European Foundation for the Improvement of Living and Working Conditions

Trends and drivers of change in the biomedical healthcare sector in Europe: Mapping report

emcc european monitoring centre on change

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Introduction

Modern biotechnology is one of the key enabling technologies of the 21st century. In relation to human health, biotechnology could potentially prevent, treat and cure a wide range of diseases – some of which today are considered to be 'incurable'; among these are heart conditions, multiple sclerosis, breast cancer, cystic fibrosis and leukaemia.[1] The potential of biotech in relation to the development of better and more accurate diagnostics and for designing improved therapies and vaccines is well recognised by the biotechnology industry.

The group of companies that use biotechnology to develop and/or manufacture products for the treatment of human beings is sometimes referred to as the 'biomedical healthcare sector' (EMCC, 2006; a more specific delineation of this sector is given in the chapter on methodology).

Biomedical healthcare in Europe

According to a recent survey, 51% of European biotechnology companies are involved in health-related activities, while other sources estimate that over 80% of biotechnology activity in Europe is healthcare-related.[2]

The importance of the biomedical healthcare sector in relation to the pharmaceutical industry is also growing: Medicines deriving from biotech innovations (biopharmaceuticals) are estimated to account for approximately 20% of all marketed medicines, and represent around 50% of all new medicines in the pipeline.[3]

In a European policy context, the biomedical sector offers a potential for establishing a knowledge base which may contribute to Europe's competitiveness in the world market. This makes biotechnology vital in the context of realising the major European goal of becoming 'the most competitive and dynamic knowledge-based economy in the world capable of sustainable economic growth with more and better jobs and greater social cohesion and respect for the environment'.[4]

Aim of the mapping report

The present mapping report is part of a study on the biomedical healthcare sector. In addition to the present report, the study features four case studies, two cluster case studies as well as four scenarios. The study aims at improving the understanding and anticipation of change in the biomedical healthcare sector in Europe.

The purpose of this mapping report is to give a concise overview of the biomedical healthcare sector and to identify the main trends and key drivers of change in the industry. A SWOT analysis is carried out as a part of the mapping report.

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[1] EuropaBio, *Healthcare Manifesto*, **http://www.healthcare-manifesto.org/intro.html**

[2] European Commission, MEMO/05/389, 2005, **http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/05/389&format=HTML&aged=0&language=EN&guiLanguage=fr**

[3] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_facts.htm**

[4] Günter Verheugen, Vice-President of the European Commission, *Biotechnology's Contribution to an Innovative and Competitive Europe*, Concluding Session of the European Track, Lyon, 14 April, 2005, **http://europa.eu/rapid/pressReleasesAction.do?reference=SPEECH/05/226&format=HTML&aged=0&language=EN&guiLanguage=en**

Methodological considerations

One of the main challenges in relation to the present sector study is that the sector is not well defined. In order to evaluate the future economic and labour market potential of the sector, statistics on past performance of the sector are required. However, the sector does not exist in statistical terms, insofar as the companies in it are included in several different statistical categories in the European NACE codes of industrial sectors and sub-sectors.

Biomedical sector and biotechnology

While broad definitions are useful in relation to capturing the comprehensiveness of a sector (i.e. by including companies from related or supplying sectors that may be involved in biotech-related activities), narrow definitions are useful when trying to determine which companies are and are not in fact engaged in biomedical research and production thus providing a picture of the core of European biotech activities.

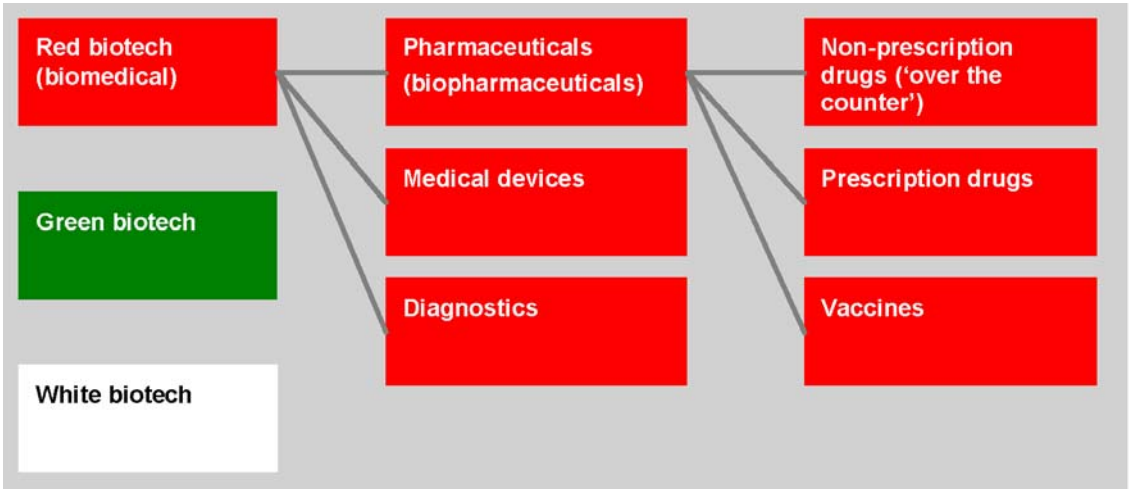
Starting from an observation, that the term 'biomedical' is used to refer to biotechnology-derived medical instruments, devices and other products that are primarily purchased by the medical field, this report first looks at what defines biotechnology.

Biotechnology can be defined as 'the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or nonliving materials for the production of knowledge, goods and services' (OECD, 2005).

Defining the biomedical healthcare sector

Biotechnology dedicated to the treatment of human beings is often referred to as 'red biotechnology'. This includes the diagnosis of health risks and the prevention and treatment of illnesses (EMCC, 2006). 'Green' and 'white' biotechnology on the other hand refer to the use of biotechnology in agriculture (e.g. making plants resistant to certain diseases) or for industrial purposes (e.g. environment-friendly washing powder).

Figure 1: *The biomedical healthcare sector – technologies and products*



Red biotech can be further divided into three sub-sectors: pharmaceuticals, medical devices and diagnostics based on biotechnology. Furthermore, pharmaceuticals can be divided into prescription drugs sold in pharmacies and to hospitals, and non-prescription drugs sold to individual customers via retail chains, etc. Pharmaceuticals also include vaccines that are sold to national institutions such as the military.

Whereas it is fairly easy to describe the sector from a technology perspective or a product perspective, it becomes more difficult from the commercial perspective. There are several reasons for this:

1. **Companies producing biotechnological products are not necessarily biotech companies.** According to the EuropaBio study, the number of pure-play biotechnology companies in the agricultural and environmental sectors is extremely limited; however biotechnology-based techniques are both a widespread and an increasingly vital part of the technology mix in those sectors (EuropaBio, 2006).
2. **Biotechnology companies are not necessarily 'red', 'green' or 'white'.** Often they develop and employ technologies which are generic in nature and potentially relevant for agriculture or industrial production as well as human health. For example, Direvo Biotech AG[5] generates and optimises proteins and enzymes for industrial applications and for human healthcare. In other cases, companies 'migrate' from one sector to other sectors, e.g. when Novozymes – a white biotech company – enters the market for biopharmaceuticals. As a consequence, a mapping of all red biotechnology activities in Europe will include companies that are also 'green' and 'white'.
3. **Not all employment or R&D in companies belonging to the population of 'biotechnology' firms is 'biotechnology related'.** It is perhaps a reasonable assumption for small firms, but it is not without problems when it comes to large multinational firms for which biotechnology could be only a small part of their total R&D, employment or sales (ETEPS, 2006).

Value chain

The biomedical healthcare sector relies on a wide range of supporting sectors and interacts with public administrations in all phases of the development, manufacturing and selling of a product. Thus, to some extent the sector – or biotechnology in general – can be understood as a system or network. Innovative activities, as well as production and commercialisation, rest on and involve, either directly or indirectly, a large variety of actors: different types of firms, research organisations like universities and non-industrial research centres, financial institutions, regulatory authorities, healthcare systems, consumers, etc.[6]

[5] Direvo Biotech AG website, **http://www.direvo.com/company/**

[6] Allansdottir et al., Innovation and competitiveness in European biotechnology, 2002, **http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_07_2002.pdf**

Figure 2: *The value chain*

Typology

The literature review does not point to any generally accepted way to categorise companies in the biomedical healthcare sector. This study has therefore developed a typology based on the following aspects: size of the company; position in the value chain; and sub-sector/markets. On this basis, the study identifies the four types of companies described in Table 1 below.

Table 1: *Description of company types in the biomedical healthcare sector*

Company type	Description
The small knowledge supplier	This type of company is small and focused on research. The company supplies knowledge and development services to other biomedical companies or the pharmaceutical industry. If the company takes products to the market, it is in strategic partnership with other companies.
The full-blown biomedical healthcare company	This medium-sized or large company covers the whole value chain, e.g. undertakes R&D activities and manufacturing of the company's own products. Companies are typically specialised within one type of disease.
The service company	This type of company does not undertake R&D activities but offers assistance in clinical trials or manufacturing of substances on a contract basis to other companies (e.g. clinical research organisation or contract manufacturing organisation).
The healthcare giant	The very large research and production company with a broad portfolio (i.e. focuses on a range of different types of diseases). Biotechnology-derived products constitute a growing part of the company's portfolio. However, the company does not necessarily conduct biomedical R&D on its own, but cooperates with small knowledge suppliers on a licensed-in basis.

Depending on size, role in the value chain, and sub-sector (pharmaceuticals vs diagnostics) and even diseases (cancer vs inflammation) within the same sub-sector (pharmaceuticals) the challenges facing companies vary. These challenges will be further highlighted through the four company case studies which form part of this sector study.

Data sources

In the official statistics such as Eurostat, biomedical companies (and also green and white biotechnological companies) are indistinguishable from non-biomedical companies (pharmaceutical industry, chemical industry, etc.), and therefore no official 'hard data' are available for this specific sector. Instead, the study of the biomedical sector has to rely on

official statistics covering more than the biomedical healthcare sector and analyses covering the pharmaceutical industry or specific studies of the European biotechnological industry as a whole.

The mapping report is based on reports, articles and web sites from amongst others: EMCC, EuropaBio, EFPIA, OECD, the European Commission, national and international research institutions, scientific journals and consultancies. In addition, stakeholders and experts have reviewed the mapping report in order to develop and validate the findings.

The OECD provides comparable country data on biotechnology activities, and EuropaBio's survey from 2006 is also of interest to this study (EuropaBio, *Biotechnology in Europe: 2006 Comparative study*). The study deals with the whole biotechnology industry and provides very few figures specifically about biomedical healthcare. However, the findings and conclusions of the study should be applicable to the biomedical healthcare sector, since this is the most prominent sub-sector of the biotechnology industry (EMCC, 2006).

The mapping report intends to provide a statistical overview over the sector. For this purpose, data from EuropaBio and Eurostat are considered to be the best available data. However, in relation to the collection of Eurostat data, it is necessary to identify relevant NACE codes.

Selecting relevant NACE codes

A survey of (Danish) companies in Medicon Valley,[7] one of Europe's strongest life science clusters located in the Danish/Swedish Øresund region indicate that 15 different NACE codes are relevant for the statistical mapping of the sector. These 15 NACE codes have been cross-checked with codes included in a life science cluster study from Montana, USA .[8]

Table 2: *Overview over biomedical-related NACE codes*

NACE code	Description [9]	No. of companies in Medicon Valley	Included in Montana study
244100	Manufacture of basic pharmaceutical products	6	X
244200	Manufacture of pharmaceutical preparations	4	X
246600	Manufacture of other chemical products	3	X
332090	Manufacture of instruments and appliances for measuring, checking, testing, navigating and other purposes, except industrial process control equipment	1	–
366390	Other manufacturing	1	–
514600	Wholesale of pharmaceutical goods	7	–
518790	Wholesale of other machinery for use in industry, trade and navigation	1	–
519000	Other wholesale	1	–
722200	Other software consultancy and supply	1	–
730000	Research and development	46	X
741490	Business and management consultancy activities	2	–
742090	Architectural and engineering activities and related technical consultancy	3	–
748790	Other business activities	1	–
851490	Other human health activities	1	–
980000	Not specified	1	–

[7] Medicon Valley website, **http://www.mediconvalley.com/**

[8] The only NACE code from the Montana study not represented in the Medicon Valley survey is 23.30 – Processing of nuclear fuel – radioactive in vivo diagnostic substances (Regional Technology Strategies, Inc. 2003).

[9] RAMON - Eurostat's Metadata Server, **http://ec.europa.eu/eurostat/ramon/index.cfm?TargetUrl=DSP_PUB_WELC**

Since all the NACE categories obviously include companies that do not belong to the biomedical healthcare sector, mapping the sector on the basis of these NACE codes will tend to grossly overestimate the sector's size. Consider, for example, the categories 'other wholesale' and 'research and development', which both include a vast number of companies having no relation whatsoever to the biomedical healthcare sector.

According to EuropaBio's recent survey of 18 European countries, the number of biotechnology companies in Europe is 2,163. Of these companies, 37% are in the human healthcare sector. The survey includes only companies 'whose primary commercial activity depends on the application of biological organisms, systems or processes, or on the provision of specialist services to facilitate the understanding thereof'.[10]

In contrast, as we can see from the table above, the total number of companies within the actual NACE codes used by biomedical healthcare companies is well in excess of 310,000, i.e. more than a hundred times as large. But given that these codes include very large segments of industry and trade which are totally unrelated to the biomedical healthcare sector, it is not meaningful – it may indeed prove very misleading – to draw statistical evidence from all these NACE codes.

