are (for instance, in education and training there are a considerable number of systemic failures that deal with human resources involving various parts of the system).

It may be noted that what we have termed as concrete systemic deficiencies in Table 6.2. are remarkably similar to the situation in several other countries which lack the presence of large pharmaceutical corporations (for the Netherlands, see the country report of this project; for Australia, see Rasmussen and Sweeny 2002; for Canada, see Industry Canada 2001).[25] What is rather unique in the Norwegian context is that there have been historic occurrences of a non-systemic nature acting as a temporary alleviation for traits which could otherwise turn into long term deficiencies. Most notably, this is the post-1997 match between increasing spin-offs of ideas from the university sector linking to surplus manpower available after the large scale merger between a domestic and foreign firm in 1997.

[25] E.g. the Canadaian situation and the list of ”major challenges for governments and industry” is almost identical to our list: Strengthening long term investment in biomedical, genomics and bioinformatics research and encouraging multi-disciplinary research; increasing financial support for laboratory infrastructure; encouraging the formation of academic spin-off companies through incubator facilities; increasing linkages between institutions and companies to better exploit Canadian research; fostering technology transfer through training of such officers in universities, teaching hospitals and government laboratories and by improving access to technologies available for licensing; strengthening technology intelligence and forecasting initiatives in firms; optimizing commercial benefits for Canada from government and industry investment in R&D; establishing pricing and reimbursement levels that contain health care expenditures without damaging the viability of the industry; ensuring Canada’s patent regime is competitive with other jurisdictions; improving regulatory efficiency; addressing human resource requirements through expanded immigration and better co-ordinated education and training programs (Industry Canada 2001, section 4.4).

Table 6.2. Policy implications.

Systemic imperfections	Concrete systemic deficiencies	Policy implications
Absent/ inappropriate functions	-Marginal firm growth.	- Evaluate reasons, and subsequently in the case of problematic non-growth trends consider support actions.
	-Lack of managerial skills: Not enough emphasis on management and marketing.	- Stimulate learning and knowledge transfer between firms, e.g. instruments that support small firms to learn/profit from large firms' expertise in managerial and downstream business functions skills. Improve/extend university and higher education curriculum with management courses.
	- Insufficient exploitation of academic research. Not enough emphasis on basic research in biotechnology in the past. Imbalance between basic research and applied development.	- Stimulate further exploitation of IPR as high priority in academic system. Realise uniformity in university IPR policies and systems. Enable institutions to develop proper support infrastructures.
Absent/ inappropriate actors	- Lack of large integrated pharmaceutical firms	- Initiatives to attract foreign companies, or, more realistically, provide for linkages between domestic SMEs and foreign potential partners.
Absent/ inappropriate institutions and framework conditions	- Need of risk capital especially between the start and seed phase. -Few public/semi-public funding programmes.	- Bridge the gap between first stage and follow-up financing (or between public funding and private equity). Possibilities of additional tax measures and incentives for investors to invest in high-tech firms. Improve mutual understanding of the needs and demands of biotech firms and providers of private equity
	-Education system producing few graduates in life sciences.	- Stimulate students in choosing natural sciences, and improve the career opportunities and terms of employment at public research institutes.
	-Weak entrepreneurial climate.	- Improve entrepreneurial climate.
Too much/little interaction and co-ordination	-Little coordination or promotion of patenting activities.	- Implement and enforce EU Directive on biotechnology patenting, remove regulatory barriers, shorten application procedures, improve communication and information supply on regulatory procedures, and improve transparency of the regulatory system.
	-Too little interaction between universities and industry, between different government agencies, and between ministries; no clear biotechnology policy	- Remove inconsistencies in public biotechnology policies. Realise more co-ordination in policy-making and implementation.

