

The Pharmaceutical Biotechnology Industry in France

French Ministry of Research and New Technologies
Technology Directorate
Bio-engineering Department
January 2004

by

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INTRODUCTION

1.1 Objectives

This report has been drafted for the Working Party on National Policies towards Innovation in the Biotechnology Sector. The aim of this Working Party is to determine and describe innovation structures and mechanisms in the pharmaceutical sector in order to establish, on the basis of national analyses, the public policy components or actions likely to prove effective in furthering the development of biotechnology.

This report therefore consists primarily in an overview of the sector describing the economic environment, the pharmaceutical industry, research, national and sectoral policies, the actors involved, and the cultural, socio-economic and regulatory contexts of the market.

The purpose of this description is to identify all the factors which stimulate or constrain the dynamics of the sector so that, by gaining a greater insight into the distinctive dynamic properties of the system, a number of axioms can be formulated independently of specifically national characteristics in order to provide a basis on which to recommend public policies to promote the development of the biotechnology industry.

These axioms will therefore be formulated on the basis of the national reports from individual OECD Member countries, whose presentations are governed by a charter drawn up by the Working Party and common to all participating countries.

These national sectoral reports will therefore allow the OECD to establish an initial analysis that will attempt to answer the following question:

Is it possible to identify the main differences and similarities in the structure and dynamics of national biotechnology innovation systems between OECD Member countries which would explain the performances of those systems, and what are the implications in terms of public policy?

This analysis has been conducted and presented according to the same procedure by the individual countries participating in this Working Party, namely: Belgium, Finland, Germany, Japan, Netherlands, Norway and Spain.

1.2 Approach

The structure of this report is based on that set out in the "Guide Book" (December 2002) drafted by the OECD Working Party on Innovation Systems in the Field of Biotechnology. France joined this Working Party in November 2003.

The approach can be broken down into four lines of enquiry:

- A descriptive analysis of the national innovation system for biotechnology. This section describes the actors (organisations) involved in the pharmaceutical biotechnology innovation system, their relations, actions and conditions of involvement.
- An analysis of patents and published papers in order to establish an overview of the performance of the national biotechnology system, with indicators that can measure the scientific and technical output of the system.
- A survey of partnership arrangements between firms. In addition to seeking information on the structure of biotechnology innovation systems, the survey should ask firms in the pharmaceutical sector to describe their strategy towards co-operation with other firms as well as universities and research organisations.
- Interviews with selected firms, experts on the sector and market actors.

The French report follows this approach by drawing on information and data sets taken from the existing literature, and primarily the large volume of statistical and survey data available. The main sources of the data aggregated in this report are as follows:

- OECD;
- INSEE (National Institute for Statistics and Economic Studies);
- Xerfi;
- Ernst & Young;
- Eurostaf;
- French Ministry of Industry;
- French Ministry of Research;
- French Ministry of Education;
- ANVAR (French Agency for Innovation);
- LEEM (Les Entreprises du Médicament);
- France Biotech;
- European Union;
- Cofacerating;
- Caisse des Dépôts et Consignations;
- OST (Science and Technology Statistics Office);
- Chambers of Commerce and Industry;
- Social welfare agencies;
- Euronext.

1.3 National characteristics

1.3.1 Context and general environment, situation and prospects

Sources: OECD, INSEE;

Economic background and prospects for potential growth

On 1 January 2003, metropolitan France had a population of 61.2 million inhabitants, making France the 21st largest country in the world and the 3rd largest country in Europe after Germany and the United Kingdom. In addition, a further 1.7 million people live in France's overseas départements.

France's gross domestic product in 2002 amounted to EUR 1 520 billion. The rate of growth in the French economy (1.2% in volume, and 1.8% in 2001) is well below the average within the OECD area. Household consumption is only rising slowly in volume terms and this particular engine for growth appears to be at a standstill. Despite a relaxation of budgetary policy, France is experiencing an economic and structural slowdown and has one of the highest unemployment rates in Europe.

Table 1.1 Macroeconomic indicators

Total population in 2002	61 231 million inhabitants
GDP in 2002	EUR 1 520 billion (1)
Imports in 2002	EUR 380 billion (1) (2003S1 = EUR 200 billion FOB)
Exports in 2002	EUR 412 billion (1)
Variation in GDP in volume terms in 2002	+1.2%
Variation in imports in volume terms in 2002	+0.6%
Variation in exports in volume terms in 2002	+1.5%
Unemployment rate	9.1% (June 2002)

(1) Nominal value

(2) Constant prices compared with the previous year

Source: INSEE.

From 1989 to 1999, total salaried employment in France grew at an annual rate of 1.1%, increasing by a total of 10.8% over the period. At the beginning of 2002, metropolitan France had a labour force of 26.7 million workers (as defined by the ILB), consisting of 24.3 million employed workers and 2.4 million unemployed. This labour force has risen by 1.5 million over the past ten years, accompanied by a shift from employment in industry to jobs in the service sector.

The labour force should peak at 27 million in 2007 when the trend will be reversed and the labour force will shrink by 30 000 employed workers/year until 2010 before rising rapidly to 50 000 and then to 80 000 employed workers/year by the 2025.

By the year 2050, provided that the demographic trends observed in recent years continue unabated, metropolitan France should have a population of 64 million inhabitants, *i.e.* 5 million more than in 2000. During this period, the French population will continue to age. By 2050, one out of every three people will be aged 60 or over, compared with one out of five in 2000. According to INSEE, in view of the strong growth forecast in the over 60s population, the support ratio is set to gradually decline from 2.2 in 2002 to 1.5 in 2020 and should continue to fall from that date onwards.

This trend should lend powerful support to the prescription drugs market provided that there is no change in health policy.

Current Research and Development effort

Source: Ministry of Research

Domestic Expenditure on Research and Development (DERD) measures the research effort conducted on national territory. It amounted to EUR 32.9 billion in 2001 and is estimated at EUR 33.4 billion in 2002.

National Expenditure on Research and Development (NERD) measures the financing of research by French actors regardless of the location where the research is conducted. It amounted to EUR 33.6 billion in 2001 and is estimated at EUR 34.2 billion in 2002, *i.e.* approximately 2.2% of GDP broken down into 0.83% by the State and 1.37% by firms.

France ranked fourth in the world for R&D expenditure in volume terms in 2001, after the United States, Germany and Japan.

- The main sectors for R&D expenditure, in decreasing order, are as follows: car industry, telecommunications, pharmaceuticals, aeronautics, measuring instruments and chemicals. These first six sectors accounted for 50% of research expenditure.
- 124 firms employ more than 99 researchers. They account for:
 - $\frac{2}{3}$ of domestic R&D expenditure;
 - Almost 60% of researchers;
 - 86% of public funding.
- The top 13 French groups in terms of research alone account for half of the R&D expenditure by firms;
- Over the past ten years, the sharpest reductions in R&D budgets in France have been in the energy, materials and office automation sectors;
- The balance of foreign trade in R&D (resources versus expenditure) was positive over the entire period 1992-2001. However, over the same period, growth in R&D expenditure abroad outpaced that in the flow of resources into France.
- Growth in R&D expenditure abroad was partly attributable to the relocation policy of French firms, the type of relationships they have with their subsidiaries and the formation of groups at the European level.

The pharmaceuticals and aerospace sectors were those where foreign R&D expenditure was highest and continually growing. The same sectors also enjoyed the highest levels of R&D expenditure by firms outside France.

Table 1.2 Indicators of R&D and innovation in all areas

	France	European Union	United States	Japan
Number of researchers per 100 jobs (2000)	7.1	5.8	8.6 (1999)	9.7
Public expenditure on R&D as a % of GDP (2000)	0.84	°.65	°.71	°.58
Expenditure on R&D by firms as a % of GDP (2000)	1.15	1.06	1.88	2.16
Share of patent applications as a % (1998)	5.1	33.5	35.7	25.3
Technology balance of payments in USD millions (2001), income from royalties, licences, marks, etc.	501	Unavailable	22 309	5 403 (2000)

Source: INPI in 2nd Symposium Pharmaceuticals and Biotechnologies, The Economist, November 2003.

In 2001, domestic expenditure on R&D by civil administrations amounted to EUR 11.2 billion and accounted for 93% of total domestic expenditure on R&D by civil administrations and the military.

- A distinction is made between three institutional sectors within civil administrations: government, higher education and non-profit organisations (NPOs).
- The main actors are Public Establishments of a Scientific and Technological Nature (EPST), Public Establishments of an Industrial and Commercial Nature (EPIC), universities and Grandes Ecoles, and NPOs, which respectively account for 29%, 27%, 36% and 4% of research funded by civil administrations.