The best alternative approach is to select the most relevant NACE codes. The following four NACE codes have been selected, based on their relation to main parts of the biomedical value chain:

Table 3: *NACE codes included in the present mapping exercise*

Sector	NACE	Title
Industry	244100	Manufacture of basic pharmaceutical products
	244200	Manufacture of pharmaceutical preparations
Trade	514600	Wholesale of pharmaceutical goods
Services	730000	Research and development

Conclusions based on these four NACE codes still need to be conservative, since the selected NACE codes also include non-biomedical companies, resulting in an overestimation of the sector's size. Existing sector studies such as EuropaBio's survey of the European biotechnology companies will on the other hand tend to underestimate the sector since relevant companies are not part of the survey.[11] As a result, the 'true' size of the biomedical sector is probably somewhere in between.

[10] EuropaBio, *Biotechnology in Europe: 2006 Comparative study*, 2006, **http://www.europabio.org/CriticalI2006/Critical2006.pdf**

[11] The survey includes only companies whose primary commercial activity depends on the application of biological organisms, systems or processes, or on the provision of specialist services to facilitate the understanding thereof. As a result, clinical research organisations, suppliers of biological reagents for research purposes, medical device companies, and those drug companies which use little biology are not included in the survey. The survey also excludes consultancies, technology transfer organisations, incubator centres, investors in biotechnology companies, and organisations that are active in biotechnology companies but which do but do not have a formal corporate legal identity. Furthermore, big pharmaceutical companies, other major corporations, and companies for whom biotechnology is an important but, nonetheless, minor part of their business, are not included in the study. However, dedicated biotechnology subsidiaries of major corporations are included (EuropaBio, 2006).

Overview of the sector

Biomedical companies engage in an expensive and long-term endeavour – especially if they work with drugs. Drug development can cost between 400 and 900 million US-Dollars for a single product. It is also a risky business: The failure probabilities are 80–90% in the first phases of clinical trials and time-to-market can reach 15 years. Data on product attrition rates indicate that the probability of a drug candidate passing from pre-clinical stages to market is 6% or less.[12]

The biomedical healthcare sector is a knowledge-intensive sector that benefits from networking and collaboration. Networked firms and firms that collaborate are quicker to generate discoveries and commercialise products than firms that do not network. They also have better access to technical information, capital and alliance opportunities (Massachusetts Biotechnology Council & the Boston Consulting Group, 2002).

Importance to the European economy

The biomedical healthcare sector is a relatively small sector in the EU. According to a study of the biomedical healthcare sector, the sector's total revenue in 2003 amounted to 10 billion euro.[13] On the other hand, the biomedical healthcare sector is a source of innovation in other sectors such as the pharmaceutical industry and the food and beverage industry ('functional foods'), and thus the real contribution to the European economy is presumably larger than the estimated 10 billion euro.

The European biotechnology industry is lagging behind the biotechnology industry in the US. Although there are approximately the same number of companies in the two regions, the US biotechnology industry employs almost twice as many people and generates more than twice the revenue of the European industry.

The difference between Europe and the US is even more notable when comparing the development and production of biopharmaceuticals:

Table 4: *Biopharmaceuticals in the EU and the US (2005)*

	NACE	Title
Revenue (€ million)	7,862	38,413
Number of employees	33,340	137,400

Source: *EFPIA, the Pharmaceutical Industry in Figures, 2006*

Size of the sector

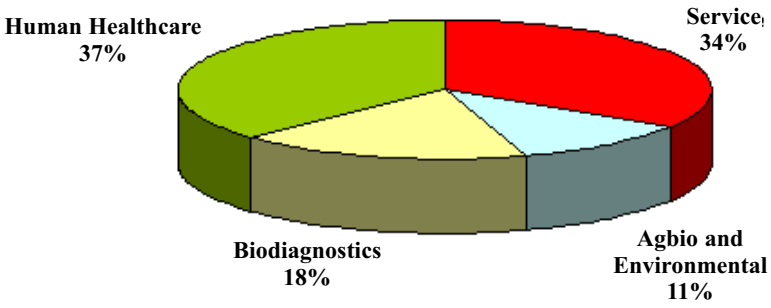
A recent survey conducted by EuropaBio identified 2,163 companies in the European biotechnology industry. The biotechnology industry in general is a very research-intensive sector with 44% of all employees employed in R&D functions (EuropaBio, 2006).

[12] The Innovative Medicines Initiative, *Strategic Research Agenda: Creating biomedical R&D leadership for Europe to benefit patients and society*, **http://ec.europa.eu/research/fp6/pdf/innovative_medicines_sra_final_draft_en.pdf**

[13] European Foundation for the Improvement of Living and Working Conditions, *The biomedical healthcare sector – what future?*, 2006.

Furthermore, the survey revealed that more than 800 biotechnology companies employing more than 50,000 people are involved in healthcare-related activities.[14] This figure does not include biodiagnostics, so the share of biotechnology companies involved in healthcare is probably higher.[15] Other sources estimate that over 80% of biotechnology activity in Europe is healthcare-related.[16]

Figure 3: *European Biotechnology companies by sub-sector*



Source: *EuropaBio, Biotechnology in Europe: 2006 Comparative study, 2006*

Germany, the UK and France account for the largest number of biotechnology companies in Europe. This is not surprising given the relative size of these three countries. On the other hand, relatively small Member States such as Sweden, the Netherlands and Denmark account for a significant number of companies given their size. The distribution of companies across Europe is shown in Figure 4 below.

According to EuropaBio, the number of US biotechnology companies increased by 1% from 2003 to 2004, while the number of European biotechnology companies declined by 2% during the same period. However, there are substantial national differences between the European countries. Greece (+25%), Italy (+19%), Ireland (+17%), and Spain (+16%) have experienced a significant increase in the number of companies, while Sweden (–9%), the UK (–6%), Germany (–6%), and Norway (–5%) are among the countries that have experienced the largest decline (EuropaBio, 2006).

Eurostat data for the biomedical-related sectors show that the number of companies in biomedical-related sectors reached 65,069 in 2004. R&D accounted for the largest share of the enterprises in the sectors (53%), while wholesale and manufacturing accounted for 41% and 6% respectively.[17]

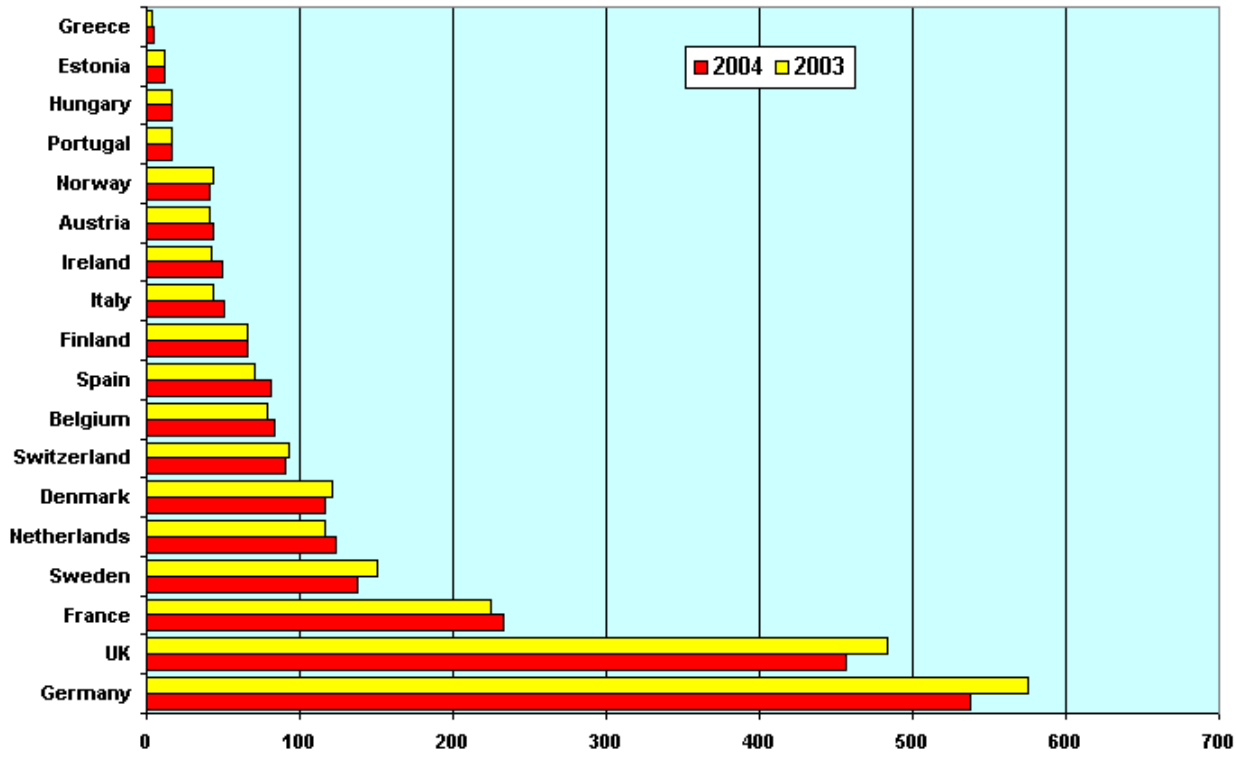
[14] Defined as biomaterials, drug delivery, drug discovery, gene therapy or healthcare cell therapy, genomics, vaccines and red biotech.

[15] EuropaBio, *Biotechnology in Europe: 2006 Comparative study*, 2006.

[16] *Biotech: Unleashing the enormous potential*, **http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/1324&format=HTML&aged=0&language=EN&guiLanguage=en**

[17] Data covers 23 EU Member States: Belgium, Bulgaria, the Czech Republic, Denmark, Germany, Estonia, Ireland, Spain, France, Italy, Latvia, Lithuania, Hungary, the Netherlands, Austria, Poland, Portugal, Romania, Slovenia, Slovakia, Finland, Sweden and the United Kingdom. However, data series for manufacturing are often not complete and thus will tend to underestimate the relative size of industry vis-à-vis R&D and wholesale.

Figure 4: *Distribution of biotechnology companies in European countries*



Source: *EuropaBio, Biotechnology in Europe: 2006 Comparative study, 2006*

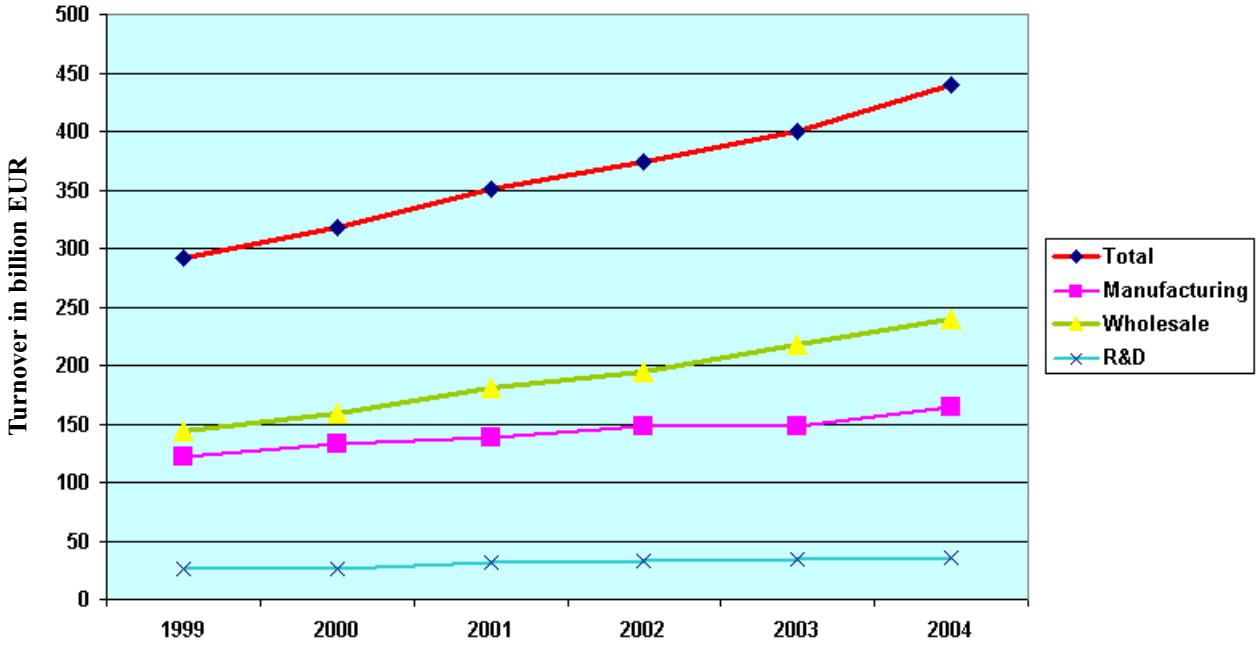
Turnover

Total turnover in the biomedical-related sector reached close to 440 billion euro in 2004. The share of R&D activities in total turnover is relatively small – only 8%. Wholesale accounted for the largest share of total turnover in 2004 (55%), while manufacturing accounted for 37% of total turnover.[18]

Turnover has been steadily increasing in the biomedical-related sectors since 1999 as shown in Figure 5 below. Growth rates have been highest in wholesale (67% increase in turnover from 1999 to 2004), while manufacturing and R&D has shown more 'modest' growth rates (34% and 36% from 1999 to 2004 respectively).

[18] Data covers 19 EU Member States: Bulgaria, Denmark, Germany, Ireland, Spain, France, Italy, Latvia, Hungary, the Netherlands, Austria, Poland, Portugal, Romania, Slovenia, Slovakia, Finland, Sweden and the United Kingdom. However, data series for manufacturing are often not complete and thus will tend to underestimate the relative size of industry vis-à-vis R&D and wholesale.