Asking whether there are any policy implications to be drawn specific to the biopharmaceutical sector, and asking the extent to which innovation policies should be customised to the particular needs and features of the biopharmaceutical innovation system, we find it necessary to sum up and subsequently pursue these questions based on an assessment of what kind of firm population we are actually dealing with in this context. Several studies have categorized firms relevant to the biopharmaceutical sector in various ways, where one way of categorizing is the somewhat rough division - like in this OECD project - between diversified and dedicated firms. A slightly more nuanced way of dividing between different types of firms is to distinguish between dedicated biotechnology firms, traditional pharmaceutical companies marketing drugs developed by biotechnology firms, and "a specialized tier of companies serving both the pharmaceutical and biotechnology industries with platform technologies that can speed up the drug discovery process or improve drug delivery" (Industry Canada 2001).

Table 6.3. Types of firms and appropriate policy implications

	Type A-firms	Type B-firms
Innovation project	Incremental innovations. Small projects and target market niches. Low to medium risk.	Radical innovations. Research-intensive. Larger projects targeting broader markets. High risk.
Business concept	Need to maintain profitability, which forces them to limit R&D investments. Sells products and/or services .	Profitability of the large projects feasible only when downstream targeted market is broader (e.g. Genentech, Chiron, Millenium)
Strategy	Targeting is niche based in order to avoid direct competition with larger firms.	Either (1) contract research/alliance with large firms, or (2) independent large research programme.
Commerciali-sation	Continuous direct sales.	Either (1) contract with partner about rights to results, (2) partnering at the time of moving into the industrial and marketing phase, or (3) independent IPO.
Organizational mode	Requires specific resources (co-operative or commercialisation networks, reputation or scientific visibility) in order to run the operational activity. Has to convince specific kinds of commercial parthers to ensure development.	Requires specific resources (human resources on continuous basis, access to scientific competencies and techniques developed by academic research, and access to capital markets, in addition to co-operative or commercialisation networks and reputation/scientific visibility) in order to run the operational activity. Has to convince specific kinds of financial partners to ensure development.
Policy implications	Focus restricted to mainly start-up phase since SMEs focusing on a market niche and conducting small research programmes will experience steady growth if it is able to reach financial equilibrium fairly quickly. Less risky, and The SME probably makes less use of the founders' knowledge.	Focus on follow-up in addition to start-up, since development is possible in the context of SMEs embarking on large research programmes in partnership or competition with major companies only when outside capital and the participation of venture capital firms exists. Founding members' experience is a key factor if the SME is to enter into certain partnerships:

Source: Based on Mangematin et al. (2003), with selected minor modifications.

Mangematin et al. (2003) have theorized further based on the more detailed way of categorization, and also deliberated on the policy implications resulting from this way of analysis (Table 6.3.). They perceive of two essentially different business models, each with its own likely

dynamics and development patterns, and, hence, appropriate policy implications. We find it useful to assess the Norwegian situation according to this more detailed way of categorization.

Although all of the firms in Table 6.4 may be classified as dedicated biopharmaceutical firms in one way or the other, there is in the Norwegian context a significant overall dominance when it comes to the Type A firms aiming at incremental innovation and a relatively quick launch on the market of products or services. Within therapeutic biopharmaceuticals seen in isolation, however, the Type B firms dominate. Within enzymes, the Type B firms are still a far way off commercialisation. For example, the firm Thia Medica AS was recently created in order to develop the discovery of a modified fatty acid (TTA) for potential use within treatment of metabolic disorders. The development process is, however, still in the very first stages. It is likewise within antisense and cell therapy, where Type B firms exist without having any products on the market yet. Within therapeutic biopharmaceuticals there is in fact only one firm out of 11 Type B firms which already has developed and marketed a product as of 2003 (Affitech AS, with its monoclonal antibody Protein-L and technology platform for further discovery and engineering).[26]

Within diagnostics there are three major Type B firms, as described in Ch. 3. These firms may even perhaps be classified outside this schemata altogether, since they have a product portfolio, have grown into considerable sizes, and behave more like independent pharmaceutical firms in their own right. Within diagnostics there are two smaller Type A firms as well. Type A firms, not surprisingly, dominate the segment equipment and services.[27]

Table 6.4. Types of firms within Norwegian biopharmaceutical system.