1.3.2 Main industries

Over the past ten years, the manufacturing and building sectors have lost 13.8% and 11% of their employees respectively, whereas a net total of 2.7 million jobs were created in the tertiary sector, *i.e.* 21% growth in employment over the past ten years (+9.6% in the trade sector and +24% in the services sector). The agricultural sector grew at an average annual rate of 3%.

Table 1.3 Main industries

Total turnover in 2002	EUR 1 252 billion (1)
Total foreign balance of trade in 2002	EUR 31.4 billion (1)
Total for industry (including energy)	Total turnover in 2002: EUR 277.4 billion (2) Balance of foreign trade in 2002: +EUR 1.1 billion
Agro-food industry	Total turnover in 2002: EUR 29.1 billion (2) Balance of foreign trade in 2002: +EUR 6.8 billion (1)
Motor industry	Total turnover in 2002: EUR 23.7 billion (2) Balance of foreign trade in 2002: +EUR 11.3 billion (1)

(1) Nominal value
(2) Constant prices
Source: INSEE.

France allocates 7% of its GDP to education, 9% to healthcare and 2% to research. French car manufacturers produced over 5.5 million units in 2001, making France the 4th largest manufacturer and 3rd highest exporter in the world. The French aeronautical engineering sector is particularly dynamic and exports in 2001 included 184 Airbuses worth a total of more than EUR 13 billion, an increase of 18% compared with the 2000.

In 2001 France had a foreign trade surplus of EUR 1.2 billion for goods and EUR 21.9 billion for services. The foreign trade balance rose to EUR 31.4 billion in 2002.

France is also the number one tourist destination in the world with 76.5 million foreign visitors, ahead of Spain (49.5 million) and the United States (45.5 million). France's export activity has led to a significant raising of the level of qualifications required for jobs in commercial management and development compared with those required for products sold on the domestic market. Manufacturing processes also require higher skills levels, although to a lesser extent that cannot readily be identified statistically.

France has an active financial market. At the end of 2001, Euronext (the pan-European exchange created through the merger of the Paris, Amsterdam and Brussels stock exchanges) ranked fifth in the world in terms of stock market capitalisation with a total worth of USD 1 843 billion.

1.3.3 The pharmaceutical industry

In 2001, the turnover of the pharmaceutical industry grew by more than 9% in France, coupled with an exceptionally high rate of growth in exports of over 33%. Overall turnover in the sector in 2001 increased by 18.2% in value terms.

In 2003, growth in sales of reimbursable drugs and medication remained buoyant (+6%), but was lower than 2001 due to the limited number of innovative molecules, the impact over a full year of price reductions decided upon in November 2001 and the doctors' strike at the beginning of the year. Exports remained at a very high level and overall activity grew by 12% in value terms in 2002.

Turnover grew at a rate of around 7% over the period 2003/2002, primarily driven by exports which rose by 10%. Three quarters of turnover came from sales to wholesaler distributors.

Overview

The French pharmaceutical industry generally emerged from the dispensaries, unlike the case in other countries where it was an off-shoot of the chemicals industry.

The share of world production accounted for by the French pharmaceutical industry currently stands at 6.5%, whereas the world share of the French market is merely 5%. French production has therefore benefited from globalisation. France is also the leading producer in Europe, accounting for 22% of the drugs and medication sold in Europe, although it needs to be borne in mind that the share of this market accounted for by France is both large and protected.

Table 1.4 Top 20 French pharmaceutical companies in 2002

Ranking	Turnover in 2002 in EUR 1000s	Name of company	Group
1	2 722 393	SANOFI WINTHROP INDUSTRIE	SANOFI-SYNTHELABO
2	2 680 000	AVENTIS PHARMA SA	AVENTIS
3	2 616 866	LABORATOIRE GLAXOSMITHKLINE	
4	2 100 000	LES LABORATOIRES SERVIER	
5	2 000 000	AVENTIS PASTEUR	AVENTIS
6	1 825 174	LABORATOIRE AVENTIS	AVENTIS
7	1 382 637	SANOFI-SYNTHELABO FRANCE	SANOFI-SYNTHELABO
8	1 319 905	LILLY FRANCE	
9	1 318 919	BRISTOL-MYERS SQUIBB	BRISTOL-MYERS SQUIBB COMPANY
10	1 201 372	ASTRAZENECA	
11	1 200 000	MERCK SANTE	E. MERCK
12	1 044 891	USIPHAR	AVENTIS
13	1 026 073	AVENTIS PHARMA SPECIALITES	AVENTIS
14	957 627	LABORATOIRES MERCK SHARP & DOHME	
15	941 302	AVENTIS PROPHARM	AVENTIS
16	934 120	PAITS-NOVARTIS	NOVARTIS AG
17	750 000	LABORATOIRES FOURNIER SA	
18	690 909	PIERRE FABRE MEDICAMENT	
19	636 012	ROCHE	F. HOFFMANN-LA ROCHE AG
20	627 391	PHARMACIA SAS	PHARMACIA SEARLE CORPORATION

Source: Cofacerating

However, the pharmaceutical industry faces strong competition on the supply side which has led to efforts to achieve productivity gains, by exploiting the expiry of certain patent rights and licences as they fall into the public domain, and restrictive policy contexts with regard to health expenditure. For example, over the next few years, 42 drugs licensed in the United States, which generate a combined annual turnover of USD 80 billion, are due to return to the public domain.

In line with the trend observed at the international levels, as the number of patents expiries increases pharmaceutical laboratories tend to restock their product portfolios to strengthen their strategic position or to move closer together. These transactions are not sufficient and laboratories are launching new molecules to replace products facing competition from generic drugs, which on average are sold 30% cheaper. At the same time, biotechnology (bio-informatics, genomic and proteomic systems) is expected to multiply the number of potential new drugs discovered by a factor of 10 or 20 and to reduce the cost of failure during the development stage.

In 2000, the turnover of the French pharmaceutical industry amounted to EUR 36 billion, of which the production of drugs and medication alone amounted to EUR 31 billion. 80% of the workers in this industry were involved in production.

In 2002, according to INSEE, the LEEM and the Ministry of Industry, the French pharmaceutical sector generated an annual turnover of EUR 34.4 billion and value-added of EUR 10 billion (2001).

In terms of financial capitalisation, over the past twenty years the French pharmaceutical industry has experienced a sharp increase in its capital value, which increased three-fold before halving in value when the Internet bubble burst. At the global level, the financial situation of these companies is currently improving and they now have a financial autonomy of 40%. The top twenty global groups in the world rankings include two French groups, namely Aventis and Sanofi which had a 4% and 1.5% share respectively of the world market in 1999.

Structure

Source: LEEM, Sessi, Cofacerating.

The number of pharmaceutical companies in France varies according to data source, although all sources concur in reporting a steady decline in number attributable to mergers and acquisitions over the past ten years, firms winding up and the expiry of patent rights, as well as the gradual process of restructuring that has been under way since the 1950s.

In October 2003, the Cofacerating and LEEM databases listed 309 companies in the pharmaceutical sector (excluding biotechnology firms), compared with 1 000 in 1950; 422 in 1970, 365 in 1980 and 349 in 1990. In addition to that number there were also 148 biotechnology firms specialised in healthcare among the 296 firms listed by the Ministry of Education in 2001, a figure close to that given by the France Biotech database.

Table 1.5 Number of pharmaceutical companies

Year	Number of pharmaceutical companies
1950	1 000
1970	422
1980	365
2003	457 (with 148 biotechnology/pharmaceutical companies)

Source: Documentation Française 2001.

Table 1.6 Main mega-fusions involving French companies

Sanofi Sterling Winthrop	1994
Bristol UPSA	1994
Rhône Poulenc Fison	1995
Rhône Poulenc Hoescht	1999
Sanofi and Synthelab	1999

Table 1.7 Start-ups/failures of companies in the pharmaceutical industry in the "drug manufacturer" category (as of the end of November 2003)

Number of	2000	2001	2002	Over continuous period of 12 months
Start-ups	11	9	8	8
Failures	3	2	3	1
Firms wound up	13	18	15	15
Net balance	-5	-11	-10	-8

Source: Cofacering.

French groups

Compared with the situation in other countries, the trend concentration remains relative due to the variety of products, markets and technologies. While the leading group operating in France has a market share of around 14%, the 50 top firms in France account for 83.3% (61.5% in 1980) and the top 50 groups 90.5% of the total. In 1999, out of the top twenty companies, 10 were French owned by for the most part were part of the two leading French groups Aventis and Sanofi. Aventis is the 8th largest group in the world and Sanofi is ranked in 17th position. These two leading French groups account for 28.5% of French production.