Figure 5: *Changes in turnover in biomedical healthcare-related sectors, 1999–2004*



Source: *Eurostat*

Employment structure

According to EuropaBio, biomedical companies employed around 96,500 people in 2004, but this number has been bigger since the European red biotech sector saw a 6% decline in total employment and an 8% decline in R&D employment between 2002 and 2003 (EuropaBio, 2005).[19]

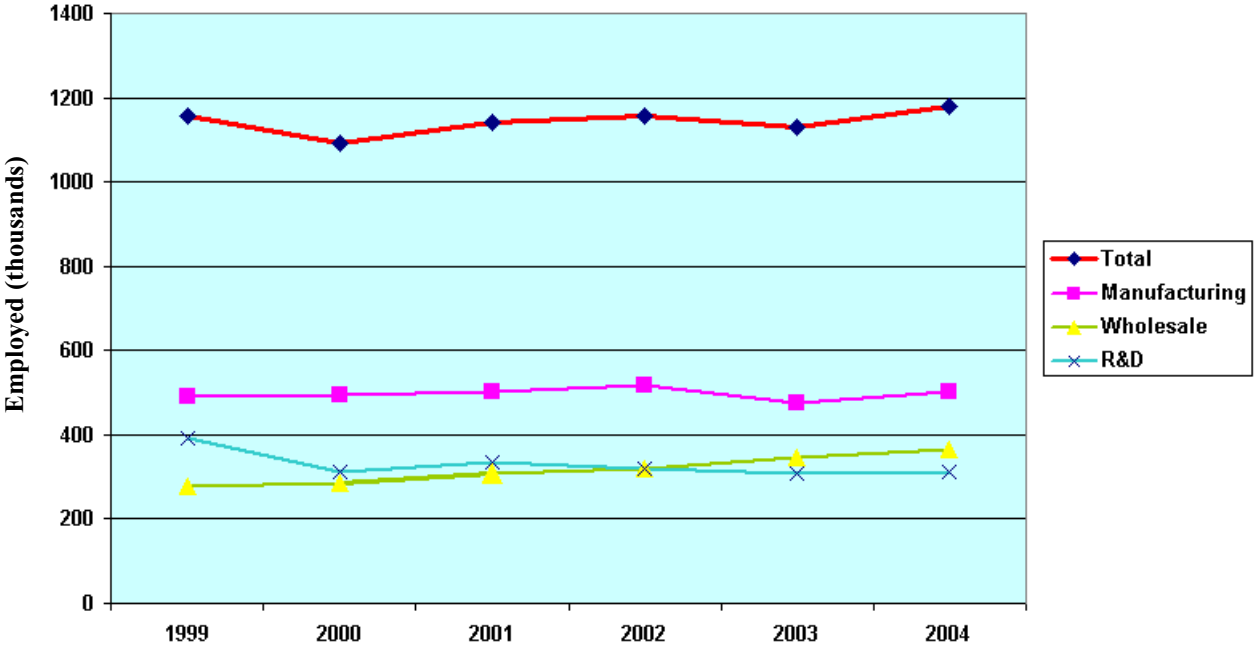
According to Eurostat, the number of employees in 2004 in biomedical-related sectors was 1,180,045. Manufacturing accounted for 42% of all the employees in the biomedical-related sectors, while wholesale and R&D accounted for 31% and 27% respectively[20].

Total employment in the sector has fluctuated in the biomedical-related sectors in recent years, but in 2004 employment for the first time since 1999 increased above the 1999 level. The development is illustrated in Figure 6 below.

[19] This conclusion is based on data covering seven countries due to limited availability of country-specific data.

[20] Data covers 18 EU Member States: Bulgaria, Denmark, Germany, Ireland, Spain, France, Italy, Latvia, Hungary, Austria, Poland, Portugal, Romania, Slovenia, Slovakia, Finland, Sweden and the United Kingdom. However, data series for manufacturing are often not complete and thus will tend to underestimate the relative size of industry vis-à-vis R&D and wholesale.

Figure 6: *Changes in employment in biomedical healthcare-related sectors, 1999–2004*

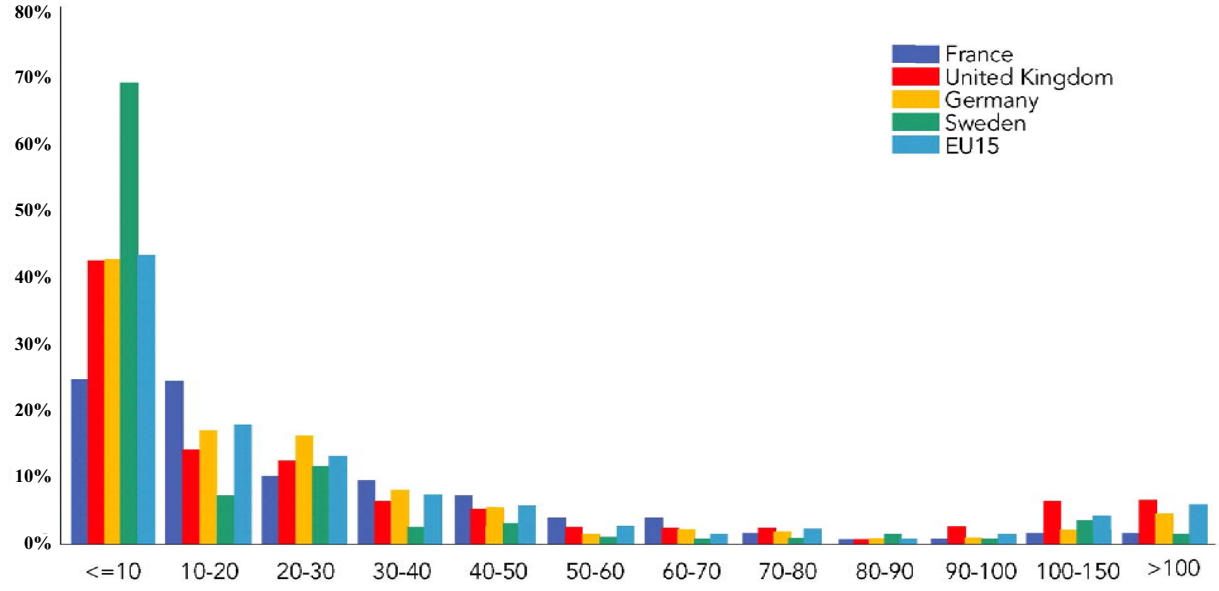


Source: *Eurostat*

Market structure

The European biotech sector is dominated by young and small companies: 55% are less than 5 years old[21] and most European biotechnology companies are micro-enterprises with fewer than 10 employees or small, with fewer than 50 employees. Just 10% of the companies have more than 50 employees.

Figure 7: *Biotechnology companies by size class (number of employees), 2001*



Source: *EuropaBio website,* **http://www.europabio.org/images/EmploymentHR.jpg**

[21] EurActive, European biotech industry pressed by lack of funding, 6 December 2006, **http://www.euractiv.com/en/science/european-biotech-industry-pressed-lack-funding/article-155646**

R&D and innovation

According to EFPIA, Europe has lost its major place as a global hub for biomedical research. In fact, over the last decade the US has invested far more in public sector sponsored biomedical research than Europe has.[22]

Among the major difference between the US and Europe is the higher innovation intensity of US companies compared with European companies. When companies launch new products on the market, the share of revenue that they devote to R&D tends to be lower than the share devoted by companies that are still wholly in the phase of developing new products. US companies, however, are not only bringing more new products onto the market than European companies, but they also devote a higher share of revenues (almost 40%) to R&D than European companies (31.6%) (EMCC, 2006). While R&D investments in Europe grew by 2.6 times between 1990 and 2003, the corresponding increase in the US was more than fourfold.

At the same time, new leading-edge technology research units are being transferred out of Europe, mainly to the United States. In 1990, major European research-based companies spent 73% of their worldwide R&D expenditure in EU territory. In 1999, they spent only 59% in EU territory. The United States was the main beneficiary of this transfer of R&D expenditure.

Trends and drivers of change

Companies in the European biomedical healthcare sector face a range of political, regulatory, economic, social and technological challenges to growth and consolidation: new public regulation, intense global competition for market shares, lack of European researchers, global competition for high-skilled employees, availability of venture capital, etc. These factors are drivers of change in the sector, and policy-makers and stakeholders need to get a good understanding of these changes in order to ensure the best possible conditions for sustainable growth.

Key research questions are: what are the consequences of changes, what new challenges arise for the companies in the sector, and how do companies in the sector respond to these challenges? Answering these questions is the first step in the formulation for an agenda for change in the sector.

The changes in the sector impact on society in many ways. New, innovative products can help many people improve their health situation and achieve a better quality of life. In addition, improved public health can reduce public healthcare costs and, by that, increase financial resources to be allocated to other purposes. On the other hand, there are significant negative socio-economic effects on local communities when biomedical healthcare companies decide to shut down manufacturing sites and move their activities to other countries in order to reduce costs. Thus, companies in the biomedical healthcare sector are not operating in an isolated arena, but operate in a socio-economic context in which their strategic choices affect the welfare of many Europeans.

[22] EFPIA, Creating biomedical R&D leadership for Europe to benefit patients and society, 2004, **http://ec.europa.eu/research/fp6/p1/innovative-medicines/pdf/vision_en.pdf**

Figure 8: *Change in the biomedical healthcare sector*

Political and regulatory developments

Biotechnology is a political priority in Europe. In 2005, Commission Vice-President Günter Verheugen, responsible for enterprise and industry policy, stated that biotechnology could potentially become a driving force in a European knowledge-based economy.[23] This makes the European biotechnology industry an important sector when it comes to the realisation of the Lisbon agenda and the overall policy goal of making the European Union 'the most dynamic and competitive knowledge-based economy in the world'.

Developments in the European policy framework

The EU has taken several policy initiatives to encourage the development of the biotechnology industry. In 2002, the Commission adopted 'Life sciences and biotechnology – A strategy for Europe' (European Commission, 2002). This is a strategy for 'green' and 'white' as well as 'red' biotechnology, and addresses major issues such as R&D, regulatory aspects and the lack of venture capital for SMEs.

The Commission has focused on ensuring closer cooperation with stakeholders (e.g. Member States, academia and the biotechnology industry) in order to secure the objectives of the strategy. In particular, the biotechnology industry contributes with ideas and feedback through the Competitiveness in Biotechnology Advisory Group. Also, an informal network with Member State officials responsible for competitiveness issues in biotechnology has been established. The network monitors the impact on European competitiveness of legislation and policy measures and reflects on further development of the strategy.[24]

A mid-term review of the biotechnology strategy is scheduled for 2006–2007. In addition, the Commission is carrying out a comprehensive cost-benefit analysis of the economic, social and environmental effects of modern biotechnology in Europe. The study – *Bio4EU* – aims at providing policy-makers and industry with an evaluation of opportunities and challenges brought by biotechnology and of its potential contributions to EU policy objectives.[25] The final synthesis report is scheduled for April 2007.[26]

7th European Framework Programme and the Innovative Medicines Initiative

The European Union's main instrument for funding research in Europe is the 7th Framework Programme for Research and Technological Development also known as FP7. The programme will run from 2007 to 2013 and has a budget of 50.5 billion euro. The framework programme supports research in selected priority areas, among them biotechnology.[27]

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[23] European Commission, *Biotech: Unleashing the enormous potential*, 2005, **http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/1324&type=HTML&aged=0&language=EN&guiLanguage=en**

[24] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_commit.htm**

[25] Joint Research Centre (JRC) Bio4EU study website, **http://bio4eu.jrc.es/**

[26] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_intro.htm**

[27] European Commission website, **http://ec.europa.eu/research/fp7/home_en.html**

Although there have been huge breakthroughs in life science research they have not resulted in the creation of many new therapies for patients. This is known as the 'pipeline problem'. In the last decade, large-scale initiatives in Europe (*The Innovative Medicines Initiative*) and in the US (*Critical path to new medicines*) have been launched to enhance and accelerate the development of medicines. The Innovative Medicines Initiative consists of a proposed partnership between the European Commission and the European Federation of Pharmaceutical Industry and Associations (EFPIA). The initiative's objective is to support faster discovery and development of medicines for patients and to enhance Europe's competitiveness by ensuring that its biopharmaceutical sector remains a dynamic high-technology sector.

To implement the recommendations of the Strategic Research Agenda of the initiative will require an investment of about 460 million euro per year, or more than three billion euro in all.

Regulatory framework

The biotechnology sector is highly regulated. For legislators, one of the main regulatory challenges is to develop and implement a timely science-based regulatory framework without creating unnecessary burdens on industry, in particular on SMEs.

The biomedical healthcare sector and the biotechnology industry in general are subject to both regulation covering all European sectors (e.g. competition law, consumer protection, intellectual property rights) and sector-specific regulation. In relation to the biomedical healthcare sector, the legislative body includes public regulation of biotechnology research, product approval and commercialisation as well as regulation related to public health.

In 2006 the European Commission published a guide to European regulation in biotechnology. This guide aims to provide a basic overview of the Community regulatory system for biotechnology, and guidance as to how it operates. This, in turn, helps companies identify routes to regulatory compliance for their products and processes, thus reducing both uncertainties about relevant regulation and basic regulatory procedures and – in effect – the costs of compliance.[28]

Public regulation affects the competitiveness of the biomedical sector, innovation, and – in a broader perspective – public health, e.g. by promoting the development of advanced therapies or lowering prices on medicines. One example of innovative European regulation is the new European legal framework for generic versions of biotechnology-derived drugs – so-called biosimilars – described in the box below.

Competitive advantage through innovative regulation: the new European policy and legal framework for biosimilars

Medicines enjoy a patent, but patents are only valid for a specific number of years. After the expiry of a patent, other companies are allowed to develop and manufacture these medicines. Until recently, no legal framework existed for biosimilars, but this was changed in 2006 with the introduction of a European policy and legal framework for biosimilars. Since patents and data protection for the first biopharmaceuticals have just expired or are about to expire in Europe, a new market for biosimilars is gradually opening.