Biotechnology category	Type A-firms	Type B-firms
Therapeutic biopharmaceuticals	**7**	**13**
- enzymes	4	4
- antisense	0	2
- monoclonal antibodies	1	1
- vaccines & antigens	2	4
- cell therapy	0	2
Diagnostics	**5**	**3**
- diagnostics	5	3
Equipment and services	**27**	**0**
- equipment	13	0
- services	14	0
Total	**39**	**16**

Source: Own assessment based on fieldwork (see Appendix 2 for further details.

[26] An additional firm, PhotoCure ASA, here classified as belonging to the vaccines and antigens group since it also has activities within this activity has marketed several products, but these are as far as we can evaluate within a different business area.

[27] Indeed some types of equipment invloves very large scale research project. This is, however, as far as we can see, not the case in the types of equipment hitherto developed and marketd by Norwegian firms.

Remembering the theoretical argumentation in Table 6.3, the resource needs of the Type A firms would in varying degrees be mostly related to co-operative or commercialisation networks and reputation/scientific visibility, and the policy target in terms of timing will mainly be the start-up phase. For Type B firms, the resource needs would in varying degrees be wider, and mostly related to acquiring and developing human resources on a continuous basis, have access to scientific competencies and techniques developed by academic research, and have access to capital markets. The main policy target in terms of timing would be various stages of the follow-up phase in addition to the start-up phase.

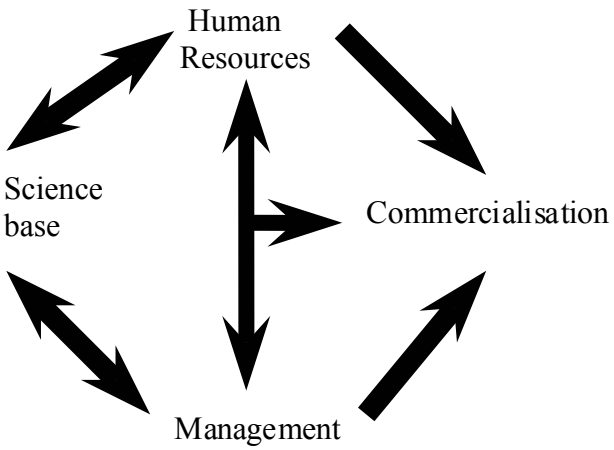
Nevertheless, one remaining overall observation is that the total number of firms is not extensive, and there is within the Type B firm population also a large proportion of firms still within the emerging phase. An overall concern should thus be to foster and maintain a critical mass of firms in order to benefit from clustering benefits. In contrast to the level of detail provided in Table 6.2., it is possible to summarise the four main factors that lead to current and potential persistent systemic failures in Norway as follows and as shown in Figure 6.1. This applies to the needs of the Type B firms and the emergence and maintenance of a biopharmaceutical innovation system with type B firms as main actors:

(1) absence of linkages between firms;
(2) lack of relevant human resources;
(3) lack of management skills; and
(4) lack of commercialisation abilities.

Assuming that the scientific set-out basis for the project is adequate, the crucial policy implication in this context is to focus on the need for facilitating linkages between each of the middle two factors, with the aim of enabling commercialisation of innovative products. Indeed, these linkages may be between partners in Norway and abroad (perhaps especially in other Scandinavian or North European countries),[28] and not only within the domestic context. But we will here for clarity's sake outline potential linkages in a mainly domestic context.

[28] It has been argued that biotechnology innovation systems in general and biopharmaceuticals systems in particular are inherently global, and not national, systems since knowledge invariably has to be sourced on a wide and cross-border basis (Bartholomew 1997; see also Narula 2003: 205).

Fig. 6.1.Factors relevant for linkages facilitation policy.