French Independent laboratories

There are therefore a greater number of SMIs, but their weight is decreasing. According to a Eurostat report published in 2001, the decline of the French independent laboratories is chiefly attributable to disposal operations since the mid 1990s. Since 1999, their share of the pharmacy market has fallen below the 20% mark. Their overall product portfolio is outdated and focused on a limited number of specialities and pharmaceutical classes. These laboratories are heavily dependent on the French market, given their general lack of international reach, which makes them more vulnerable to more constraining measures to control expenditure and to the aggressive competition from foreign firms.

These French independent laboratories also have limited R&D resources and their drugs portfolios are made up of old products. These firms have no significant diversification and rely on sales of reimbursable products; their market share has fallen from 54% to 18% over the past thirty years.

Foreign groups

France ranks 4th in the world in terms of the size of its prescription drugs sector. The French market is therefore also an attractive one for many subsidiaries of foreign groups, including those working in the area of biotechnology in that France offers what is far and away one of the choicest targets for growth.

Table 1.8 Share of French market held by foreign groups in 2000

United States	24%
Germany	13%
United Kingdom	8%
Switzerland	8%
Others	9%

Source: Documentation Française and Ministry of Industry, 2001.

In 1999, 80 foreign groups had registered offices in France. Their presence in France had been facilitated by the changeover from administrative price controls in 1994 to negotiated prices. Moreover, France is a production platform offering access to the European market as a whole. Two thirds of the drugs and medication market in France is supplied by foreign groups.

Production

The production of firms in the sector is relatively undiversified and is specialised in either:

- Drugs manufacturing; or
- Production of basic products in collaboration with other firms in the sector; or
- Production of other pharmaceutical products.

The use of sub-contracting is widespread (94% of firms in 2000) and almost exclusively concerns specialist activities within the same group. Concentration operations have increased the use made of sub-contracting by groups. Devoting ever-increasing funds to R&D, the major laboratories have also found themselves forced to restructure their industrial plant and make greater use of highly skilled sub-contractors for their production activities.

Labour force

The pharmaceutical industry employs some 98 000 people (2001), two thirds of whom are concentrated in the Ile de France, Rhône-Alpes and Centre Regions. This labour force is broken down as follows:

- R&D (14%);
- Production (32%);
- Distribution (35%);
- Administration (19%).

The R&D component has enjoyed its highest rate of growth in terms of relative share, rising from 5 000 employees to 15 200 employees in 1999.

Table 1.9 Top 20 pharmaceutical companies in France by number of employees in 2002

Ranking	Number of employees in 2002	Name of company	Group
1	7 366	AVENTIS PHARMA SA	AVENTIS
2	4 600	MERCK SANTE	E. MERCK
3	3 649	AVENTIS PASTEUR	AVENTIS
4	3 446	SANOFI WINTHROP INDUSTRIE	SANOFI-SYNTHELABO
5	3 100	LABORATOIRE AVENTIS	AVENTIS
6	3 064	BRISTOL-MYERS SQUIBB	BRISTOL-MYERS SQUIBB CIE
7	2 677	LABORATOIRE GLAXOSMITHKLINE	
8	2 676	LILLY FRANCE	
9	2 524	LABORATOIRES MERCK SHARP & DOHME	
10	2 353	BOIRON	
11	2 104	VIRBAC SA	
12	1 816	SANOFI-SYNTHELABO FRANCE	SANOFI-SYNTHELABO
13	1 723	GLAXO WELLCOME PRODUCTION	
14	1 717	MERIAL	AVENTIS
15	1 695	PAITS-NOVARTIS	NOVARTIS AG
16	1 583	PIERRE FABRE MEDICAMENT	F. HOFFMANN-LA ROCHE AG
17	1 545	ROCHE	
18	1 486	LABORATOIRES FOURNIER SA	
19	1 430	PFIZER PGM	
20	1 387	SANOFI CHIMIE	SANOFI-SYNTHELABO

Source: Cofacerating

Competitiveness

Sources: INSEE, Sessi.

Faced with growing competition, the pharmaceutical industry has developed two strategies, namely: moving into the generics market and/or seeking to exploit the new markets offered by biotechnology.

With regard to the former, since the 1990s many French laboratories have pursued a strategy of developing generics which, while cheaper to develop, require a larger sales and marketing budget. This strategy has had an impact on the registration of marks. The French pharmaceutical industry ranks first in terms of applications for brand protection.

The pharmaceutical industry faces numerous challenges at the international level:

- Adapting the industry to cost-cutting policies;
- Expiry of patent protection for certain molecules;
- Rising R&D costs;
- Growing importance of marketing and related expenditures;
- Pressure from private health insurance systems;
- Structuring of the sector through mergers and acquisitions;
- Search for new outlets;
- Wider portfolios and concentration of research efforts.

Technological competitiveness

In such a context, groups are seeking new strategies to improve productivity and research. Pharmaceutical groups are major consumers of research and development, and R&D expenditure accounts on average for 14%-38% of their turnover. The R&D conducted by the leading pharmaceutical companies must now meet new challenges, namely to:

- Increase the number of molecules in the initial stages of development;
- Meet the increased costs of R&D through greater investment. The number of patients needed for trials has risen to 50 000 compared with 1 300 ten or so years ago, while the cost of researching a new product has risen to over USD 500 million;
- Research into new technology to reduce the length of R&D cycles;
- Network in order to globalise R&D;
- Outsource;
- Focus research on molecules offering major sales potential, *i.e.* blockbusters.

Out of 40 blockbusters at the international level in 2000, only one was owned by a French group (La Documentation Française 2001), despite the fact that half of the companies in the sector innovate and every year invest a total of EUR 3.3 billion (2002) in research and development. 40% of the R&D conducted by SMEs is sub-contracted and 69% of that carried out by pharmaceutical companies. 43.6% of their turnover is protected by patents.

Commercial competitiveness

Production is led by exports and concentrated within groups (25% of turnover in 2000). The trade surplus is primarily attributable to trade with Western Europe and the growth in exports corresponds to growth in intra-group trade. In France, pharmaceutical specialists are ranked 5th in terms of sales after the car-making, aeronautics and space, electrical goods and perfume sectors.

Table 1.10 Top 20 resident French groups in terms of exports in 2002

Ranking	Revenue from exports in 2002 in EUR 1000s	Name of company	Group
1	1 331 212	SANOFI WINTHROP INDUSTRIE	SANOFI-SYNTHELABO
2	1 131 734	LABORATOIRE GLAXISMITHKLINE	
3	912 797	LILLY FRANCE	
4	689 536	LES LABORATOIRES SERVIER	
5	452 480	LABORATOIRES MERCK SHARP & DOHME	
6	280 300	VIRBAC SA	
7	275 016	BRISTOL-MYERS SQUIBB	BRISTOL-MYERS SQUIBB CIE
8	232 469	MERCK SANTE	E. MERCK
9	165 382	USIPHAR	AVENTIS
10	162 250	PIERRE FABRE MEDICAMENT	
11	159 628	GEURBET	
12	159 393	NOVO NORDISK PHARMACEUTIQUE	
13	158 560	PHARMACIA SAS	PHARMACIA SEARLE CORP.
14	154 585	PAITS-NOVARTIS	NOVARTIS AG
15	149 703	BIO-RAD	
16	143 189	BOEHRINGER INGELHEIM FRANCE	BOEHRINGER INGELHEIM

17	125 722	LABORATOIRES FOURNIER SA	KG
18	115 419	SCHERING SA	
19	108 600	RHODIA FOOD	RHODIA
20	106 176	ROCHE VITAMINES FRANCE	F. HOFFMANN-LA ROCHE AG

Source: Cofacerating

Over the past ten years the share of exports in turnover within the sector (medication, serums and vaccines for human and veterinary use) has doubled to 33%, mainly in exports to European countries (66%). The balance of trade in the sector amounted to EUR 6.3 billion in 2002 compared with EUR 3.6 billion in 2000. This surplus was attributable to the activities of French companies only, in that foreign groups imports equalled their exports. Two thirds of foreign trade consisted in intra-group trade.

2. NATIONAL POLICIES TOWARDS R&D AND TECHNOLOGICAL INNOVATION

According to OECD's recommendations for France, maintaining a long-term production potential capable of responding to the ageing of the population also calls for:

- Productivity gains to be stimulated through continued R&D efforts;
- An easing of the rigidities in the allocation of research expenditure between areas or programmes through a policy aimed at reducing the fiscal burden on firms.

Two thirds of French biotechnology firms receive national and European assistance for their R&D activities in the form of grants for the transfer of knowledge, patent and licence applications, research personnel, equipment, and incentive and tax measures.