'Omnitrope' – a biosimilar drug containing growth hormone intended for the treatment of growth disturbance in children and adults – was the first biosimilar drug to get an EU market authorisation by the European Medicines Agency (EMEA). The drug is manufactured by Novartis AG's generics unit Sandoz GmbH and has been deemed of comparable quality, safety and efficiency to the reference medicinal product Genotropin, which is manufactured by Pfizer. The expiry of patents and launching of biosimilars ends big drug-makers' monopoly in biopharmaceuticals and could lower prices for biotech medicines due to market competition.

[28] European Commission, User Guide to European Regulation in Biotechnology, 2006, **http://ec.europa.eu/enterprise/phabiocom/docs/user_guide_biotech.pdf**

The EU is the first in the world to have defined a policy and legal framework for biosimilars. Absence of such regulation and biosimilars' approval process in other countries, in particular in the United States, can lead to a competitive advantage for the EU biosimilars industry. The European Generic Medicines Agency (EGA) thinks that the EU is now set to become 'the global centre for R&D and production of this new generation of affordable, biotech pharmaceuticals, giving the EU a huge competitive advantage over other countries like the United States and Japan'. Moreover, biosimilar medicines are an opportunity for governments to control national healthcare expenditure[29].

However, the current EU framework does not address issues such as labelling of biosimilars. EuropaBio has pointed to this as an outstanding issue and highlights the need for a unique name and label for a biosimilar: 'Clear and distinct labelling is essential to avoid confusion between the innovator product and a biosimilar and to facilitate pharmacovigilance obligations.'

EurActiv, **http://www.euractiv.com/en/health/biosimilar-drug-gets-eu-market-authorisation/article-154524**;
European Commission, Biotech medicines: first biosimilar drug on EU market, 2006

The following special regulatory issues have been identified by the Commission:[30]

- Ensuring the transposition and application in Member States of existing legislation, e.g. the new GMO legislation
- Regulating the development and use of genetically modified organisms (GMOs)[31]
- Securing intellectual property rights

Slow implementation of EU regulation

The European Commission has identified some weaknesses in the implementation of the European biotechnology strategy:[32]

- Slow national implementation of internal market legislation (especially the directive on the legal protection of biotechnological inventions) is seriously hampering the development of the biotech industry.
- Slow progress on the Community Patent has prompted companies to turn to the US for protecting patents.
- Member States need to implement the new GMO legislation.
- Access to finance for biotechnology companies must be improved as the market matures.

Industry representatives in the biomedical sector have also expressed concerns related to the implementation of the European biotechnology strategy and sector-specific EU regulation: the inadequate implementation of EU regulation in the biotech sector hinders innovation and blocks SMEs' access to the market.

[29] European Commission, *Biotech medicines: first biosimilar drug on EU market*, 2006, **http://europa.eu/rapid/pressReleasesAction.do?reference=IP/06/511&format=HTML&aged=0&language=EN&guiLanguage=en**

[30] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_gar.htm**

[31] The EU has been legislating on GMOs since the early 1990s.

[32] European Commission, *Life Sciences and Biotechnology – A Strategy for Europe. Third Progress Report and Future Orientations*, 2005. **http://europa.eu.int/eur-lex/lex/LexUriServ/site/en/com/2005/com2005_0286en01.pdf**

These concerns have led the industry to launch a '*Healthcare Manifesto*'. The manifesto calls for EU policy support to 'ensure innovative healthcare (innovative medicines, orphan drugs such as those developed to treat rare diseases, advanced therapies), engagement with society and creation of wealth through a friendly environment for SMEs in the sector'.[33] According to Patricia Pellier from Serono International, a biomedical company based in Switzerland, 'Europe is the only region in the world to have a real strategy on biotechnology and that strategy is worth its weight in gold if, and when, implemented'.[34]

Patents and IPR in the biomedical sector

The number of patent applications has increased tremendously over the last decade. In 2004, 10% more patents were applied for at the European Patent Office than in the previous year (OECD, 2003). However, good intellectual property policy is not the same as maximal intellectual property rights. Poor patent quality can lead to a reduction in investment and commercialisation of innovations. It can slow progress in cumulative technologies and increase the level of rights fragmentation. As a result, patent systems could become barriers to follow-up research. Biotechnology, in particular the field of genetic inventions, is one of the sensitive areas. In fact, DNA patents have been frequently criticised for having a detrimental impact on follow-up or continuing research (Thumm, 2005).

However, surveys of industry representatives reveal that the industry perceives the phenomena of overly strong dependencies among patents, patents blocking entire technological fields and problems with overlapping patents only to a moderate degree. This could lead to the conclusion that the patent system as it stands today does not need overall reorganisation but rather continued fine-tuning on the basis of existing regulations (Thumm, 2005).

Biotech patents in Europe

Patents provide an incentive to innovation and without the safeguard provided by patents, industry and other inventors would be unwilling to invest their time and money in research and development. This applies to all areas of technology but especially to biotechnology given the considerable amount of high risk investment that is often required in this area. In the EU, Directive 98/44 on the legal protection of biotechnological inventions constitutes the legal framework for biotechnology patents.

In 2005, the EU Commission published its 2nd report on the EU Biotechnology Patents Directive. The report specifically investigates the issues of patenting of human DNA, and patenting of human stem cells. According to EuropaBio, these issues have for a long time been at the centre of a debate as to whether inventions comprising human gene sequences or human stem cells can be patented. On both issues the Commission recommends continuing to monitor the developments. However, the Commission has refrained from taking a position, leaving it up to the Member States themselves to legislate on these issues.[35]

EuropaBio has criticised the absence of European-wide legal harmonisation. In relation to gene sequences, two EU Member States, France and Germany, have in different ways limited the scope of patent protection for human gene sequences to the specific use disclosed in the patent application. France has completely banned the patenting of human gene sequences. The remaining countries provide absolute product protection for human gene sequences that gives a scope covering possible future uses of that sequence.

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[33] Healthcare manifesto website, **http://www.healthcare-manifesto.org/**

[34] EurActive, Biotech industry wants better implementation of EU regulations, **http://www.euractiv.com/en/health/biotech-industry-wants-better-implementation-eu-regulations/article-144738**

[35] EuropaBio position paper, Uncertainty reigns as biotech patents remain unharmonised, 2005, **http://www.europabio.org/articles/Gene%20patenting%20050719_FINAL.doc**

National biotech policies

European regulation is not the only source of public regulation. In many areas of importance for the biomedical healthcare industry, the institutional setting including conditions under which biomedical companies operate and national systems for healthcare, is provided by the Member States. The conditions vary considerably between Member States, especially as regards restrictions on entrepreneurial activity in this field and acceptance and regulation of relevant technologies (EMCC, 2006).

Such differences affect the development and competitiveness of national biomedical healthcare industries. While the UK's biomedical healthcare industry is ahead, the German industry is in an early state of development with a large number of small research companies, but a comparatively small output of products. If Member States want their national biotechnology industries to flourish, they need to provide an adequate policy and legal framework for biomedical companies.

In a study entitled 'Benchmarking of public biotechnology policy' delivered to the European Commission in April 2005, the effectiveness of various policies in EU Member States is assessed by comparing the national policy measures with national performance in biotechnology.[36]

The report's main conclusions are:

- A comparison of national policy portfolios indicates a reinforcement of public policies in favour of biotechnology in recent years. Most countries foster the exploitation of public biotechnology research via the stimulation of entrepreneurship, spin-offs and collaborative biotechnology research between industry and public sector research organisations.
- Policy instruments to support industrial development are related mainly to improving the availability of financial capital and various forms of business support for start-ups. Policies aiming at creating biotechnology clusters are less favoured policy instruments.
- In general, the policy portfolios of the new Member States are less comprehensive and patchier than those of the old Member States.
- Dedicated instruments for policy coordination and policy impact assessment are not widespread in the European Member States.
- The analysis of policies fostering the knowledge base for biotechnology indicates that a strong financial commitment to supporting biotechnology is an important but not sufficient precondition for effective policies. Well-performing countries (e.g. Denmark, Sweden, Finland, Belgium and the Netherlands) have implemented a mix of generic and biotechnology-specific measures.
- When designing policies to support infrastructures for biotechnology, it pays off to combine such measures with support of service functions (e.g. advice on patenting, management, financing and regulatory issues).
- In order to improve social acceptance of biotechnology, Member States could adopt comprehensive policy approaches which include a broad variety of different measures (technology assessment, foresight, workshops and infrastructure) as was the case in Denmark and the Netherlands.

[36] Fraunhofer ISI, Benchmarking of public biotechnology policy, Final report, 2005, **http://ec.europa.eu/enterprise/phabiocom/docs/benchmarking_of_public_biotechnology_policy_-_final_report_april_2005.pdf**

Reforms of European healthcare systems

National healthcare systems define the 'rules of the game' for biomedical companies due to their tremendous economic importance: the public healthcare system's share of the total healthcare market is as high as 80% in some Member States and about 65% in others (EMCC, 2006). For many reasons, European countries are reforming the public sector and public healthcare systems. While the reform of national social insurance systems and health markets might be necessary for cutting costs and ensuring 'value for money', such reforms are also changing the demand for healthcare products and services.

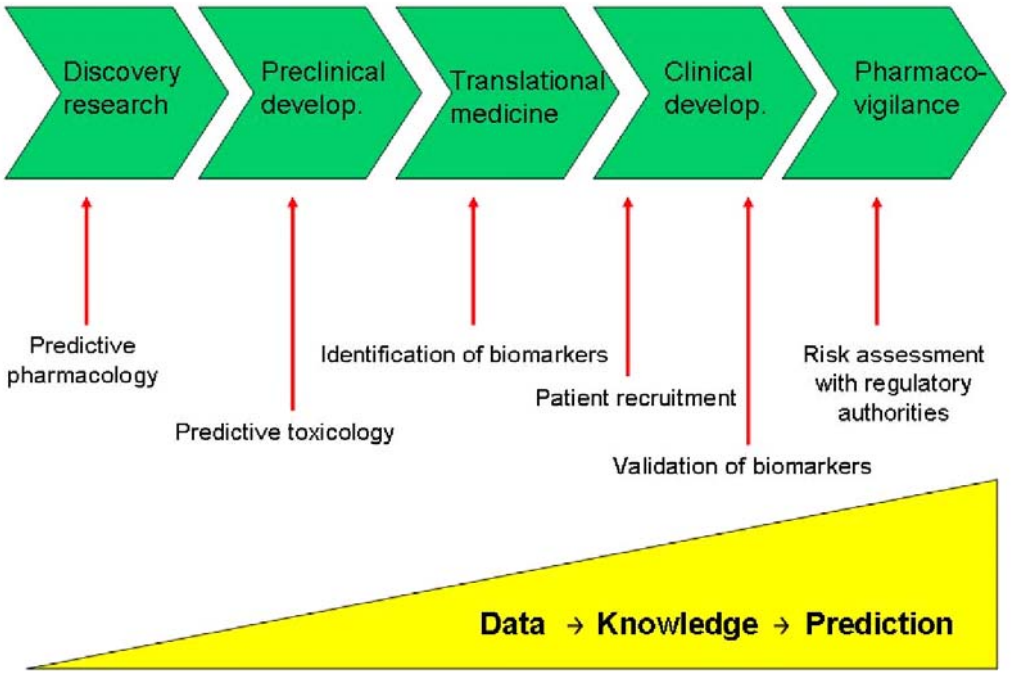
The introduction of financial restrictions in national healthcare systems could limit the demand for expensive medicines while on the other hand increase the demand for biosimilar drugs. It could also result in the elimination of certain types of healthcare services such as the financing of treatments for very rare ('orphan') and hereditary diseases that the biomedical healthcare industry is – and could be – especially providing the cures for (EMCC, 2006). Since patients might not be able to pay for the treatments themselves, such restrictions could worsen the health condition of people with such diseases. This eliminates market opportunities for biomedical companies, and companies that have specialised in rare diseases will need to rely on private funding for future R&D activities.

Bottlenecks in the development and sale of biomedical products

There is a range of bottlenecks in the biomedical R&D – the key bottlenecks are shown in Figure 9 below.

Addressing these bottlenecks is a great concern for biomedical companies. The Innovative Medicines Initiative has proposed a Strategic Research Agenda (SRA) that addresses key areas, which are linked to the bottlenecks in current drug development, including regulatory aspects.

Figure 9: *The pharmaceutical R&D process and key bottlenecks*



Source: *EFPIA, Creating biomedical R&D leadership for Europe to benefit patients and society, 2004,* **http://ec.europa.eu/research/fp6/p1/innovative-medicines/pdf/vision_en.pdf**

The proposed Strategic Research Agenda will be organised around four key areas, addressing the key bottlenecks in the R&D process:

- Safety, addressing the bottlenecks of predictivity in safety evaluation and pharmaco-vigilance with the authorities
- Efficacy, addressing the bottlenecks of predictive pharmacology, biomarkers identification and validation, patient recruitment and risk assessment with the authorities
- Knowledge management, leveraging the potential of new technologies to analyse a huge amount of information in an integrated and predictive way
- Education and training, addressing certain gaps in expertise which need to be resolved in order to change and support the biopharmaceutical research and development process

If these key areas are dealt with, it will be possible to get medicines to patients more quickly, to discover and develop better medicines (safer, with improved efficacy and better adapted to patients needs), and facilitate risk/benefit evaluation by the authorities to accelerate the access of patients to innovative medicine.[37]

In terms of regulatory bottlenecks, one of the main difficulties faced by small and medium-sized (bio)pharmaceutical companies is the procedure of applying for product authorisation. Among the important European initiatives in this area is the establishment of the European Medicines Agency (EMEA) in 1995.[38] The EMEA has been engaged in streamlining the process to authorise medicinal products in the Single Market and removing the need to make multiple applications on behalf of the same product.