Linkages between firms may be relevant in terms of R&D or in connection with other collaboration efforts in order to compensate for the lack of large domestic firms, as well as in order to compensate for the lack of critical mass mentioned previously in the report. Such potential linkages are thus relevant in the cases of, firstly, domestic biopharmaceutical firms and foreign pharmaceutical firms with activities in Norway. Secondly, linkages of another type may be conceivable, namely linkages between the dedicated biopharmaceutical firms and domestic firms within the marine biotechnology sector in Norway. Although rather different in many respects (see Vol. II of this report on marine biotechnology) there might nevertheless be synergy effects from limited and carefully targeted linkages. Thirdly, a considerably different type of linkages might materialize provided the conditions are present, namely linkages between domestic, dedicated biopharmaceutical firms and domestic "national champions" within entirely different businesses (e.g. oil drilling, mechanical engineering). The role of policy-makers then becomes to evaluate the feasibility of facilitating such different types of linkages, and subsequently act as facilitators for the development and maintenance of selected linkage patterns.

The two input factors, lack of management skills and human resources, are, as identified in the report, identical to the two most prominent systemic failures. Science based firms are often lacking management skills, and there is thus a need for policies that facilitate learning and knowledge transfer between firms. Indeed there have existed programmes within this realm directed at SMEs, such as the BUNT programme. Learning by way of linkages may come as a supplement to such programmes. Such learning of management skills in a wide sense is especially relevant to the firms we deal with here due to the fact that biopharmaceutical firms are outside the main framework of Norwegian "locked-in" National System of Innovation, which is centred on oil-related and mechanical engineering businesses. Linkages to firms within this network may thus result in important assets for the firms in the forms of personal contacts, in addition to the learning outcome. In addition, therapeutic biopharmaceutical firms also stand partly outside the diagnostics industrial cluster in Norway, since the latter firms are focusing more on equipment and processes rather than biotechnical research and development per se.

In the case of human resources the situation is, as reviewed above, a coincidental post-1997 adequacy or even surplus of labour, but there will inevitably be a shortage in the medium or long term. Indeed, direct policy measures such as facilitating increased levels of life science graduates or making it easier for immigration of specialist labour may be warranted for. However, cross-cluster networking both between biopharmaceuticals and the traditional industries as well as between therapeutic biopharmaceuticals and diagnostics may be a valuable addendum and result in the utilization of a cross-sectoral mobility of labour which has hitherto been virtually non-existent.

The main goal of favouring such linkages is obviously the need for increasing the probability of commercialisation. The post-1997 generation of firms have generated some products by now, but there is in quantitative terms more products at the planning stage or in the pipeline rather than already launched products. For Type B firms this may be understandable in terms of the long development period needed, but an unavoidable issue is whether firms with feasible products-in-process will survive until they actually are able to launch the products themselves. There currently seems to be a vicious current leading from (a) the lack of products on the market, leading to (b) lack of trust from investors. This is especially so when investors might tend to refer to former generations of "blockbuster products", such as X-ray and ultrasound agents and the Ugelstad beads. If increased probability of commercialisation is the target, one of the main guiding issue in the Norwegian context and for Norwegian policies becomes to construct and maintain a critical mass (i.e. construct and maintain the biopharmaceutical system itself), and in such a process it might be necessary to think in terms of linkages such as outlined here.

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Appendix 1: The 2003 Biotechnology Use and Development Survey

Question #1 Biotechnology use

			IF YES				IF NO	
			Do you use them for:				Do you plan to use it within the next 5 years?	
Has your firm used the following biotechnologies since 1999?	***yes***	***no***	*Product/process development*	*Current production*	*Environmental purposes*	***Indicate the years in use since 1999***	***yes***	***no***
DNA: The coding (genomics, pharmaco-genetics, gene probes, DNA sequencing/synthesis/amplification, genetic engineering)								
Proteins and molecules: The functional blocks (protein/peptide sequencing/synthesis, lipid/protein glyco/engineering, proteomics, hormones and growth factors, cell receptors/signalling/ pherormones)								
Cell and tissue culture, and engineering (cell/tissue culture, tissue engineering, hybridisation, cellular fusion, vaccine/immune stimulants, embryo manipulation)								
Process biotechnologies (bioreactors, fermentation, bioprocessing, bioleaching, bio-pulping, bio-bleaching, bio-desulphurization, bio-remediation and, bio-filtration)								
Sub-cellular organisms (gene therapy, viral vectors)								

Question #2 Background information

When was your company established? _____

Is your firm a part of an enterprise group? (Enterprise group consists of a mother company and at least one daughter company; the mother company controls the daughter company by share of ownership)