Grants and tax incentives consist in the national competition for the creation of innovative and technology-based firms, incubators, national research networks, the research tax credit, national and regional start-up funds, as well as development grants to firms.

2.1 Main actors in public policy

There is no government agency in France providing centralised co-ordination of measures to promote innovation. Innovation programmes are drawn up by individual Ministries within their own sphere of action. Innovation and R&D activities are supported by individual Ministries, research organisations and agencies that translate R&D findings into applications. This apparent complexity must not be allowed to overshadow the basic simplicity of the way in which the rules for intervention are to be applied, a simplicity that has been further enhanced by the Act on Innovation as well as the new Innovation Plan for 2003.

Consequently, in the pharmaceutical sector, as in all sectors with high-tech value-added, the respective roles are assigned as follows:

- The Ministry of Research is responsible for conducting scoping research programmes and, where appropriate, laying down strategic lines of direction in collaboration with representatives of industry, academic research and universities;
- The Ministry of Industry's responsibility lies further downstream in the field of technological innovation, focusing in particular on pre-competitive programmes designed to lead to the development or the improvement of new products to be launched on the market;
- The Ministry of Health is responsible for regulating and managing collective health expenditure in partnership with social welfare agencies;
- Lastly, with regard to green biotechnology, the Ministry of Agriculture can also be called upon to set up research programmes in collaboration with the Ministry of Research.

In organisational terms, government actions are targeted on either the supply of health products or demand for health products: on the demand side, prerogatives are assigned according to the time needed to develop or bring to market a product resulting from research in progress; while on the supply side, actions are assigned according to the degree of maturity of innovations. The systemic organisation of these actions clearly reflects the separation of health policy (healthcare supply) from industrial policy.

The main actors in public policy towards innovation in the pharmaceutical biotechnology sector are therefore currently as follows:

- Ministries of Research, Industry and Health;
- Research agencies:
 - French Institute of Health and Medical Research (INSERM);
 - Life sciences division of the CNRS (National Centre for Scientific Research);
 - Life sciences division of the CEA (French Atomic Energy Commission);
 - French Institute for Agricultural and Food Research (INRA);
 - Institut Pasteur
 - Institut Curie;
- National Agency for Innovation (ANVAR);
- Caisse des Dépôts et Consignations (CDC);
- Universities;
- Local and regional government;
- European Union.

2.2 Main measures to support innovation

France's innovation policy was set out in the 1999 Innovation Act, together with the series of measures described below.

2.2.1 *The 1999 Innovation Act*

Source: French Ministry of Research

The Innovation Act was inspired by:

- A situation of moderate but steady growth in the world market;
- An international economic context characterised by strong growth in the new financial markets dedicated to new technologies (NASDAQ, New Market). The Act was designed to support and encourage the emergence of new innovative enterprises against a background of growth in the value of high-tech companies;
- A stable geopolitical context without uncertainty;
- Awareness of innovation theories among politicians and decision-makers;
- Development of an international approach by industrial groups to R&D management.

A new legal framework to allow research personnel to develop applications for research findings

Source: Ministry of Research

In order to support the research effort of public laboratories, the July 1999 Act on Innovation and Research provided a legal framework which allowed researchers to participate in business projects while at the same time pursuing a scientific career. The Act provided for three types of participation: civil servants were allowed to be partners or managers of start-ups; they could participate in the activity of a firm by providing scientific expertise and/or up to 15% of the start-up capital; and they could sit on the Board of Directors or the Supervisory Board of a private company.

As a result of this legislation approximately 120 researchers became involved in the biotechnology sector over a period of four years. The reasons for this development have not yet been determined.

Incentives for the creation of innovative firms

Source: Ministry of Research

The national competition for assistance in the creation of firms specialised in innovative technologies was set up in 1999. It is organised by the Ministry of Research in collaboration with ANVAR. The competition is held annually and the winners are selected by regional and national juries. The aim of the competition is to promote the creation and development of innovative firms and to encourage individuals with a project involving innovative technology to set up a company.

31 incubators for public research findings have been set up and are currently operational. They were inaugurated by the Ministry of Research and the Ministry of the Economy, Finance and Industry in March 1999. These incubators were put in place by Universities working together at the regional level with regional and local authorities. Their purpose is to promote the creation of innovative firms to develop applications for public research findings. This system can provide financial and material assistance for the winners of the national competition so that they can proceed with their project and set up a firm. These incubators cover several sectors, but focus on certain sectors such as biotechnology or equipment. Two incubators are exclusively dedicated to biotechnology, namely Paris Biotech in the Ile-de-France region, and Eurasanté in the Nord-Pas-de-Calais region.

In addition to this system of incubators and in view of the fact that the creation of firms requires investment capital as soon as projects start up, in 1999 the State provided approximately EUR 20 million under the Innovation Act for the creation of:

- Three national venture capital funds for specific sectors (biotechnology, information and communication technologies);
- A further seven general venture capital funds for investment in firms relating to public research findings.

The venture capital funds provide the investment needed to set up a firm. These private funds are specialised in providing venture capital for innovative firms and their role is to participate in the initial financing of such firms.

These incentives for new start-ups can work synergistically. Competition winners can set up firms that will spend a specified period of time in an incubator. Regional and national venture capital funds acquire shares in firms set up by the winners of competitions or by researcher benefiting from the new legal framework for the development of applications for research findings.

Incentives for the development of partnerships

Research and technological innovation networks, which now have a legal basis, provide value added through the pooling of resources, the concentration of collaboration between public and private research sectors and support for research programmes. The proposal of topics for internal discussion, assiduous efforts to foster dialogue and generate information, as well as the sharing of best practices are all ways in which the network steering system can be enhanced. Besides the above, recommendations are made on practical measures to improve network operation, calls for proposals, financing, recruitment and assessment, with the aim of improving operational efficiency.

Networks receive incentive funding and provide significant support for co-operation in research activities and the structuring of the research effort. Networks make it possible to:

- Improve the transfer of upstream research findings to industry by removing the technological barriers to the joint development of products and services based on new technologies;
- Accelerate the use of new technologies;
- Lend structure to and co-ordinate research policy;
- Support comparative advantages in economic sectors;
- Place research within the context of demand from industrial and market actors;
- Lend support to the creation and growth of innovative firms.

First impacts of networks

The network policy was first adopted in order to foster synergies between major programmes posing challenges which were beyond the capacities of individual private and public partners. This was an unprecedented initiative in terms of the resources deployed. Networks provide access to major sources of funding and allow research capacities to be focused on major issues.

Networks have earned the gratitude of the industrial world despite the deployment of what are often modest resources compared with those of firms. Against a background of fierce competition, networks have proved to be instruments that unite individual actors and encourage laboratories to match each other's efforts. In addition, industry may begin to adopt a policy of purchasing research and of creating competition between laboratories. Driven by such forces, laboratories align their research directions more closely with those of networks and thereby increasingly start to consider applications for priority areas of research. In terms of the pooling of resources and fostering of synergies, networks seem to be both meeting and exceeding initial expectations.

Overall, networks make it possible to improve:

- The outreach of research organisations. As a general rule, a research organisation does not have sufficient resources to cover the full range of activities in its remit and is therefore unable to assume sole responsibility for co-ordination at the national level;
- The relationship between private and public research, given the opportunity gains offered by a closer relationship. The network concept is therefore an instrument that allows closer links to be forged between institutions, researchers and laboratories, given that the network is a forum for discussion.

Lastly, besides the above-mentioned objectives, networks meet several needs:

- The on-going need to synchronise the activities of partners, which the network concept meets through its ability to unite;
- The need to remedy deficiencies. SMEs, for example, find it hard to conduct certain types of research because of the induced cost. They tend to work on a just-in-time basis, lack staff and have difficulty in expressing their needs in terms of science. The obligation that an SME be involved in projects encourages the inclusion of SMEs and SMIs in the processes of innovation and public research;
- Lastly, the need for complementarities within the same research discipline.

In terms of overall support for the research effort, as a general rule it would seem that the policy of creating networks also provides a basis on which to undertake multi-disciplinary programmes to develop new areas of knowledge at the interface between individual disciplines. These interconnections are primarily developed within the framework of technology platforms and more particularly in areas relating to telecommunications and to the new information and communications technologies.

Alongside these networks, there are several systems that are similarly designed to establish bridges between public research and industry:

- 18 National Technological Research Centres set up between 2000 and 2002;
- 41 Technological Research Teams created since 1999;
- 14 Commercial and Industrial Activity Services (SAIC);
- 200 Regional Centres for Innovation and Technology Transfer (CRITT).

These amount to a total of 265 structures designed to foster partnerships, with over eight different denominations. This is a specifically French approach in which any new idea or proposed improvement is used to complement the systems already in place, without having to worry about the actors addressed losing sight of all the measures and services available.