There is now a European system with a centralised procedure of mutual recognition. The certification of medicines is to be carried out in conformity with the arrangements laid down by the World Health Organisation (WHO). The EMEA and the national authorisation bodies form a network which is responsible for the approval and supervision (pharmaco-vigilance) of medicinal products in the market.

Moreover, cooperation between the European Commission, the EMEA and EBE has resulted in a proposal to implement fee reductions and administrative support to SMEs which are taking their products to the EMEA. This is of vital importance for biomedical healthcare companies since the high costs of their product dossiers are a heavy burden on them (EMCC, 2006).

Role of research coordination, tax credits and other policy-related European incentives

EU Member States are increasingly using tax credits to stimulate the development of innovative companies with high R&D expenditure, such as biotechnology companies. Tax incentives for R&D stimulate the growth of innovative companies by lowering the effective cost of investment in R&D.[39] In parallel, industry is increasingly cooperating across borders, in particular in the high-tech sector. But the diversity of national schemes introduced has resulted in an increasingly complex landscape for R&D tax treatment in Europe, hindering trans-European collaboration.

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[37] The Innovative Medicines Initiative (IMI), *Strategic Research Agenda: Creating biomedical R&D leadership for Europe to benefit patients and society*, 2005, **http://ec.europa.eu/research/fp6/pdf/innovative_medicines_sra_final_draft_en.pdf**

[38] EMEA website, **http://www.emea.eu.int/**

[39] The Swedish Institute for Food and Biotechnology, *Promoting Innovation by Tax Incentives. A review of strategies and their importance to biotech growth*, 2006, **http://www.sik.se/yicstatus/Reports/Tax_incentives_for_RD_YIC_project_report.pdf**

The European Commission has adopted a Communication on the more effective use of tax incentives in favour of R&D in order to boost R&D investments and enhance job creation and economic growth in Europe. It encourages Member States to improve the use and coordination of tax incentives on specific R&D issues.[40]

Biomedical research is coordinated at both the European and the national level. As described above, the European institutions play a large role in terms of research coordination. At the national level, there is a myriad of initiatives related to biotechnology research activities. One example is the Swedish Government's sector strategy for pharmaceuticals, biotechnology and medical technology.[41] As a part of this strategy, the Government has initiated a research programme, SAMBIO. The aim of the SAMBIO programme is to promote cooperation between industry and universities in the life sciences domain.

There is also a range of European organisations working to promote research at the European level. Among these is the *European Science Foundation* (ESF). The ESF acts as a catalyst for the development of science by bringing together leading scientists and funding agencies to debate, plan and implement pan-European initiatives. In the context of the ESF Strategy Plan 2006–2010, the association of European Medical Research Councils (EMRC) has developed a strategy covering the biomedical field.[42] The strategy aims to:

- foster an interdisciplinary approach towards the Functional Genomics domain;
- focus on biomedical applications emerging from these and related domains, such as e.g. nano medicine and structural medicine, molecular imaging, genetic epidemiology and pharmacogenetics in order to advance the promising field of personalised medicine;
- develop translational research to overcome boundaries between basic research/science and clinical applications;
- gather expertise and advance the methodology for the evaluation of the socio-economic value of research in the above-mentioned fields;
- develop new partnering to support and leverage these activities, e.g. with European agencies, intergovernmental organisations (EMBO), charities, science advocacy groups and pharmaceutical and biotechnological industries.

In addition, further attention will be paid on the identification of related regulatory and ethical issues and to the promotion of biomedical research to the European general public and political stakeholders.

Since 1990, the EC-US Task Force on Biotechnology Research has been coordinating transatlantic efforts to guide and exploit the ongoing revolution in biotechnology and the life sciences. The task force was established in 1990 by the European Commission and the White House Office of Science and Technology. In the past 15 years the Task Force has acted as an effective forum for discussion, for coordination and for developing new ideas.[43]

[40] European Commission, *Tax incentives: Commission promotes an effective use of tax incentives for R&D*, 2006, **http://europa.eu/rapid/pressReleasesAction.do?reference=IP/06/1598&format=HTML&aged=0&language=EN&guiLanguage=en**

[41] Swedish Government website, **http://www.regeringen.se/sb/d/5677/a/45831**

[42] European Science Foundation website, **http://www.esf.org/esf_domain_home.php?section=2&language=0&domain=2**

[43] EC-US Task Force on Biotechnology Research, **http://ec.europa.eu/research/biotechnology/ec-us/index_en.html**

Finally, the European Federation of Biotechnology (EFB), a non-profit organisation founded by European scientists in 1978 aims to expand collaboration between academic and industrial researchers, to strengthen education and promote innovation. The EFB has established several task groups, including the task group on public perceptions of biotechnology, and the task group on safety in biotechnology.[44]

Political and regulatory developments – implications for the biomedical sector

- Regulatory requirements are resulting in growing administrative burdens.
- Different regulatory regimes make it difficult for biomedical companies to operate in the European market. There is a need for better implementation of European strategy and legislation.
- Innovative regulation, such as the policy and legal framework for biosimilars, is providing European companies with a competitive advantage.
- Bottlenecks in the development and commercialisation of new products are obstacles to growth and need to be addressed.

Social and demographic developments

While the use of biomedical products might be in the hands of medical doctors, allocation of public funds for R&D and public biotechnology policies in democratic societies depend on the public attitude towards the use of biotechnology-derived products and biotechnology as such. To some people, biotechnology is seen as a risk to human health and the environment. For others it is not compatible with religious beliefs. Finally, some see biotechnology and thus biomedical products as solutions to global problems such as hunger, diseases and environmental problems.

These attitudes are reflected in different attitudes towards biomedical companies. People may want innovative treatments, but some are not willing to accept high prices for the innovative products, especially when it comes to drugs needed in developing countries.

Demographic change

Due to declining birth rates and improved health, European populations are becoming smaller and older. As the baby-boom generation ages, America, Europe and Japan are set to face an explosion in healthcare costs. Alzheimer's is an illustrative case – the cost of caring for patients with the disease is estimated at 250 billion US-Dollar a year globally.[45]

At the same time, the changes in demographic composition also mean that the labour force is declining relative to those depending on others for their subsistence. Hence, the tax base is declining (EMCC, 2006). This puts a potential limit to the financial resources available for advanced treatments.

Risk society (migration, tourism, terrorism)

Global warming resulting in the spread of diseases to Europe (e.g. malaria discoveries in southern Europe), pandemics such as Avian flu, threats posed by terrorists and rogue states acquiring biological weapons of mass destruction, and the spread of exotic diseases through migration and global tourism, all constitute potential risks to public health while at the same time representing opportunities for growth for biomedical companies. An illustrative example is the increased

[44] European Federation of Biotechnology website, **http://bio4eu.jrc.es/documents/Stakeholderdialogue230506Summary_000.pdf**

[45] The Economist, From bench to bedside, 2 November 2006.

demand by citizens for 'Tamiflu', a biopharmaceutical used to prevent and treat flu, during a recent outbreak of Avian flu in Europe.

Hospitals and institutions such as the military buy vaccines to prepare for crisis situations such as outbreaks and bio-terror attacks. However, biomedical products – and biotechnology-derived products in general – constitute potential risks to public health themselves. The unknown side effects on human health of biomedical drugs are a matter of concern, and could constitute a barrier for the take-up of new drugs on the market.

Another dimension of the potential misuse of biomedical research is represented by research aimed at countering pandemics but which could result in the unleashing of life-threatening viruses. Recently researchers have constructed viruses containing several of the 1918 influenza virus's genes in order to get a better understanding of deadly pandemics. The gene sequences of the virus were retrieved from victims who had been buried in Alaska's permafrost and from preserved tissue samples. The 1918 flu killed more than 40 million people – especially young people – and the research into such diseases could be fatal if terrorists got hold of such viruses or if they spread from research facilities by accident.[46]

Ethical dimension

The risk dimension aside, biotechnology is also controversial for ethical reasons. The debate about the use of human stem cells for the development of innovative treatments has especially been sparking controversy. The European Commission has adopted a very cautious stance on the introduction of controversial technologies such as stem cell technology into EU research programmes after opposition from the European Parliament (EMCC, 2006).

Animal rights organisations are critical of the use of animals in clinical trials, and clinical trials involving human beings are also subject to criticism. In particular, clinical trials conducted in developing countries, where people are poor and not very well protected by law, have been criticised by human rights groups. So, in 2005, the Council of Europe agreed on the Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research. According to the protocol, the parties to the protocol shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to any research involving interventions on human beings in the field of biomedicine.[47]

Public attitude towards biotechnology

Whereas the opinions referred to above may be very visible in the media, they may not be representative of the opinions of European populations. The Eurobarometer 2005 survey[48] shows that EU citizens are, in general, more optimistic about technology than previously. The survey shows large support for the development of nanotechnology, pharmacogenetics and gene therapy, which most Europeans consider as 'useful to society and morally acceptable'. The claim that European public opinion is a constraint to technological innovation and contributes to the technological gap between the United States and Europe is therefore, according to the report, invalid.

[46] National Institute of Allergy and Infectious Diseases (NIAID) website, **http://www3.niaid.nih.gov/news/focuson/flu/research/pandemic/toxictraces.htm**

[47] Council of Europe website, **http://conventions.coe.int/treaty/en/Treaties/Html/195.htm**

[48] Eurobarometer surveys on biotechnology and life sciences are conducted every three years.

Health-conscious society

Rapid advances in science and technology, an increase in lifestyle-related diseases, an ageing population and a rising interest in attaining wellness through diet are among the key factors fuelling the growing interest in lifestyle drugs and functional foods. The increasing health awareness among European citizens constitutes an emerging market for biomedical companies.

'Lifestyle drugs' refers to any drugs intended or used for a problem that falls into the border zone between medical and social definitions of health. Secondly, drugs intended to treat diseases that result from a person's lifestyle choices (e.g. obesity) may also fall under the category of lifestyle drugs. The increased use of lifestyle drugs implies that the distinction between the social and medical dimensions of health is increasingly blurred. Expanding the definition of what constitutes a treatable medical problem will have a variety of consequences. For example, there may be a change in how general practitioners balance the risks and benefits of pharmacotherapy. No drug is without side effects, but the acceptability of those side effects usually increases with the severity of the illness being treated. The acceptable side effects of treating socially defined problems (including 'defects' that are results of the normal variation in the population) are on the rise.[49]

With a rising health awareness – as well as credible scientific research indicating many potential health benefits from functional foods – health claims on foods have arrived on the scene. However, the public scepticism in Europe in relation to GM foods indicates that the US market is more interesting for companies wishing to focus on functional foods.

Social and demographic developments – implications for the biomedical sector

- Demographic changes affect the recruitment of employees – competition for European brains and muscles is increasing and could hinder growth.
- Threats to public health and the ageing population are providing new market opportunities for biomedical companies.
- The increasing use of lifestyle drugs provides new market opportunities.
- The convergence of technologies resulting in innovative products such as functional foods could provide a market opportunity.

Economic developments

Biomedical products are relatively expensive due to the amount of research done in relation to the development of the products. Therefore, the demand for the products will depend on the financial resources available in the public healthcare system and citizens' economic situation in general. Also, international efforts in relation to trade liberalisation imply that market access barriers are increasingly removed, paving the way for competitors from third countries. This increases international competition and puts pressure on European biomedical companies.

International competition

The European biomedical industry is under pressure from international competitors: US companies dominate the global biotechnology markets, and the US biomedical sector consistently achieves strong output growth. In addition, the competitive pressure on the European biomedical sector is increasing with the emergence of new biotechnology players such as India and Shanghai that benefit from low costs and access to a highly qualified labour force.

[49] http://www.cmaj.ca/cgi/content/full/164/10/1449

Indian companies are particularly successful in the development of active agents, i.e. substances that produce chemical reactions, as intermediate products for the manufacture of generics, i.e. medicines marketed without a brand name, and most of these products are delivered to European or US pharmaceuticals companies. Furthermore, Indian companies are poised to enter the US market with generics, and are also entering knowledge-driven market segments with innovative products based on their own expertise. Indian companies have also become interested in the acquisition of smaller European pharmaceuticals firms in order to get access to their distribution channels (EMCC, 2006).

However, the emerging economies also constitute a growth opportunity for the European companies – in terms of both the number of potential costumers and the possibility of relocating parts of the production and clinical testing to low-cost countries in order to achieve a higher degree of global competitiveness. For instance, late-stage clinical trials are increasingly moving to Eastern Europe, Latin America and Southeast Asia.[50]

Enlargement process

The European Union has undergone considerable changes in recent years. Not least in regard to the number of Member States. Ten new European countries joined the Union in 2004 and on 1 January 2007 Romania and Bulgaria became members, bringing the number of Member States up to 27. In time Croatia and perhaps Turkey could join.

The enlargement process is affecting the competitive situation of biomedical companies. On the one hand biomedical companies face increased competition from companies in the new Member States. On the other hand the enlargement process results in access to new markets and provides an opportunity for companies to move activities to low-cost Member States. Relocation activities in the biomedical sector are focused on manufacturing activities and other labour intensive activities in general.

Competitiveness of European companies

According to a research report, *Innovation and Competitiveness in European Biotechnology*, Europe lags significantly behind the US in all facets of the commercial development of biotechnology.[51] This to some extent could be a reflection of its late entry into the biotechnology field. However, another reason for this situation could be the availability of leading-edge scientific capabilities. In particular, new European biotechnology companies are generally smaller than their US counterparts, less active in global networks and collaborative relationships, and fewer are present in markets for these technologies.

One of the important conclusions of the report is that the European research environment is unattractive to US research: comparatively little US research is done in Europe. The European research system in the life sciences and in biotechnology is too fragmented – probably due to regulatory, entrepreneurial, fiscal and financial factors. In addition to these factors, the supply of cutting-edge scientific research may be inadequate.