Yes ☐ No ☐ If yes, what is the country of the home office? _____

	1999	2001	2002
Employment			
How many employees do your firm employ?			
Number of employees engaged full-time in biotechnology activities			
Number of employees engaged part-time in biotechnology activities			
Number of full time employees engaged in biotechnology R&D			
Number of part-time employees engaged in biotechnology R&D			
Financial characteristics			
Total firm sales/revenues from all sources			
% of revenues from biotechnology			
Total R&D spending			
% of total R&D spending on biotechnology R&D			

Question #3 Venture capital

How much capital was raised by your firm for biotechnology related purposes from 1999 to 2002?

Question #4 Innovative activities

	1999 to 2001		*2002 to 2003*		*Plans for 2003 to 2005*	
	Yes	***No***	***Yes***	***No***	***Yes***	***No***
a) Did you have biotechnology products/processes on the market?						
b) Did your firm develop products that require the use of biotechnologies?						
c) Did your firm develop processes that require the use of biotechnologies?						
d) Did you consider biotechnology central to your firm's activities or strategies?						

e) How many biotechnology products did or will your firm have in the following stage of development at the end of . . .	2001	2002	2003
Research and development			
Pre-clinical trials			
Regulatory phase			
Approved/ On the market/ In production			

Question #5 Obstacles to commercialisation

Rate the following obstacles to advancement of biotechnology commercialisation activities in your firm ***(scale of importance from 1 (low) to 5 (high)***

	1999					2003				
	1	2	3	4	5	1	2	3	4	5
Inputs										
Access to capital										
Access to technology/information										
Access to human resources										
Markets										
Domestic market too small										
Lack of access to international markets										
Lack of distribution and marketing channels										
Constraints										
Public perception/acceptance										
Regulatory requirements										
Time/cost										
Patent rights held by others										
Lack of patent protection										
Lack of appropriate sources of finance										
Excessive perceived economic risks										

Question #6 Public funding

Has your firm received any public financial support for innovation activities since 1999?

	1999-2001		2002-2003	
	Yes	No	Yes	No
Local or regional authorities (counties, municipalities)				
Central government (ministries, directorates, Norwegian Research Council, SND)				
The European Union (EU institutions)				

Question #7 Intellectual property protection

How many biotechnology-related patents or pending patents does your firm have in 2002?

Question #8 Collaborative arrangements from 1999 to present (see notes on page 4)

A. What organisations do you co-operate with in biotechnology[1] R&D? *(please mention your most important partners)*	**B. Since when does this co-operation exist?**	**C. In what country is your partner resident?**	**D. What is the type of co-operation?** *(please tick 1 or more of the following options)*							**E. What is the goal/reason of the co-operation?** *(please tick 1 or more of the following options)*					
Name *(* if you wish to keep your partner's name secret then just tick the type of organisation)*	Year	Country name	Joint venture[1]	Joint R&D projects[2]	R&D contract / Research funding[3]	Licensing[4]	R&D outsourcing[5]	Exchange of employees	Other	Scientific (basic) research	Development of products	Development of processes	Development of (research) techniques	(Pre) clinical research	Non R&D (manufacturing/marketing/sales)
Research organisations[6]															
1															
2															
3															
4															
5															
Large enterprises (>500 employees)															
1															
2															
3															
4															
5															
Small and medium sized enterprises (<500 employees)															
1															
2															
3															
4															
5															
Other organisations															
1															
2															
3															
4															
5															

Notes for Question #8

1. This is a firm's decision to establish a formal joint venture with equity involvement. A third corporation is created with a definitive objective of innovation. 2. Agreement between partners to jointly carry out research and development on a definite technology or technological discipline. This mostly regards joint projects in which both partners contribute e.g. in the sense of finance, technology and/or research capacity. Important characteristic is that often both partners set the project's goals, means, methods etc. There is no equity involvement. 3. This regards a firm's decision to participate in another organisation's (exploratory) research and development activities to pursue opportunities and ideas for innovation by providing financial means. Dependent on the extent of financing, the firm will mostly not become (sole) proprietor of the research outcomes. The financing firm only has a limited influence on the project set-up. 4. This includes licensing in, licensing out or cross licensing of specific technologies. 5. This regards a firm's decision to externalise a part of its R&D activities to another organisation. Mostly in this situation, the outsourcing firm will become the (sole) proprietor of the research outcomes as it simply acquires the relevant output. Examples are the involvement of clinical trial organisations and of commercial laboratories. 7: This includes universities and (semi) public research organisations.