The Research Tax Credit is a tax incentive that has been in place since 1983. This measure is designed to encourage firms to make a greater research effort. It benefits major industrial groups and above all SME/SMIs which receive a credit equal to 50% of the increased in R&D spending by a firm.

2.2.2 *The 2003 Innovation Plan*

Source: Ministry of Research

The Innovation Act was designed to provide support for projects in a way that would encourage projects to emerge, and not to resolve structural and economic problems. However, the environment in which this Act was to take effect suddenly suffered a number of blows:

- A crisis in the stock markets;
- A decline in the attractiveness of new technologies to financial markets;
- An international geo-political crisis;
- A review by major industrial groups of their R&D policy, whose budgets were the first victims of economic measures, restructuring, regrouping of sites, and the search for new know-how and skills in emerging countries such as India, Brazil and China (cf. IBM, Cap Gemini, etc.);
- The pursuit by industrial groups of a policy aimed at internationalising their R&D effort.

Due to the change in the international climate, it would seem that the new aid measures rapidly failed to attract support from venture capital funds, seed capital funds or business angels.

In areas relating to biotechnology alone, it would seem that 148 firms were created as a result of aid measures (competitions and incubators), out of which 28 attracted seed and venture capital in return for a net outlay of EUR 22 million of public money over a four-year period, *i.e.* EUR 790 000 per firm. Between 25 and 31 patents, at least, should ensue. These firms represent from 6% to 8% of start-ups in the biotechnology sector over the past four years.

Twice the amount of secondary funding would have made it possible to increase the number of firms and sharply reduce new start-up costs. Despite the fact that the public sphere had created venture capital funds and bio-incubators, the intervention by government was out of step with the trend in the economic environment; this shortcoming was addressed by the Innovation Plan.

Consequently, the policy was adjusted by means of the 2003 Innovation Plan which will strengthen the provisions of the 1999 Innovation Act, namely:

- An effort to achieve greater synergy with European poles of excellence;
- Continued pursuit of the policy of creating innovative firms;
- Support for the CDC-PME (a subsidiary of the Caisse des Dépôts et Consignations) which has announced financial aid of EUR 30 million for young firms;
- Actions to raise researchers' awareness of patent policy and to give them a financial interest in patents.

The Innovation Plan follows on directly from the 1999 Innovation Act by establishing new legal statuses and by introducing new tax provisions.

The new status of "business angel"

The legal and fiscal status of business angel sole proprietorship (*société unipersonnelle d'investissement providential* or SUIP) allows business angels to actively manage their investments. This status has tax benefits (in particular an exemption from corporation tax for the first ten financial years) provided that the capital is invested mainly and for a long period of time in innovative firms.

Aid for R&D projects conducted by "young innovative firms"

This aid is for SMEs that have been in existence for less than 8 years and that have viable R&D projects based on R&D expenditure of at least 15% of their operating costs. Among other things, firms received such aid are granted total exemption from employer contributions for a period of eight years with regard to staff working on R&D projects.

New aid aimed at innovation

Reduced tax rates are linked to the R&D expenditure of all firms seeking to innovate, regardless of the size and age of firms and the sectors in which they are active. It has been confirmed that in 2004 R&D investment will be exempt from professional tax; the rules on decreasing depreciation of R&D investment have been restored to the level prior to 2001 (40%).

"Foundation of a Scientific Nature"

In March 2003, the National Assembly passed a tax reform in favour of patronage and foundations.

To complement the measures in the Innovation Plan aimed at increasing R&D expenditure by firms, the Ministry of Research has defined a new status of a variant form of "Foundation of a Scientific Nature", which has been accepted by the Council of State in principle and whose specification is currently being finalised. These research foundations of a scientific nature will allow the funding of research into priority subjects to be increased through civil actions.

Simplification of aid for innovation

ANVAR will be allowed to co-ordinate and supervise the network of local innovation developers, which will be relayed by the Chambers of Trade and Industry to disseminate information to the firms closest to the ground. This measure will be implemented through the new multi-annual contract between the State and ANVAR from 2004 onwards.

Practical measures to better capitalise on R&D in firms and laboratories

- Introduction of work placements in firms for Ph.D. students;
- Increase in the number of CIFRE scholarships;
- Encouragement of public-private scientific programmes;
- Encouragement of patent applications for researchers in the public sector;
- Greater recognition of innovation in the careers of public sector researchers;
- Renewed funding for successful incubators, after appraisal;
- New funding for seed capital (EUR 30 million) through the Caisse des Dépôts et Consignations.

3. STRUCTURE, DYNAMICS AND PERFORMANCE OF THE BIOTECHNOLOGY SECTOR IN FRANCE

3.1 Public research

70% of the civil R&D budget for life sciences is allocated to research conducted by research agencies:

- CNRS: 28%
- INRA: 19.7%
- INSERM: 18.7.

In all, approximately 25% of the civil R&D budget for life sciences is assigned to biotechnology and human health, *i.e.* some EUR 350 million in 2002. This figure should be compared with the EUR 3.3 billion assigned by the pharmaceutical industry to research activities and the additional sum of around EUR 100 million of aid provided by the Ministry for these areas of research in the form of incentives and other measures.

Table 3.1 Annual national budget for R&D in the life sciences

In EUR millions	2000	2001	2002
Civil R&D budget	1 708	1 839	1 994
Other	717	732	793
Pharmaceutical industry	2 903	2 897	3 299
Associations	119	119	119
Total	5 446	5 586	6 205

Source: Ministry of Finance

3.2 The private biotechnology sector (a3-a5)

3.2.1 Situation

There is uncertainty over the number of biotechnology firms specialised in healthcare:

- A France Biotech survey lists around 80 biotechnology firms currently specialised in healthcare;
- Ernst Young and the Evaluation and Forecasting Directorate of the Ministry of Education lists 296, although this figure includes biotechnology activities directed at human health, animal health, or the food and vegetable sectors;
- A survey by France Biotech and Deloitte Touch estimated that there were 255 biotechnology firms in 2002, of which approximately 125 were specialised in human health.

This latter study also specifies the main activities in the health sector of biotechnology firms specialised in human health in 2002 (Table 3.2).

Furthermore, a large percentage of research activities are conducted in public laboratories where a large number of clinical studies are conducted (296 listed to date and primarily concerning molecules designed to treat orphan diseases).

Table 3.2 Main activities of biotechnology firms specialised in healthcare

% of firms	Therapy	Diagnosis
Oncology	15%	17%
Infectious diseases	13%	7%
Immune system	10%	9%
Genetic diseases	7%	12%

Source: Deloitte 2001.

In 2001, a national overview of the biotechnology industry was drawn up on the basis of a survey (DEP) of a selection of 1 400 firms from the sector. This overview produced a list, for 2001, of 625 firms whose activity related to biotechnology and the supply of products, processes, services and instrumentation.

Out of these 625 firms:

- 72% produced products or used new processes;
- 28% sell equipment and services to other firms;
- 92% conduct biotechnology R&D in-house, and 47% outsource R&D;
- 329 have a related biotechnology activity;
- 296 develop products or use new processes, there would currently appear to be 350 to 400 such companies at present.

Table 3.3 Number of firms and employees in the biotechnology and pharmaceuticals sectors

In 2001	Total	Biotechnology firms	Biotechnology firms specialised in healthcare	Pharmaceutical industry
Number of firms	625	296	80-125	329
Employees	98 000	9 954	≈ 1 400/3 000	88 046
R&D workers	17 940 (18%)	3 338 (34%)	> 2 000	14 602 (16%)

Source: DEP.

The main attributes of these 296 firms are as follows:

- They have fewer than 500 employees;
- 50% have fewer than 10 employees, the average number being 34;
- 50% were set up less than 6 years ago;
- They employ a total of 9 954 people (2001);
- 95% have an in-house R&D activity;
- 45% outsource R&D work, 42% sub-contract R&D work to another firm;
- 66% receive or have received public aid in the form of:

- Assistance with the transfer of skills, patents and licences (41%);
- Assistance with the recruitment of research staff (22%);
- Grants for plant and equipment (48%);
- 58% of biotechnology firms specialised in human health provide services both for own account and for third parties by making their skills available to contractors. Biotechnology firms thereby generate income that can be used to fund their own R&D work;
- 26% of these firms work solely for third parties;
- 16% work exclusively for own-account;
- 51% have made human health their sole area of interest;
- 20% are active in more than two areas (animal health, agriculture, cosmetics, food, the environment);
- 32.4% have organised their activities to cover all stages in R&D ranging from basic research to pre-clinical testing;
- 23% are semi-integrated firms covering at least all stages in the innovation cycle up to phase II clinical testing;
- 31% are specialised in R&D or sub-contract R&D.