If this is the case, the specific problem could be addressed not only through higher levels of research funding but also through higher degrees of pluralism in funding sources, lower dependence on closed national systems, and higher integration of research with teaching, clinical research and medical practice. This emphasises the need to establish a European Research Area enabling European biotechnology companies to access and make efficient use of networks of collaborative research.

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[50] Thiers, Fabio, *The globalisation of clinical drug development*, **http://web.mit.edu/cbi/publications/Thiers.html**

[51] European Commission, *Innovation and competitiveness in European biotechnology*, 2002, **http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_07_2002.pdf**

Besides the lack of an effective pan-European research infrastructure, companies are also facing rising labour costs, lack of finance for R&D, and extensive public regulation of the industry. In addition, the geographical location of the companies has an effect on their competitiveness. One of the success factors for companies seems to be the clustering around large corporations ('big pharma' in the case of biomedical companies). Large corporations are not only the fundamental source of demand for the products and services of biotechnology companies, but they also provide essential capabilities (e.g. technological and managerial competencies). The importance of the relationship between biotechnology companies and large companies indicates that policies for biotechnology should be much more strongly linked to policies aiming at raising the competitiveness of 'downstream' industries, such as pharmaceuticals and agriculture.[52]

The US biotechnology industry is characterised by a high degree of concentration of firms in a restricted number of regions. A similar process of clustering took place across Europe. However, integration of smaller bio-clusters into bigger ones and increased cooperation between bio-clusters, as well as stronger technology transfers from academia to industry both within and between different European clusters, are needed.[53]

European 'elite companies'

Europe has experienced some success – especially in relation to the promotion of biotechnology start-ups. However, the growth of many biotechnology companies in Europe appears to be hindered for the reasons described above.

Some European companies on the other hand have done well in the competitive challenge for market shares. In the 2006 EuropaBio study, the concept of a 'European elite company' was defined as follows: elite companies are those outperforming the typical US company[54] by 100%.

[52] European Commission, Innovation and competitiveness in European biotechnology, 2002, **http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_07_2002.pdf**

[53] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_comp.htm**

[54] 'The typical US company' has been identified by stripping out the best and worst 10% of the companies in each of four age groups. The mean values for employment, R&D employment, R&D spending and revenue of what remains becomes the profile of a 'typical' company (EuropaBio 2006).

According to the study, 33 European biotechnology companies under 15 years old meet the definition of a European elite company:

Table 5: *European elite companies in the biotechnology industry, 2004*

Company name	Country	Year Founded	Company name	Country	Year Founded
Biovertis	Austria	2003	Igeneon AG	Austria	1999
Inyx Pharma Limited	UK	2003	Solvias AG	Switzerland	1999
Addex Pharmaceuticals SA	Switzerland	2002	Artus GmbH	Germany	1998
CXR Biosciences Limited	UK	2002	Epigenomics AG	Germany	1998
Indivumed GmbH	Germany	2002	GW Pharmaceuticals plc	UK	1998
CMC Biopharmaceuticals A/S	Denmark	2001	Actelion Pharmaceuticals Ltd	Switzerland	1997
TARGET HIT	Belgium	2001	Biogemma S.A.S	France	1997
Zentaris GmbH	Germany	2001	Biotage AB	Sweden	1997
Argenta Discovery Limited	UK	2000	Intercell AG	Austria	1997
Basilea Pharmaceutica AG	Switzerland	2000	Vectura Limited	UK	1997
Genmab BV	Netherlands	2000	Cytos Biotechnology AG	Switzerland	1995
Henogen	Belgium	2000	ProStrakan Group Limited	UK	1995
Renovo Ltd	UK	2000	MediGene AG	Germany	1994
Astex Therapeutics Limited	UK	1999	Advanced Medical Solutions Group plc	UK	1991
Biolitec AG	Germany	1999	Flamel Technologies S.A.	France	1990
Galapagos Genomics BV	Netherlands	1999	Cerep SA	France	1989
Genfit SA	France	1999			

The list shows that most of the companies are located in either the UK (9 companies), Germany (6 companies) or Switzerland (5 companies).

Economic developments – implications for the biomedical sector

- European biomedical companies are losing out in the global healthcare markets. This increases the need for strategic initiatives.
- Competitive pressure from countries outside Europe is driving the need for product and process innovation.
- The enlargement process is an opportunity for growth, but also increases competition from biomedical companies in the new Member States with the development of their national industries.

Market developments

As already mentioned, most European biotech companies are micro or small, research-intensive firms, and on average smaller than their US counterparts.[55] However, the strength of the biomedical healthcare industry differs widely between European countries. The UK is ahead, with a total of 636 new biotech healthcare products in clinical tests, even though there are no more biomedical companies in the UK than in Germany. The UK industry, however, is more mature and its companies are larger. There are 43 quoted companies among its 334 biomedical healthcare companies, while the corresponding figures for Germany are 11 and 350 respectively.

Europe's capacity for breakthrough innovation

According to data on patents and collaborative R&D projects, the US has accumulated and maintains a dominant advantage in innovative activities in biotechnology compared with Europe.[56]

One of the main determinants of innovation is research activities. However, European R&D activities are not able to keep up with R&D activities in the US. According to Sir Tom McKillop, former Chief Executive of AstraZeneca, US spending on biomedical R&D has increased from 2.4% to 2.8% of GDP over the past two decades. Over the same period in Europe it has fallen from 2.4% to 1.9%. This is resulting in an innovation gap between the US and Europe.[57] Other reasons for this innovation gap include:

- slow take up of new products;
- bureaucratic clearance processes;
- structural problems: laws and regulations; delayed implementation of biotechnology directive in some Member States;
- talk for over 15 years of a European patent which still has not been achieved;
- no integrated strategy for biomedical R&D across Europe;
- no solution, despite strong support from government and elsewhere, to the worrying problem of animal activists;
- very little facilitation across Europe of academic–industrial collaboration, which was achieved in the US a decade ago;
- underinvestment in education and training.

This has resulted in a situation where the North American pharmaceutical market in 2002 was significantly bigger than that of Europe, a reverse of the situation a decade previously. Given that 70% of the worldwide total sales of innovative pharmaceutical products are in the US, it is natural for European companies to look abroad.

Generic drugs

A generic drug is a drug which is bioequivalent to a brand name drug with respect to pharmacokinetic and pharmacodynamic properties.[58] In 2006 Apotex, a Canadian drugs firm, launched a generic version of the world's

[55] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_comp.htm**

[56] European Commission, *Innovation and competitiveness in European biotechnology*, 2002, **http://ec.europa.eu/enterprise/library/enterprise-papers/pdf/enterprise_paper_07_2002.pdf**

[57] *Can Europe compete in biomedical research?* Summary of the second Annual Forum Lecture given by Sir Tom McKillop, FMedSci, Chief Executive of AstraZeneca, on 31 March 2004, **http://www.acmedsci.ac.uk/images/event/1121788418.pdf**

[58] Wikipedia, **http://en.wikipedia.org/wiki/Generic_drug**

second-bestselling drug, 'Plavix'. For a few weeks in August the generic version captured nearly three-quarters of the American market for the $6 billion-a-year drug – until Sanofi-Aventis and Bristol-Myers Squibb, the makers of Plavix, asked a judge to halt sales.

The Plavix case shows that generic drugs are brought to the market even though a perfectly valid patent is in place. Obviously, the potential prize is so large that the reward outweighs the risk of legal defeat. The multi-billion dollar sales of today's blockbuster drugs have invited greater legal scrutiny of patents and encouraged generics firms to find ways to innovate around them. The result is a relentless legal attack on branded drugs.

However, rather than using the law to defend their patents, big firms often settle out of court. One reason for this could be that some drugs giants regard settlements as a way to bribe a generics firm to delay its introduction of a cut-price product. Another explanation is that the cost and legal uncertainty associated with patent trials are simply too great. Finally, big firms may know that a patent is based on too minor or too obvious a discovery to really deserve a patent. With this in mind, branded firms try to extend their lucrative monopolies by filing less rigorous secondary patents designed to block generics.[59]

Developments in the value chain

There is evidence of biomedical companies playing a new role in the value chain – biomedical companies are not necessarily involved in R&D but rather take care of the manufacturing of biological substances for pharmaceutical companies to be used in the production of biopharmaceuticals. Pharmaceutical companies need these substances, but are often not able to develop or manufacture them themselves. In effect, they need to rely on external suppliers with expertise in this field.

Prospects for this market are good: biopharmaceuticals are driving growth in the pharmaceutical industry – showing growth rates of up to 20% per year, and this type of drug is expected to constitute 50% of the market for pharmaceuticals within the next ten years. However, it is a very competitive market and the development and manufacturing of such substances is very difficult – scaling up production and complying with the tough standards applying to the pharmaceutical industry are among the main challenges in this market.[60]

Companies in the biomedical sector – especially the large ones – to an increasing degree have to rely on subcontractors in order to speed up the product development process and compensate for lack of specialised knowledge in specific areas. As a result, the value chain is becoming more complex. Since subcontractors are required to comply with the safety and quality standards that apply to the company buying their services, the biomedical companies to an increasing extent have to spend resources on ensuring and documenting compliance with standards in all parts of the value chain (value chain management). Moreover, these standards and the required documentation are not harmonised at the international level. As a result, companies have to comply with both US and European regulation, and provide documentation to European and/or national authorities as well as the FDA for product approval.

[59] The Economist, Under attack, 7 September 2006.

[60] Ingeniøren, *Kraftig vækst i markedet for ny biofarmaka*, 1 December 2006.

Strategic alliances

Entering strategic alliances with pharmaceutical companies on a 'licenses-for-funding' basis is a way for small biomedical companies to stay in business when funds run out or to help with the commercialisation of a new product. Pharmaceutical companies on the other hand need the know-how of the biotechnology companies.

In the past, the major pharmaceutical companies may have passed on opportunities in the field of speciality products in order to wait on the next big thing – the blockbuster drug. But now 75% of the drugs in the pipeline are specialty medications, and pharmaceutical companies need to focus on these speciality products rather than waiting for the new blockbuster. As pharmaceutical companies typically do not have in-house expertise in the development of this type of product, they will consider strategic alliances with biotechnology companies as a way to gain access to such expertise.[61]

However, the prospects of entering strategic alliances also depend on the biotechnology companies' pipelines. Pharmaceutical companies want proven drug candidates in late-phase clinical trials, since the success probability of such drug candidates is higher than early-stage drug candidates and, not least, they can be brought to market more quickly. The UK biotechnology industry is smaller yet older and more established than its German counterpart, and as a result the number of experimental drugs for sale in the UK is much higher than in Germany (more than 150 compared with about 15). Moreover, most of Germany's experimental drugs are in the early stages of development. This implies a probability of failure as high as 90%, so reducing the market value of these drugs compared with drugs in the late stages of development. Some biomedical companies such as Medigene, a German biomedical company, have decided to completely abandon early-stage research and have licensed-in late-stage products (Sasson, 2004).

Mergers and aquisitions activities in the biomedical healthcare sector

From the mid-1990s onwards the number of biotechnology companies has increased and in fact almost doubled. However, since 2001 the biomedical healthcare sector has been characterised by consolidation and a decrease in the rate of new company creation. This change was due to the burst of the high-tech bubble in 2000, together with clinical trial failures, fewer drug approvals and corporate scandals.

Companies in the biomedical sector and in the pharmaceutical industry are trying to get bigger through mergers. Volume helps in marketing and distribution, and can also benefit R&D: firms with big budgets and better laboratories attract more talented researchers. On the other hand large companies can kill the entrepreneurial spirit and flexibility that fosters great discoveries. This has led GlaxoSmithKline, a British drugs giant, to create smaller research units to recreate a more intimate environment. As a result its pipeline has improved.

As a part of the ongoing consolidation process, mergers and acquisitions (M&A) increased worldwide in 2003 and 2004. Both public and private biotech companies in Europe have shown an increase in M&A activity, with 42 mergers in 2004. Many of the mergers are between European companies although the share has varied strongly over the years (from 27% to 74%). North American companies acquiring European companies amounted to 12 deals in 2004 or 29% of all European mergers and acquisitions, compared with 18% in 2003. European companies acquiring American counterparts also increased from two to seven deals in 2004.[62]

[61] Deloitte consulting website, **http://www.deloitte.com/dtt/article/0,1002,sid%253D109091%2526cid%253D125231,00.html**

[62] European Commission website, **http://ec.europa.eu/enterprise/phabiocom/comp_biotech_facts.htm**

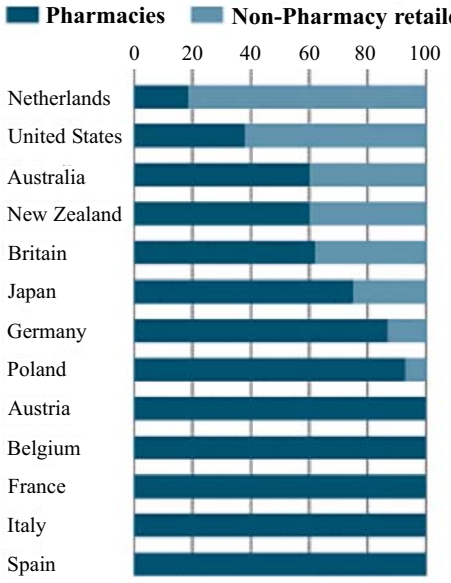
Recent European mergers include UCB's takeover of Germany's Schwarz Pharma, the purchase of Swiss Serono by German Merck, and the purchase of the drugs business of Altana, another German firm, by the Danish Nycomed. Schwarz, Serono and Altana have been under pressure to sell because of the rising cost of marketing and R&D, increasing competition from makers of generic drugs as patents expire, and the efforts of European governments to lower their healthcare costs by cutting expenditure on drugs. Other companies face the same pressure and more mergers are expected. Analysts predict that companies such as British Shire, French Ipsen, Danish Lundbeck, and Finnish Orion could all be taken over in the near future.[63]

Developments in drug sales

Among the main global trends in the value chain is the vertical integration of drug 'outlets' that could increase the pricing power of pharmacies. CVS, the biggest pharmacy chain in the US, has revealed that it intends to buy a drugs middleman, Caremark Rx, a big pharmacy-benefits manager which would give CVS access to 90 million customers and would enable CVS to direct personalised pitches at them based on their health profile.