Appendix 2: Overview of biopharmaceutical and related firms in Norway.

Part A: Explanatory notes.

Table A2-1

Category	Activity area	Notes
Hormones and enzymes	Fertility hormones	
	Enzymes	
	Human growth hormones	
	Human insulins	
	Tissue plasminogen activators	
	Thyroid stimulating hormone	
	Dnase	
	Blood clotting factors	
Cytokines	Colony stimulating factors	
	Interleukins	
	Interferons	Proteins interfering with a cell's ability to produce, and serving as basis for drugs for osteoporosis, multiple sclerosis, and other diseases
Vaccines & antigens	Vaccines/antigens	Recombinant antigen vaccines where the antigen is produced in bacteria or yeast rather than extracting it from chronic human or animal carriers (e.g. hepatitis B); recombinant vector vaccines using weakened viruses; DNA vaccines; RNA vaccines.
Monoclonal antibodies ("MAbs")	Monoclonal antibodies	Laboratory made version of the naturally occurring protein that binds to and neutralizes foreign invaders. I.e. individual antibodies for recognizing and binding to foreign invaders, singling them out for elimination by immune defences.
Antisense	Antisense	Drugs which interfere with the communication process that tells a cell to produce an unwanted protein. I.e. peptides (macro-molecules composed of 50 amino acids or less) which interfere with the production of a specific protein by binding to its mRNA.
Cell therapy	Cell/tissue therapy	

Source: Bibby et al (2003) (category and activity) and misc. medicinal literature (notes).

In this appendix we attempt to map the current biopharmaceutical firm population based in Norway according to activity area, types of firm. Firstly, the firms are classified according to the categories and activity area regarding therapeutic biopharmaceuticals (cf. Table A2-1):

Secondly, we add include firms within a category which is not the main focus of the national reports within this project, but which we have nevertheless included due to its strong presence in Norway, diagnostics (Table A2-2).

Table A2-2

Category
Diagnostics

Thirdly, the table includes one category which consists of miscellaneous equipment development and service functions (Table A2-3).

Table A2-3

Category	Activity area
Equipment	Misc. equipment
	Bioinformatics software
Services	Databases/data mining tools
	Biobanks
	Sequencing etc.

The overview contains also information regarding the firm and its products (Table A2-4):

Table A2-4

Firm	Address	Type	Est.	Emp.	Product(s)
Name of firm and any information about its organizational mode (subsidiary v independent etc.)	Internet address	A versus B type of firm, as discussed in Ch. 6 of the report regarding different types of firms classified according to the size of their innovation project.	Year of establish-ment	Number of employees in 2002	Product(s) in development and/or on market as of 2002

The information collected on financial matters is uneven and complicated, and is therefore not included.

Sources are: Materials from Norwegian Bioindustry Association, field notes/surevy responses, and firm home pages.

Part B: Overview of dedicated and diversified enterprises in Norway according to biopharmaceutical categories

Category	Activity	Firm	Address	Est.	Emp.	Product(s)
Hormones and enzymes	Enzymes	Biotec Pharmacon ASA	www.biotec.no	1990	48	Bioactivite compounds & DNA modifying marine based enzymes. Candidate in Phase II (2003)
		Ami Go As				Splitting fish protein into free amino acid by using enzymatic methods.
		Aqua Biotech Technology AS				Enzymes
		Thia Medica AS (UiB-spin-off)	-			Modified fatty acid (TTA) for metabolic disorders
		Clavis Pharma AS	www.clavispharma.com	2001	8	Lipid Vector Technology involving the chemical binding of specific fatty acids to pharmaceutical agents, thereby creating new chemical entities with improved biological properties such as increased cellular uptake, reduced toxicity and slow release of the active compound. (application: skin cancer, lung cancer)..