At the same time, many R&D laboratories have opted to focus their research efforts on generic drugs that are less expensive to develop. Despite government incentives aimed at facilitating R&D efforts, the situation in the financial markets has reduced the number of biotechnology firms reaching maturity.

Table 3.4 Specialisation of biotech firms in the human health sector in 2000

Recombinant vaccines	9.4%
Gene therapy	16.2%
Cell therapy	13.5%
Diagnostic instruments and products	10.8%
Functional genomics	24.3%
Pharmaco-genomics	12.2%
Structural genomics	6.8%
Combinatorial chemistry and magic bullets	4.1%
Drug delivery and galenics	21.6%
Therapeutic proteins	16.2%

Table 3.5 Trends in R&D expenditure 1995-1999

Trend increase	France	United States	Europe
1995	n/d	6.6%	3.4%
1996	5.4%	14.7%	6.6%
1997	3.8%	13.6%	18.3%
1998	4.7%	11.7%	7.9%
1999	6.5%	16.8%	7%
2000	6%	11%	6.5%
2001	5.5%	9%	6%

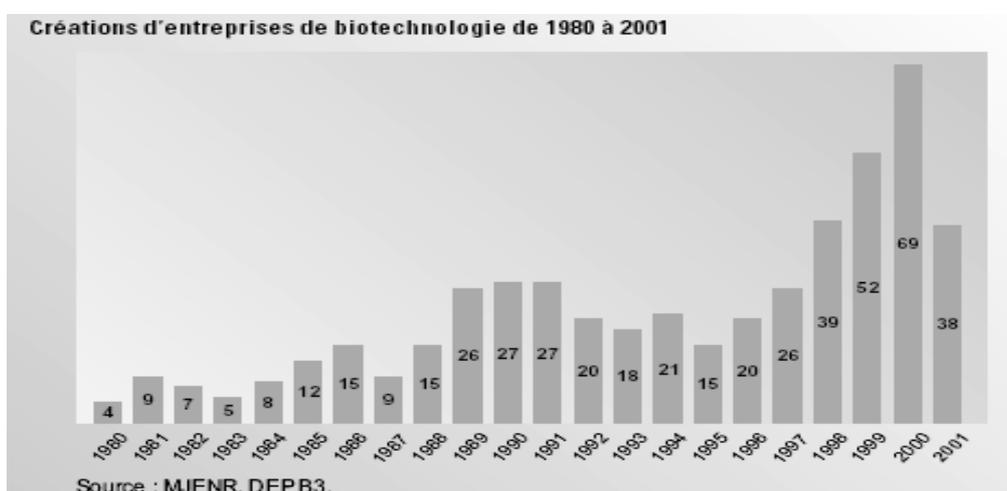
Source: Eurostat 2001.

3.2.2 *Trend in start-ups and failures (E26)*

Half of all biotechnology firms in France were founded before 1999 and the new wave of start-ups since 1998 can be attributed to:

- The sub-contracting and outsourcing strategy pursued by the pharmaceutical industry;
- A satisfactory economic and financial environment in which the expansion of financial markets was accompanied by a wave of new start-ups in 1999 and 2000;
- The emergence in 1999 of a policy aimed at promoting innovation with the adoption of the 1999 Innovation Plan.

Table 3.6 Start-ups of biotechnology firms from 1980 to 2001



3.2.3 *The international dimension (d20-d21)*

Total European exports rose from EUR 7 billion in 1980 to EUR 63 billion in 1999. Foreign groups established in France account for half of French pharmaceutical output. Turnover is growing at an annual rate of 7% and growth in sales is primarily driven by increased exports, which amounted to 10% over the period 2003/2002.

According to the 2001 Deloitte study, a third of all biotechnology firms have no partners, while 30% have between 3 and 5 partners. These partners, where they exist, are domestic firms in 60% of cases, European firms in 25% of cases and US firms in 11% of cases. 84% of the most mature firms have entered into at least one partnership agreement.

According to the Xerfi 2000 study (Table 3.5), an analysis of partnership agreement entered into by French biotechnology firms over the period 1995-1999 reveals the weakness of alliances in the sector. In addition, in 90% of cases, these partnership agreements were entered into with foreign operators, indicating the weakness of the alliances with French pharmaceutical groups.

Table 3.7 Strategic alliances entered into by leading French biotechnology firms 1995-1999

	Partnership with a biotechnology firms	Partnership with a pharmaceutical company	Total number of partnership agreements
Genset	2	6	8
Transgene	1	1	2
Cerep	3	3	6
Biotech vector pharma	3	3	6
Flamel Technologie	0	4	4
Drug Abuse Sciences	1	1	2
Total	11	17	28

3.3 Performance (a5)

Weaknesses in the biotechnology sector still remain in France due to:

- The weakness of the pharmaceutical sector;
- The trend towards concentration which reduces the potential number of partners;
- Uncertainty in financial markets;
- The distinctive nature of French R&D culture which is not sufficiently focused on the commercial and industrial dimensions.

The build-up of momentum over the past few years is not always sufficient to compensate for the lag in R&D activity and the following brakes therefore remain on growth:

- Non-existence of activist venture capital;
- Mismatch with financial markets;
- A constraining regulatory and fiscal environment;
- Lack of a culture of entrepreneurship and industrial protection;
- A clear divide between basic research and the world of industry.

Table 3.8 Performance of biotechnology firms

34% of biotechnology SMEs file patents to protect their inventions (1995-2000)	
60% of pharmaceutical groups submit patent applications	
Number of biotechnology patents filed by French firms	171 (2002)(1) 150 (2001) 158 (2000)
Annual turnover of biotechnology firms	EUR 0.3 billion (2001)
% of annual turnover of the pharmaceutical industry	1%
% of R&D budget of the pharmaceutical industry	10%

Source: INPI, DEP (Ministry of Education).

(1) Deloitte 2002: Ten firms account for over 80% of patents filed.

Each group strikes a balance in its R&D strategy between in-house research, joint research projects conducted in partnership and licence acquisitions. As a general rule, the work of the start-ups will probably

consist in finding a "candidate drug" molecule, while that of the groups will be to take care of the development and marketing stages.

Table 3.9 Status of the Biotech Santé Humaine pipeline of French biotechnology firms in 2002

Phase	Number of molecules in 2002
Pre-clinical	89
Phase 1	27
Phase 2	24
Phase 3	5
Phase 4	3
Total	148

Source: Deloitte 2002 survey

Table 3.10 Status of the Biotech Santé Humaine pipeline of French biotechnology firms in 2003

Phase	Number of molecules in 2002
Pre-clinical	111
Phase 1	18
Phase 2	22
Phase 3	7
Phase 4	6
Total	148

Source: Ministry of Research, estimate for 2003.

To defend their strategic positions, groups tend to acquire licences to produce drugs from biotechnology firms or external sources. This strategy applies on average to 35% of drugs in the R&D phase in pharmaceutical companies. The portfolios of biotechnology firms at world level in 2000 contained some 1 500 drugs, which will probably lead to the launching of 8 to 12 new products a year from 2007 onwards.

In France, the activity of these biotechnology firms remains marginal compared with that of the pharmaceutical industry. The number of molecules in the latter's pipeline apparently amounts to between 140 and 160, primarily in the pre-clinical phase. This figure excludes pharmaceutical groups and agro-food groups.

4. THE DYNAMICS OF INNOVATION

4.1 Knowledge potential (Ba8, Ba9)

The share of world patents accounted for by French patent applications to the European Patent Office (EPO) in 2000 amounted to 6.6%, four percentage points lower than in 1995.

Table 4.1 French scientific output

Field in which published	Share of world total as a %
Basic biology	5.5%
Medical research	4.7%
Applied biology and ecology	4.3%
	Trend over 1995/2000
Basic biology	-1
Medical research	-2
Applied biology and ecology	+6

Source: OST 2003.

In response to the continuous decline in patent applications by public research bodies up to the year 1999, the 1999 Innovation Act provided for:

- Business and industrial centres in universities;
- The creation of subsidiary agencies for technology transfers in research bodies (CNRS, INSERM, INRA);
- A policy aimed at raising the awareness of researchers regarding patent applications.

Since the Innovation Act was first passed, 120 researchers qualified in biotechnology have gone to work in a start-up.

4.1 Human resources (Ba9, Ba10)

In terms of the use it makes of human resources, the pharmaceutical sector is clearly a high value-added sector in view of the fact that approximately 18% of jobs in the sector are related to research.