On the other hand, general retailers such as supermarkets are increasingly entering the drug markets. One example is the big retail chain Wal-Mart, which is now making several hundred generic drugs available for just four US-Dollar for a month's supply, and clearly has ambitions to take on conventional pharmacy chains.[64] In Europe, countries differ in regard to the institutional setup of drug sales. In continental Europe pharmacies continue to enjoy an iron grip on sales of drugs – even non-prescription drugs. In contrast, the liberalisation of drug sales in a handful of European countries has put pressure on the power of pharmacies. In the Netherlands and in the Anglo-Saxon countries a big and growing proportion of drugs are sold by supermarkets and other general retailers.[65]

Figure 10: *Percentage of over-the-counter medicines sales by type of vendor, latest year*



Source: *Economist, Counter manoeuvres, 7 September 2006*

[63] The Economist, Growth pills, 28 September 2006.

[64] The Economist, Big deal?, 2 November 2006.

[65] The Economist, Counter manoeuvres, 7 September 2006.

Globalisation of the value chain

Globalisation brings many opportunities – one of them is to move manufacturing activities to low-cost countries in order to increase competitiveness. Another is to relocate research activities to countries with a strong research environment and with access to a pool of highly qualified staff. Strategic alliances across borders between independent companies (e.g. a pharmaceutical company and a biomedical company) are another dimension of the globalisation of the value chain.

According to Jacques Mulder, lead principal and Pharmaceutical R&D practice leader for Deloitte Consulting, biomedical companies no longer aim to manage the entire lifecycle of a drug's development by themselves. Rather, they are looking to global alliances to help fill key areas of a drug's development.[66]

However, the globalisation of the value chain also requires a focus on measures aimed at controlling risks and ensuring compliance with public regulation on hygiene and safety in all parts of the value chain. Companies do not want to be accused of polluting the environment, exploiting the labour force in countries with poor protection of workers, inflicting pain or hurting people participating in clinical trials, or profiting from peoples misfortune. To avoid exposure to such potential scandals a company needs to rely on risk management and internal control of the company's compliance with public regulation and, not least, ethics.

Changing locations

Low manufacturing cost is the most common reason for moving parts of the value chain to other countries or even other world regions. In addition, companies consider the risk of getting intellectual property stolen. As a result, simple manufacturing activities requiring unskilled or low-skilled and/or the less sophisticated back-end work of product development rather than research is performed in countries such as China, while most cutting-edge pharmaceutical research is carried out in western Europe, America, Israel and Japan, all of which have highly educated populations and strong intellectual property laws.

Go east! Big pharma moves to China

Novartis, the world's fourth-largest pharmaceutical company, has decided to expand to China – but reasons other than the 'usual suspects' apply. The company has announced plans to invest 100m US-Dollar in a new research facility in Shanghai. The ambition is that this new facility in Shanghai will eventually become one of Novartis's three big research hubs, alongside Cambridge, Massachusetts, and Basel in Switzerland.

According to Novartis the main reasons for moving to Shanghai include:

- The international market price for top scientists is the same wherever they operate. By locating in Shanghai, perhaps China's most expensive city, Novartis is hoping to attract globetrotting researchers.
- There will be new market opportunities. The role of the research centre will be to create new drugs for which there is strong demand in China in particular, and in Asia more generally.
- There will be marketing benefits. Because of a recent crackdown on corruption throughout China, Western companies are no longer allowed to meet purchasing directors in hospitals, which are major distribution points for drugs. Developing a reputation for advanced research into critical diseases could help its brand.

[66] Deloitte Consulting website, *The Challenges of Biopharmaceutical Outsourcing in a Global Economy*, **http://www.deloitte.com/dtt/article/0,1002,sid%253D2221%2526cid%253D125227,00.html**

- An entire generation of scientists was lost to the Cultural Revolution in the 1960s and 1970s, but now a flood of smart students is emerging once again from universities.
- None of the Chinese universities is particularly famous, but Novartis believes their standards are already world-class.
- Conditions regarding intellectual property are improving.
- A discouraging factor is the dramatic rate of employee turnover in China. However, turnover is highest among employees, such as those in sales and marketing, whose skills transfer readily from one industry to another. When it comes to attracting top-level scientists in China, the only real competition comes from academia, since the other big drug companies have not yet set up significant research centres.

The Economist, A Novel Prescription, 9 November 2006

Financial situation

Biomedical products are very expensive to develop and there is a considerable risk that potential products have to be abandoned even though that they are close to commercialisation. In addition, the European biotech sector is dominated by young, small companies, 55% of which are less than five years old. In order to develop into big, mature companies, they need more funding. As a result, the European biomedical sector needs to attract investment.

The biomedical healthcare sector and the biotechnology industry as a whole was hit hard by the worsened investment climate that resulted from the blast of the technology 'bubble' in 2000. Investors became much more risk-adverse and moved their focus from the scientific potential of new discoveries to late-stage product candidates. Biotechnology companies responded to this new climate by accelerating product development leaving companies with only early-stage candidates in the pipeline struggling to survive.[67]

European companies – especially small companies – are still struggling to get funding.[68] Comparing the EU and the US biotechnology industries, EuropaBio's recent report show that with the same number of biotech companies (around 2,000 in both the EU and the US), the US sector raises over twice as much venture capital, and has access to ten times as much debt finance than the EU sector.

The 2006 EuropaBio study states that insufficient funding of European biotech companies could result in:

- a focus on staying in business instead of building value;
- slow growth of companies;
- young companies being taken over by their competitors;
- even mature companies being acquired by their better funded US counterparts;
- companies looking to establish a presence in the US to access the more generous financial market.

[67] Ernst & Young, *Beyond Borders: The Global Biotechnology Report 2006*. According to AFIBIO ('*Access to Finance in the Biotech sector*'), a group of innovation professionals, there is a lack of early-stage risk capital in the biotechnology industry that severely hampers the formation of innovative start-up companies, **http://www.europe-innova.org/index.jsp?type=page&lg=en&from=child&classificationId=5580&classificationName=Results&cid=5320&parentClassificationId=5031&parentClassificationName=AFIBIO&parentContentId=5117**

[67] EurActive, *European biotech industry pressed by lack of funding*, 6 December 2006, **http://www.euractiv.com/en/science/european-biotech-industry-pressed-lack-funding/article-155646**

According to the Chairman of the European Association for Bioindustries (EuropaBio), Hans Kast, the EU needs to establish a reliable legal framework for approval of biotech products and clear and open market access for them, for European biotech industry to attract external funding: 'The current lack of political will, for example on the authorisation of genetically modified (GM) products, sends a totally wrong message to potential investors'.[69]

Recently, venture capital has begun flowing back to the biotechnology industry. The EU Industrial R&D Investment Scoreboard has revealed that private research investment in the EU rose by 5.3% in 2005, with pharmaceuticals and biotechnology among the leading sectors.[70] However, there are significant national differences. For instance, companies in Denmark are performing far better than companies in Germany and Sweden in terms of attracting external finance.[71]

EU and national financing schemes for biomedical companies

The number of public funding schemes dedicated to new biotechnology companies and/or SMEs in general has been increasing in recent years, with schemes available at both the national and European level. Examples of national initiatives include the Dutch BioPartner programme that has helped to create around 80 new companies and the French Jeunes Entreprises Innovantes10 (JEI) which provides tax breaks, particularly for the reduction of labour costs, to research-oriented companies. These programmes concentrate above all on seed and start-up finance (EMCC, 2006). Similar programmes exist in many countries, but their take-up seems to suggest that a main problem for new biotechnology companies is that they lack an overview of funding opportunities and experience in applying for financial support.[72]

Hence, commercial and managerial capacity building among SMEs is also a focal area for public intervention. The European initiative 'SMEs go LifeSciences' aims at supporting the successful participation of SMEs in life science related EU research projects. The initiative focuses on capacity building and the training of SMEs and researchers in EU project participation, and provides support activities for consortium building and matchmaking for SMEs and researchers preparing EU project proposals. Among its recent results is the publication of a catalogue of European incubators and biovalleys.[73] Likewise, Bioentrepreneur – a newly established portal managed by online journal *Nature* – provides biotechnology SMEs with an overview ('roadmap') of funding opportunities at national and European level.[74]

Along with the Seventh Framework Programme, the EU has launched the Competitiveness and Innovation Framework Programme (CIP). The CIP includes several potential funding sources for biotech SMEs such as the High Growth and Innovative SME facility and the SME Guarantee Facility. Other EU funding schemes include EUROTRANS-BIO and Eureka, both of which are geared specifically towards SMEs, while support initiatives include the establishment of the

[69] EurActive, *European biotech industry pressed by lack of funding*, 6 December 2006, **http://www.euractiv.com/en/science/european-biotech-industry-pressed-lack-funding/article-155646**

[70] European Commission, European Commission study shows 5% leap in European industrial R&D spending, 2006, **http://iri.jrc.es/research/docs/2006/scoreboard_2006_pr_en.pdf**

[71] Biotechmed website, **http://www.biotechmed.dk/dir05/v2/biomed.nsf/(internet_articles)/01-07-2**

[72] European Commission website, **http://ec.europa.eu/research/headlines/news/article_07_02_22_en.html**

[73] SMEs go LifeSciences website, **http://www.smesgolifesciences.be/common/home.asp**

[74] According to the roadmap, new biotechnology companies are able to get funding from several FP7 sub-programmes. For example, the Research for the Benefit of SMEs, which comes under the 'Capacities', sets aside around 1.34 billion euro; the 'Cooperation' programme allocates funds to initiatives like the health theme with an overall budget of 6 billion euro, with numerous possibilities for SME participation; and the 'People' programme gives 4.57 billion euro to the Marie Curie initiative, which supports partnerships between academia and SMEs. Competition for FP7 funding is fierce, and requires a considerable effort in putting together a proposal.

EuroBioFund which was set up in 2006 by the European Science Foundation with support from the European Commission to enable greater interaction among European life science funders and researchers.[75]

The role of financial support after the initial start-up period

When investment is not forthcoming, companies have to look for other strategies. Lack of funding has forced some companies to put cutting-edge research on hold and sell valuable technology just to stay solvent (Sasson, 2004). Other companies have merged with – or been acquired by – stronger rivals from the US who are able to raise more money than companies in Europe. In fact the take-over of UK companies by US companies has led to fears that the UK could end up 'performing the role of the research division of US multinationals' (Martyn Postle, director of Cambridge Healthcare and Biotech, cited in Sasson, 2004). Entering strategic alliances with pharmaceutical companies on a 'licenses-for-funding' basis is also among the strategic options of biotechnology companies.

Good practices in the post-start-up phase

According to EuropaBio, it is possible to create real growth from biomedical companies in just a few years by lowering the costs of starting a new business and by multiplying the rate of investment in research across all innovative technology sectors.[76] A favourable scientific, business and regulatory environment will spur innovation and ultimately result in growth in employment and economic wealth. Rather than a cost for European countries, investments in helping new companies are followed by a high economic return.

EuropaBio's Emerging Enterprises Council (EEC) focuses on providing advocacy for priorities with European authorities in order to ensure that the needs and interests of small and medium-sized biotech companies are brought up at the European level. The overall goal of the EEC is to improve the financial environment for European biotech SMEs to increase their global competitiveness. The EEC has thus created and is promoting a special programme to help young innovative companies across Europe. The aim is that EU governments should adopt this line of thought and create a specific status for young innovative companies, providing tax exemptions to entrepreneurs, employees, investors and companies across Europe to reward risk with incentives and benefits. The EEC suggests that companies younger than 15 years with an R&D expenditure of more than 15% of the total budget should be given the status of a 'young and innovative company'. In 2004 France was the first European country to implement the YIC status and in 2006 Belgium followed.[77]

[75] European Science Foundation website, **http://www.esf.org/esf_genericpage.php?language=0&section=8&domain=0&genericpage=2573**

[76] **http://www.europabio.org/bi_infokit_emerging.htm**

[77] **http://www.europabio.org/emerging_enterprises3.htm**

Economic developments – implications for the biomedical sector

- Framework conditions for innovation are deficient in Europe compared with its main competitors.
- Relocation to countries outside Europe remains an attractive option.
- Engaging in strategic alliances and consolidation through M&A require that managers focus more on strategic management.
- The amount of funding available to European companies is still negligible compared with funding available to US biotechnology companies, so considerable efforts need to be devoted to attracting investment.
- The lack of funding is forcing biomedical companies to develop new business models – considering entering strategic alliances is among these.
- Value chain management, risk management and quality control gain priority with the globalisation and increasing complexity of the value chain.
- Products are increasingly under pressure from generics – legal and illegal. This increases the need for product monitoring, sufficient legal capabilities, and not least for innovation.

Research, technology and development

The biomedical healthcare sector relies on a number of different technologies in both R&D and manufacturing activities, e.g. ICT and bacterial management systems. In addition, biotechnology in itself is combined with other generic technologies such as nanotechnology (nanobiotechnology) and sensor technology (biosensors).