Category	Activity	Firm	Address	Est.	Emp.	Product(s)
Hormones and enzymes (cont.)	Enzymes (cont.)	FMC Biopolymer AS (subsidiary of MNC)	www.fmcbiopolymer.com			Biopolymers (alginates and carrageenans) processed from seaweeds and microcrystalline cellulose processed from specialty grades of pulp.
		Biotec ASA				Immutol Beta Glucan
		Promar Aqua AS				Algae production for medicinal use
	Fertility hormones	- No firms -	-	-	-	-
	Human growth hormones	- No firms -	-	-	-	-
	Human insulins	- No firms -	-	-	-	-
	Tissue plasminogen activators	- No firms -	-	-	-	-
	Thyroid stimulating hormone	- No firms -	-	-	-	-
	Dnase	- No firms -	-	-	-	-
	Blood clotting factors	- No firms -	-	-	-	-
Cytokines	Colony stimulating factors	- No firms -	-	-	-	-
	Interleukins	- No firms -	-	-	-	-
	Interferons	- No firms -	-	-	-	-

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Vaccines & antigens	Vaccines/ Antigens	GemVax AS	www.gemvax.com	2001 ***	2	Cancer vaccine-related not yet on market
		Alpharma AS	www.alpharma.com			Antibiotics; vaccines
		Intervet Norbio AS	www.intervet.com	1985	29	Fish health related 10 products in development, 10 products on market. .
		Scanvacc				
		Inovio AS	www.inovio.com	1999	5	Gene delivery technology for skeletal muscles (detection of animal immunogenic antigens and validation of monoclonal antibody candidates/gene therapy product candidates). 1 product on market .
		PhotoCure, ASA				Including relevance to gene therapy and cancer vaccines, but main focus elsewhere (photodynamic technologies for detecting skin cancer and other skin diseases, internal e.g. bladder cancer).

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Monoclonal antibodies	Monoclonal antibodies	Diatec.com AS	www.diatec.com			Custom production of MAbs
		Affitech AS	www.affitech.com	1997	23	Drug development in cancer and infectious diseases using engineering of monoclonal antibodies, and affinity chromatography based on Protein L
Antisense	Antisense	Lauras AS	www.lauras.no	1998	7	HIV therapy based on immune stimulation. 2 products in development, 0 on market.
		Bionor Immuno AS	www.bionorimmuno.com			HIV, two candidates with one in Phase I (2003)
Cell therapy	Cell/tissue therapy	PCI Biotech AS (Subsidiary of PhotoCure AS)	www.pcibiotech.com	2000	5	Technology for transporting macromolecules into living cells. 13 in development, 0 on market.
		Algeta AS	www.algeta.com	1997	10	Alpharadin alpha emitting anticancer radiopharmaceutical (targeting skeletal metastases from prostate and breast cancer)

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Diagnostics	Diagnostics	Axis-Shield ASA	www.axis-shield.com	1999 *	80	Medical diagnostics products
		Amersham Health AS	www.amershamhealth.no	1997 **	1000 (>10)	Medical imaging, i.e. in vivo detection of disease.(soft tissue level and, increasingly, changes at cell level)
		Bionor AS	www.bionor.com	1985		Diagnostic products incl. HIV test kit
		Dynal Biotech ASA	www.dynalbiotech.com	1986	278	A. Monosized magnetic (Dynabeads) and monosized non-magnetic (Dynospheres) particles for immunology, biological and clinical research and in vitro diagnostics. B. Sample preparation etc.
		Genpoint AS	www.genpoint.no	1999	11	Diagnostics kits/tests; sample preparation; 2 products on market as of 2002 (3 as of 2003)
		DiaGenic AS	www.diagenic.com	1998	10	Gene expression: method for early detection of breast cancer etc.
		Norsk Senter for Gastro-intestinal				
		Biosense Laboratories A/S	www.biosense.no			Vitellogenin (Vtg) ELISA Kits, for quantification oestrogen effects in fish, etc.