Table 4.2 Employment in the pharmaceutical industry

Number of persons employed	98 000 (2001)
Number of managers	20 000 (2001)
Number of managers assigned to R&D	17 940 (approximately)(2001)
Managers assigned to biotechnology R&D	8 772 (approximately)(2001)
Number of theses submitted annually in life sciences and biology	1 800 (1)
Creation of skilled jobs	1 860 (2002) (710 in 2001)
Recruitment of recent graduates	335 (18%)
Recruitment for R&D	111
Recruitment for production	800 (2)
Staff turnover in pharmaceutical sector	11% (3) (2002)

Sources: APEC, OST, INSEE, LEEM.

(1) In the fields of life sciences, health and biology (except for graduates in pharmaceutical and medical sciences).

(2) Sales and marketing staff appear to be a priority for recruitment in the sector.

(3) Which is the highest rate observed in different sectors and which would suggest that there might be upwards pressure on wage costs.

Analysis of the recruitment statistics for 2001 reveals both the policy thrust of firms in the sector and the pressures exerted on the job market.

The current level of competition in the sector prompts firms to adopt a more aggressive sales policy which is reflected in the recruitment data by the high percentage of new sales and marketing staff recruited, these being the areas overwhelmingly given priority. The market situation also reflects the continuing interest shown by groups and firms in research jobs.

The job market, on the other hand, appears to be extremely tight for employers. Apparently the number of PhDs and graduates produced by the higher education system in 2003 is only just enough to meet the requirements of industry. However, this matching of requirements probably conceals upwards pressures on the wage costs for firms in that a number of these young researchers and graduates find employment in the public research sector and teaching.

The market is therefore supply-led and this situation also reflects a higher rate of turnover than other sectors in that it encourages mobility among managers in the pharmaceutical industry.

Moreover, French social contributions are the highest in Europe; however, the new status of "Young Innovative Enterprise" should reduce the rate of 60% observed in France to approximately 5% to 10% with regard to over 90% of the jobs concerned.

Table 4.3 Comparison of social contributions in a selection of European countries

Country	Employer's rate of contribution	Employee's rate of contributions	Total rate of contribution
France	40%	20%	60%
Germany	21%	21%	42%
Italy	35%	8%	43%
Netherlands	18%	36%	54%
Spain	31.6%	6.3%	37.9%
Sweden	43%	0	43%
United Kingdom	12.2%	10%	22.2%

Source: Chambers of Trade and Industry Networks.

4.3 Financing (b11-b14)

A large number of biotechnology firms make use of the financial and logistical assistance provided by venture capital funds and companies, or take advantage of the provisions of the 1999 Innovation Act.

Public funding by research and technological innovation networks

Over a period of four years, networks in the biotechnology sector have provided support worth EUR 168 million for 331 projects involving 694 partners, of which 243 firms and 63 groups; 90 of these projects were funded by private partners.

The impact of this assistance is estimated to be equivalent to a forecast 180-260 patent applications or extensions and 219 prototype products or processes. The funding provided by the State has permitted equal investment by private partners. Approximately 440 jobs have been created, *i.e.* around 8% to 10% of total R&D employment in the sector. These projects should generate EUR 22 million in income from licences and can be offset by growth of merely 0.016% in the turnover of the sector; in fact, the latter grew by 6% in 2002.

Table 4.4 Impact of national research and technological innovation networks on the biotechnology sector (2000-2003)

Budget	EUR 168 million, of which: EUR 90 million provided by private partners; EUR 78 million by the State
Number of projects	331
Number of partners	694, of which: 243 SMEs; 63 industrial groups.
Forecast impact of national networks	
Number of patents	Between 180 and 260
Number of new products, prototypes and processes	219
Number of new jobs created	Approximately 440 (1)
Income from licences and duties	EUR 22 million

(1) Approximately 5% of R&D personnel in the pharmaceutical sector.

Other sources of public financing: ANVAR and Research Tax Credits

ANVAR's budget for biotechnology firms amounts to EUR 88 million (1999-2002), primarily aimed at young firms less than 3 years old and with fewer than ten employees, that is to say:

- Assistance for 395 projects involving new start-ups, transfers of technology or innovative projects;
- Approximately 430 jobs created directly and 27 biotechnology firms.

The Research Tax Credit (EUR 527 million in 2002) provided assistance worth EUR 15 million a year to pharmaceutical companies and biotechnology firms that had declared an increase in their R&D spending. The amounts involved should double with the introduction of new arrangements.

Venture and seed capital funds

Out of an initial budget of EUR 44 million, public capital venture and seed capital funds (primarily the BIOAM) have invested EUR 15 million in 7 biotechnology firms for an expected return on private investment by the first financing rounds of approximately EUR 60 million.

The CDC, alongside research agencies and other major investors, promotes 15 venture and seed capital funds whose portfolios include 40 firms specialised in the life sciences (2002), among which 16 received renewed funding in 2002. In 88% of cases, these firms were set up to develop spin-offs from public research, 78% of them have also benefited initially from public incubator facilities.

This system is designed to generate a knock-on effect on the market and economic actors. Seed capital funds primarily invest in the equity of innovative firms with a high-tech agenda and high growth potential, when the firm is first created or during the initial financing stage, that is to say the stage at which in most cases they have not yet started to develop their products or to generate any significant income.

BIOAM is the national seed capital fund for biotechnology. Aid is subsequently provided by non-sectoral regional funds, of which there are seven. Investment in the field of the life sciences amounted to EUR 4 million in 2002 compared with EUR 3.6 million in 2001; the share of refinancing in this sector is virtually nil. Average leverage amounts to 2.2 on venture capital provided by other investments, which are primarily companies specialised in such funding and, to a lesser extent, research agencies, financial establishments, industry and foreign investors. Investment funds retain their equity holdings in SMEs for three to five years on average.

Private financing (b11 & b14)

Venture capital investment in France amounted to EUR 758 million in 2002, compared with EUR 1 900 million in the United Kingdom, EUR 969 million in Germany and USD 9 500 million in the United States.

Approximately 30% of this expenditure was sub-contracted in 2000. Biotechnology investment funds provide EUR 169 million (2002) in France, of which 6% was invested in young firms compared with 23% in 2000-2001 and EUR 31 million during the first half of 2003.

Stock markets are tight in France after the bursting of the Internet bubble. In addition, flotations are received coolly by investors and there are virtually no business angels in France for fiscal and cultural reasons.

Table 4.5 Breakdown of R&D in the French pharmaceutical industry in 2000

	millions	% of domestic and export sales
Internal expenditure	2 402	8.7%
of which: -- fundamental research	280	1.0%
-- applied research	851	3.1%
-- experimental development	1 271	4.6%
External expenditure	948	3.4%
Total R&D expenditure	3 349	12.1%

Source: LEEM, Ministry of Research.

There are 60 companies operating in the venture capital market in France and during the first half of 2003 these companies invested a total of approximately EUR 213 million in all sectors of the economy.

159 companies received funding worth an average of EUR 1.3 million during the period, down 21% compared with 2002. Investors are focusing on the refinancing of their portfolios and are therefore giving priority to development capital until the market turns. The main venture capital companies operating in the biotechnology sector in France are as follows (Table 4.6):

- 3i;
- Sofinnova Partners;
- Apax Partners;
- Banexi Ventures Partners;
- Atlas Ventures.

A total of six biotechnology firms were quoted on the new market in 2000:

- Appligene Oncor, which has since become QBiotech;
- Cerep;
- Chemunex;
- Flamel Technologie;
- Genset;
- Transgene.

There were four companies quoted on the new market in 2003: Transgene, Nicox, Cerep and Oxis INTL.

Table 4.6 Source of investment in French biotechnology firms in 2002

Company	Amount invested in € millions	Financing phase	Investors
Proteaxis	0.9	Seed capital	Finorpa, Nord Innovation Nord creation
Hybigenics	16.7	3 rd	Life Science Partners, Banexi Ventures LFR
Carex	5.4	1 st	Sofinnova, GIVM
Faust	2	1 st	Sofinnova, Auriga Partners
Meristem Therapeutics	23	3 rd	SPEF, Innoven, LCFR, Banexi Ventures, Odyssee Ventures, CPR P E, Pechel Industries, Thetys, 3i, Sofimac
Collectis	16	2 nd	Bank Invest, AGF P E, LCFR, Odyssee Ventures
Palumed	2.15	1 st	IRDI, SOCRI, CFMT, FCJE
Innate Pharma	20	2 nd	Alta Partners, AXA P E, Sofinnova, GIMV, Auriga
Mutabilis	2.2	1 st	BioAm, AXA P E
GenOdyssee	2	2 nd	SGAM, LCFR
Thertopis	2.5	1 st	LCFR, SPEF, FCJE
Opi	5	2 nd	FCJE, Innoveris, Sofimac, Rhône Alpes Création
Proskelia	60	1 st	Warburg Pincus
Neuro 3D	20	2 nd	TVM, HealthCap, Sofinnova, APax
Aureus Pharma	1.6		BioAm, AXA P E, FCJE
Cytheris	6.9	2 nd	BioAm, CDC Innovation, AGF P E, Ventech
Aptomomics	7	1 st	BioAM, CDC Innovation, AGF P E, Ventech
Metabolix Explorer	6	2 nd	CL P E, SPEF, Innoveris, Sofimac, FCJE
IDM	20		Sanofi Synthlabo
Diatos	6.6	2 nd	CL P E, Sofinnova, AGF P E
Vivalis	3	1 st	FCJE, Crea agro, Pays de Loire Dvpt
Cellial Technologies	0.9	Seed capital	Finorpa, Nord Innovation, Nord Création, Innovam
Total	229		

Source: Kopp Report, 2002.