Technological developments are important for innovation in the biomedical healthcare sector. However, to realise the full potential of the sector, it is necessary to ensure that R&D activities are coordinated and sufficiently funded, and that new applications are in fact used. Recent analyses suggest that the actual adoption of modern biotechnology by various European industry sectors is probably lower than anticipated.[78]

Bridging the public–private divide

There are many approaches aimed at increasing cooperation between public and private research organisations, and between industry and research organisations in general. At the European level, the Council of European Bioregions (CEBR) is supporting local bio-communities through direct services including networking, incubation, partnering and cluster promotion. Its aim is to develop and implement new biotech support activities across Europe.[79]

At the national level, there is a range of activities aiming at bridging the public–private divide. An example of such an activity is the BioLogue Network[80] in Denmark.

[78] Bio4EU study website, **http://bio4eu.jrc.es/background.html**

[79] Council of European Bioregions website, **http://www.cebr.net/**

[80] **http://www.biologue.ku.dk/**

Enhancing public–private partnering: the BioLogue Network

BioLogue is a Danish pharma consortium that aims to help research-intensive biomedical companies and the academic community in Denmark to work together, and to fulfil the research and innovation agendas of both Denmark and the European Union. The consortium works across disciplines and across the public and private sectors, building knowledge networks and seeking technological synergies.

BioLogue enhances public–private partnering based research, development, education and funding opportunities by exploiting their core competencies of matchmaking, science dating and one-stop shopping for technology and competence-based resources.

Cluster building and development is another way of strengthening cooperation between public and private biomedical actors. In the 'Heartbeat of life sciences in Europe' initiative, universities and regional development agencies in the Meuse-Rhine Triangle have joined forces in order to strengthen the regional life sciences cluster more efficiently. Their aim is to promote cross-border cooperation, to bring together science and business and to attract foreign investors.[81]

Converging technologies

The latest technological development in the sector is to be found where different technologies converge with major synergetic effects as a result. Converging technologies are to be found which combine provinces of nano-, bio-, info-, and cognotechnology, which are all currently progressing at a rapid rate (Roco and Sims Bainbridge, 2002).[82]

In the East of England there is increasing interest in integrated, inter-disciplinary research that brings together biology, chemistry, engineering, electronics, software, mathematics, physics, etc. The idea is to find novel solutions to bio-related problems by investigating fields outside the traditional life sciences disciplines. Analyticon, a maths-based company that has expertise in developing maths-based models for the aerospace industry has recently adapted some of its models to provide clinical development managers with a novel tool to help improve the design of clinical trials. Other examples are Akubio and the Centre for Integrated Photonics. Akubio is a spin-off company from the University of Cambridge exploiting acoustic detection technology for enhanced drug discovery, while the Centre for Integrated Photonics in Ipswich is developing expertise in the emerging field of bio-photonics.

Personalised medicine is the future

Medical communities have laid emphasis on preventive medicine as the most efficacious and cost-effective approach to improving quality of life. In addition, researchers have realised that the most advantageous way to combat many diseases such as diabetes or cancer is to predict susceptibility and begin preventive treatment before the onset of the disease. Designing preventive screening tests will allow people to be in charge of their own health. Therefore, pharmacogenomic testing has tremendous market value.

Pharmacogenomic testing can be used to predict the chances of a disease developing, so appropriate preventive action can be taken. Pharmacogenomics provides the opportunity to manufacture customised drugs for patients, suitable for each person's individual genetic make-up. A number of factors such as the environment, lifestyle, diet and age all can influence a person's response to medicines, but determining an individual's genetic make-up is fundamental to creating personalised drugs with greater efficacy and safety (Frost and Sullivan, 2006).[83]

[81] Heartbeat of Life Sciences in Europe website, **http://www.heartbeatineurope.org/de/about_us/3.html**

[82] **http://www.wtec.org/ConvergingTechnologies/Report/NBIC_report.pdf**

[83] **http://pharmalicensing.com/features/disp/1162546586_454b0d9a676d0**

Research, technology and development – implications for the biomedical sector

- The biomedical sector relies critically on research to ensure its ongoing development.
- The convergence of technologies provides new opportunities for the sector.
- When technologies converge, education and knowledge creation also need to converge.
- Lack of critical mass in Europe is increasing the attractiveness of other regions in the world.
- In the future there will be an even greater demand for scientists skilled in more than just one area or research field.

Restructuring and human resources

Europe is rapidly losing jobs in a number of sectors. Losses are fuelled by the introduction of new technologies as well as the integration of Asia, Russia, Eastern Europe and Latin America into the world economy. New technologies and low freight rates put pressure on the competitiveness of European industries in the world markets and at the same time make it attractive for European manufacturing industries to outsource parts of the business processes to countries with lower wage levels, or to move out of Europe altogether.[84]

Up until recently, the vast majority of functions to have been outsourced demanded only basic skills levels; but countries like China and India invest heavily in education and R&D, so if a wage gap remains with these regions, there is little doubt that Europe will see an increase in outsourcing of knowledge-intensive functions.

Due to the high knowledge intensity of the biomedical sector, the first wave of outsourcing has not hit the sector with any visible effect. However, another type of reaction to competitive pressure is to increase efficiency by introducing cost-saving technologies in production and management. This type of restructuring has been ongoing in large companies in most sectors of European industry since the 1990s and the biomedical sector is no exception.

Looking further ahead, we find that outside Europe and the US, Singapore represents potentially strong competition. The biomedical sector is already quite well established in Singapore with production by local and international companies. Process and production development is present, particularly among pharmaceutical companies which are undertaking clinical development in Singapore. Medical devices make up approximately 23% of the industry, with companies like Applied Biosystems and Siemens Medical Instruments. Some medical devices companies, such as Becton Dickinson and Biosensors, already undertake new product development, process automation and product customisation (Bacon, 2003).

But China is also beginning to stir in the biomedical field: biotechnology and pharmaceutics are key R&D areas in the 10th five-year plan of the Chinese Ministry of Science and Technology, the aim of which is to enhance China's overall biotechnological R&D level and capacity by a significant margin.[85]

[84] Haahr et al., (2006).

[85] Ministry of Science and Technology of the People's Republic of China website, **http://www.most.gov.cn/eng/programmes1/200610/t20061009_36225.htm**

Restructuring activities in Europe

According to data from the European Restructuring Monitor,[86] the main sources of job losses in the sector are internal restructuring and bankruptcy/closure, while offshoring and delocalisation only contribute to a relatively small extent. The statistics include drugs giants GlaxoSmithKline[87] and the Sanofi-Aventis Group[88] which both announced large cuts during 2002–04.

National actors have taken an active part in the handling of restructuring leading to job redundancies. One such example is the Redundancy Rapid Response Team in the UK.[89]

Redundancy Rapid Response Team

A critical element of building and maintaining a bio-community is ensuring that skilled researchers and administrators stay within the community. Cambridge has seen a number of companies downsize or close and ERBI, a private, not-for-profit, membership-based company, developed a 'rapid response team' to go and talk directly to employees being made redundant. The team has a number of activities:

- talks directly to staff to give them the 'bigger picture' of biotech in the UK;
- gives examples of other companies that have downsized and the positive way that employees have moved on, setting up their own companies, etc.;
- distributes skill sets around the ERBI Human Resources network so that other companies recruiting have a detailed profile of skilled scientists;
- hosts skill sets on the ERBI website for potential employers to view;
- emails people regularly with all jobs available in the bio-community.

ERBI has ensured that the majority of people being made redundant find new jobs before they were due to leave their old posts. For example, Millennium Pharmaceuticals closed with the loss of 160 jobs. Ninety per cent of employees found new jobs immediately and several new companies were founded.

Skills needs

The ratio of R&D jobs to jobs in actual production is much larger in the biomedical sector than in other manufacturing industries. Using empirical research on the actual skills profiles of existing biomedical companies, Bacon (2003) has drawn up skills diagrams for four types of companies in the sector according to size. Research plays a major role in terms of staff and departments as do quality control and assurance and clinical/regulatory affairs; and the smaller the company, the larger the relative importance of these functions, which is quite the opposite of what we see in other industries.

[86] ERM data covering the chemical sector (including pharmaceutical companies), 402 cases. The total number of planned job reductions in the period 2002 onwards is 88,752, and the total number of planned job creations is 43,968 indicating a net loss of jobs, **http://eurofound.europa.eu/emcc/erm**

[87] ERM website, **http://eurofound.europa.eu/emcc/erm/static/factsheet_3976.html?template=searchfactsheets&page=1&sel=7&date=&totalRecords=181&issearch=&nav=&order=&type=DESC**

[88] ERM website, **http://eurofound.europa.eu/emcc/erm/static/factsheet_3897.html?template=searchfactsheets**

[89] Council of European Bioregions website, **http://www.cebr.net/goodpracticelist.htm#redundancy**

Bacon identifies a range of job functions in the Irish biotechnology industry where companies have experienced particular difficulties in recruiting. One example is employees specialised in regulatory affairs. There is a very limited supply of such people in Ireland, although the pharmaceutical industry at present may provide some potential supply. Another area that is undergoing rapid growth and is experiencing a skills shortage is bioinformatics. To fill this growing need, redundancies from ICT might be accessed, although this would entail a considerable amount of retraining.

The study concludes that – in general – there is a considerable gap between the demand for skills that would be implied by the development of a biotechnology cluster in Ireland in the medium-term, and the projected output of relevant skills over this period. This development requires policy actions in a range of areas for the biotechnology industry to realise its full potential (Bacon, 2003).

At a more general level, the shortage of scientists with the right qualifications is among the main challenges for the European biomedical healthcare sector. Projections for the future supply of scientists indicate that this problem will only get worse. Among key drivers in this area are demographic changes, the limited attractiveness of natural science education among young people in Europe, and European scientists moving to the US and Asia due to the greater availability of finance and state of the art equipment for research ('brain drain').

Globalisation and the increasing complexity of the value chain are resource demanding and require managerial skills (value chain management, risk management); and competitive pressure and market developments accentuate the need for strategic management concerning location decisions, strategic alliances, etc. The need for managerial competences is particularly conspicuous in small biotech companies where the managers often have a purely scientific background.

Development of the industry may have a major impact on employment in associated sectors, such as healthcare, where the new biomedical products may impact on the processes that take place. Also, there are significant employment possibilities in the production (bio-processing) of high value-added products resulting from underlying developments in the knowledge base. The opportunities may arise in areas such as healthcare, pharmaceuticals, chemicals and medical devices. Companies in these sectors can provide the core for an emerging biotechnology industry, in the sense of providing a labour pool with relevant experience.

A highly skilled workforce is essential for the development of biotechnology. However, in the absence of supporting policies and conditions this would not of itself be sufficient to stimulate the development of a high value-adding industry that fully utilises these skills. However, there are also important challenges that could undermine the ability or willingness of the private sector to provide the requisite investment. For example, risks and difficulties associated with protecting intellectual property (IP) have the capacity to undermine the commercialisation of new discoveries. Also, changing demographic trends entail fewer young people entering the job market or pursuing further education than previously. These circumstances pose a challenge and potential constraint on biotechnology development in Europe.

Training issues

As a result of the nature of the companies in the sector, the most urgent training issues in the sector pertain more to scientific and managerial competences and less to competences in production. However, while much focus is on compensating for the lack of scientists, quality assurance and compliance with regulation are also important topics for training.

National actors such as the UK-based ERBI are engaged in training activities in the biomedical sector[90] as the example below indicates.

Training for biotechnology companies

ERBI has developed a portfolio of training courses for biotechnology companies. The training originated from ERBI's Human Resources Special Interest Group (SIG), a group of human resource managers from the region's biotechnology companies.

Training courses are run on a not-for-profit basis and include:

- Introduction to Drug Development: adapted for both scientific and non-scientific employees, it introduces delegates to the process, both scientific and business, leading from an initial discovery through to the marketing of a drug.
- Introduction to Management: the course objective is to help participants become effective managers. It has three modules: Managing the task, Managing the team and Managing the individual.
- Training for health and safety individuals: This course provides an up-to-date knowledge of health and safety legislation and an ability to apply risk management principles in the workplace.

ERBI launched its training portfolio in 2003 and holds courses every three months. Over 675 delegates from both scientific and non-scientific roles in biotech companies have attended the 'Introduction to drug development' course.

At European level, the Innovative Medicines Initiative Strategic Research Agenda stresses the importance of education and training in the biomedical sector. Among its main recommendations is to create a European Medicines Research Academy for education and training for professionals involved in biomedical R&D, including regulatory officers, over the whole lifecycle of a medicine.[91]

Restructuring and human resources – implications for the biomedical sector

- Shortage of European scientists may hamper growth in the biomedical healthcare sector and result in the relocation of knowledge intensive activities to countries such as the US and Asia.
- Managerial skills are needed in the sector in addition to scientific knowledge.

[90] Council of European Bioregions website, **http://www.cebr.net/goodpracticelist.htm#training**

[91] The Innovative Medicines Initiative, *Strategic Research Agenda: Creating biomedical R&D leadership for Europe to benefit patients and society*, **http://ec.europa.eu/research/fp6/pdf/innovative_medicines_sra_final_draft_en.pdf**

SWOT analysis

Based on the analysis of trends and drivers of change, this study has identified the following main strengths, weaknesses, opportunities and threats for the development of the sector:

Table 6: *SWOT analysis for the European biomedical healthcare sector*

Strengths	Weaknesses	Opportunities	Threats
High level of technology use Well educated labour force Well developed networks and intra-industrial cooperation	R&D spending less than in US companies Managerial competences in sector lag behind	Ageing population and health consciousness Converging technologies Access to cheap and highly skilled labour force outside Europe Proactive biotechnology policies incl. SME support measures Generous public funding availability Risk society (bioterrorism, pandemics)	Skills needs and global competition for brains – brain drain Extensive regulation imposes administrative burdens Low attractiveness of natural science among young people in Europe Lack of private investment Pressure on patents from producers of generic products High cost level in Europe Public scepticism towards the use of biotechnology

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