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Equipment	Misc.	NorChip AS	www.norchip.com	1998	20	RNA & proteins detection kits. 5 products in development, 1 on market.
		Optinose AS	www.optinose.com			Devices for nasal delivery of vaccines etc.
		Techcap International AS/Biolink	www.techcap.no			Phytochemicals
		MedProbe AS	www.medprobe.com			Research reagents and custom services
		Biodetect AS	www.biodetect.biz			Bacteria detection instruments
		Biomolex AS	www.biomolex.com			Isotope based camera for gene expression
		Polarization Technology AS	www.polarizationtechnology.no			Fluorescence polarization immunoassay measurement systems
		Promar Aqua AS		2000		Photosynthesis bioreactor for production of microalgae
		NeoRad AS				Device for computed tomography procedures
		Optoflow				

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Equipment (cont.)	Bioinformatics software	Sencel Bioinformatics	http://www.sencel.com	2001		Software tools for genomic research and diagnostics
		Interagon (Invested by Fast Search & Transfer ASA & others)	www.interagon.com			Development of processor technology for use in classification of biological data
		MolMine AS	www.molmine.com	2000		Software for data anlysis in biotechnology research
Services	Databases/data mining tools	PubGene AS	www.pubgene.com			Genomics and proteomics data
	Biobanks	Cancer registry of Norway (Public agency)				Biobank
		Norwegian Biobank				Biobank
		GeNova AS	www.genova.no ?			Biobank and dev. tools for gene therapy
		Cattles/Bovibank AS				Animal breeding-related (cattle)
		Geno	www.geno.no			Animal breeding-related (cattle)
		Norsvin				Animal breeding-related (pigs)

Category	Activity	Firm	Address	Est.	Emp.	Prod.
Services (cont.)	Sequencing & other supplies/ services	Lingvitae AS	www.completegen.com			Method for DNA sequencing
		G&T Septech AS (UiO-spin-off)	www.gtseptech.no	1997		Micro-HPLC columns; competence in chromatography and analytical sample preparation
		GenoVision (acq. by Qiagen in 2002)	www.genovision.com	1998/ 2002		HLA/tissue typing
		TraceTag Nordic AS	www.tracetag.com	1996	12	DNA marking and tracing
		Telelab As	www.telelab.no			Contract clinical diagnostic services
		Biosentrum AS	www.biosentrum.com	1997	6	Contract fermentation
		UniTargetingResearch AS	www.unitargeting.com	2001	8	Cell-factory technology for protein production

* date for merger between Axis Biochemicals (Norway) est. 1985 and Shield Diagnostics (UK) est. 1982.
** date of merger with Amersham
*** part of larger company before that

Appendix 3: Main authorship responsibilities.

	Dobos, E.	Grønning, T.	Knell, M.	Olsen, D.S.	Veistein, B.K.
Chapter 1: Introduction					
1.1 Background and goals.		•	•		
1.2 Approach.	•	•	•		
1.3 Main traits of the Norwegian economy			•		
Chapter 2: Overview of national R&D, technology and innovation policies for biotechnology					
2.1 Main actors involved in policy making and policy programme management	•	•			•
2.2 Main vertical policies and most important horizontal policies	•	•			
Chapter 3. Structure, dynamics and performance of the biopharmaceutical system					
3.1 National public R&D system	•	•	•	•	
3.2 Business system	•	•	•		
3.3 Performance			•		
Chapter 4: Innovation barriers /drivers – Framework conditions					
4.1 Knowledge sources			•		
4.2 Human resources			•		
4. 3 Private finance and venture capital	•		•		
4.4 Regulations for biotechnology	•		•		
4.5 Entrepreneurship.			•		
4.6 Innovation barriers/drivers.			•		
Chapter 5. Demand Side Factors					
5. 1 Organisation of national health care system	•	•			
5.2 Regulations	•				
5.3 Role of users	•	•			
5.4 Lead market features		•			
5. 5 Socio-economic / ethical aspects	•	•			
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