Cerep specialises in the development of new drugs by means of a platform that allows is to discover candidate drugs both more rapidly and at lower cost. This platform is based on the following technologies: chemo-informatics, combinatorial and medicinal chemistry, drug targeting and high-flow profiling, in vitro and in vivo pre-clinical testing, and Bio-Print (relational database based on reference compounds that can determine the pharmacological and physico-chemical properties of drugs). It can also be used to carry out successive operations at high speed: identification of targets, validation of pharmacological tests and selection of the best candidates, molecular modelling and then synthesis of organic combinatorial library, high-speed drug targeting and transition to development. Cerep's revenues are derived from services (74%) and drug discovery (26%). The breakdown of turnover by geographical location is as follows: France (22%), North America (48%), Europe (23%) and Asia (7%).

The Institut Pasteur has an 8% shareholding in Cerep. Its stock market value has fallen by 70% in three years as the share value has fallen from € 22 to € 8, despite the fact that its turnover has risen from EUR 8 Million in 1998 to EUR 34 million in 2002.

Founded in 1984, **Chemunex** designs and sells rapid micro-biological analysis systems designed primarily for use by pharmaceutical and cosmetics laboratories, drinking water supply systems and the agro-food sector. The group has developed a technology for the detection and analysis of micro-organisms (bacteria, yeasts, fungi) which can produce results within 2-24 hours. The group has two main activities:

- Analysers: ChemScan, ChemFlow and D-Count;

- Reagents and other consumables: Fluorassure brand.

Chemunex generates most of its earnings in Europe and the United States. AES Laboratoire Groupe has a 60% shareholding in Chemunex. Its share value has fallen from € 1.0 to € 0.4 in three years, a 60% decline, while turnover rose from € 4 million in 1997 to € 8 million in 2000.

Appligene, Famel and Genset are no longer quoted on the new market. The share value of Genest fell from € 48 three years ago to € 8 in June 2003.

Transgene is a biotechnology company which designs and develops gene therapy technologies and products. Transgene has already developed 7 families of vector that it uses in the areas of cancer therapy (cancer of the lung, breast, ovaries, prostate, etc.) and hereditary diseases (myopathy and cystic fibrosis). The breakdown of the group's portfolio of products is as follows; 5 products for treating cancer at varying stages of development and 1 gene therapy products against myopathy undergoing clinical assessment. Transgene's share value has fallen from € 38 to € 6 in three years, while its turnover fell from € 9 million in 1998 to € 2 million in 2002.

The last stock market flotation of a biotechnology firms in France dates back to 1999 with the listing of **NicOx**, whose share value has fallen from € 30 in 2000 to € 3 in 2003. A collapse in share value of this magnitude, equivalent to a 90% reduction in its stock market value, makes the company less attractive to venture capital investors. Created in 1996, NicOx is a pharmaceutical laboratory specialised in the development of drugs which exploit the properties of nitric oxide. NicOx targets several therapeutic markets: pain and inflammation, cardio-vascular and respiratory diseases, chronic inflammatory enteropathies, urinary incontinence, osteoporosis, Alzheimer's disease and hepatic and dermatological disorders. To date, NicOx has a portfolio of 9 products undergoing clinical development: 4 in Phase I and 5 in Phase II. The group derives its earnings from partnership agreements signed with pharmaceutical groups, notably AstraZeneca (81.5% of turnover) and Axcan (18.5% of turnover).

4.4 Legislation and regulations (Bc15 and Bc16)

All activities in the pharmaceutical sector in France are subject to the stringent rules of the Public Health Code which sets out the rules for access to the market (clinical studies, pharmacovigilance).

Growth in sales within the sale is strictly controlled by the authorities. The French Parliament specifies the rate of growth in health expenditure for each year in accordance with the rate of growth in GDP. Furthermore, any drug considered to be ineffective or insufficiently effective may have its rate of reimbursement lowered or can even be reclassified as non-reimbursable.

The pharmaceutical industry is facing a difficult and increasingly constraining environment over the next few years as a result of competition from generic drugs and a more restrictive health policy in terms of spending. Nonetheless, the impact of these new constraints may be softened by the scope offered to the industry in 2003 to set prices for innovative drugs freely.

4.5 Starting up a firm (Bd17 and Bd19)

All categories of actor in the French economy are subject to a high rate of taxation: firms, employees, wealthy individuals, consumers and shareholders. SMEs must devote a large share of their energies to administrative and fiscal formalities (up to 10% of human resources according to size), and this burden becomes heavier if a firm applies to the administration for assistance, even if it is simply a grant for innovation. Admittedly there is a strong desire to simplify administrative procedures but the number of procedures is still increasing, indeed to the extent that it is worth asking whether it would be more in the

strategic interest of an innovating firm to spend time and energy on administrative procedures with a view to securing grants rather than developing its own commercial strategy (cf. section on strategic alliances). In France, rather than attempting to find non-existent financiers, the energy of firms is spent on seeking out public aid which is based on a tax income system that is unattractive to private sources of financing.

Moreover, measures in favour of innovation are in many cases tax measures which do not ease the burden imposed by previous systems, but which instead make them more complex and opaque. The result is that taxation and subsidies are now dealt with by specialists and tax officials remain unaware of the wide spectrum of specific conditions or run-of-the mill aid measures available.

Table 4.7 Rates of taxation selected European countries

Country	Corporate tax	Maximum income tax band	Wealth tax	Normal rate of VAT	Dividend tax	Average linear tax burden
France	37.3%	49.5%	Yes	19.6%	21.1%	31.7%
Germany	41.37%	48.5%	No	16%	21.1%	31.7%
Italy	38.25%	44%	No	20%	12.5%	29%
Netherlands	34.5%	52%	Yes	19%	25%	32.6%
Spain	35%	48%	Yes	16%	18%	29%
Sweden	28%	56%	Yes	25%	30%	35%
United Kingdom	30%	40%	No	17.5%	29%	29%

Source: Chamber of Trade and Industry.

The public programmes specifically put in place to facilitate and encourage the creation of innovative young enterprises are the national competition for enterprise creation and the public incubators created to support start-ups. The impact of these two measures is measured after eliminating the double accounting, given that several enterprises had benefited from both the competition and the public incubator system.

Their impact was analysed over the period 1999-2000, although the results do not discriminate between firms in the healthcare sector and those outside it. Healthcare firms are estimated to account for 25% of the total, *i.e.* the share of life science research devoted to healthcare.

Table 4.8 Impact of the national competition and incubators on the creation of biotechnology firms specialised in healthcare

1999-2000	Competition	Public incubators	Biotechnology total	Healthcare biotechnology
Number of biotechnology firms created	92	56	148	32
Number of jobs created	441	213	654	170
Total cost to State	€ 20 million	€ 12.5 million	€ 32.5 million	€ 8 million
Average unit cost to State	€ 225 000	€ 223 000	€ 219 000	€ 219 000
Average number of firms supported by venture capital funding in 2002	3	9	12	3
Number of patents or new products expected in the medium term	3	9	12	3

Source: Ministry of Research DEP DT.

It would seem that these measures receive little follow-up from venture capital funds, seed capital funds or business angels.

5. MARKETS

5.1 Situation in the French market

The development of the drugs market in France depends strongly on:

- Changes in the drugs market administration system with a view to harmonising European regulations;
- Trends in public health expenditure;
- The arrival of rival generic products;
- Changes in consumer habits should the latter start to practice self-medication;
- As a counterweight, the ageing of the population, which would seem to indicate an increase, or at the very least the maintenance at current levels, of health expenditure.

In the world market, the consumption of drugs and medication is increasing at a rate of 8% a year and the market is dominated by the United States. The administration of the European market should move towards greater harmonisation of the various regulatory systems in force in European countries, and should focus on the product licensing and approval system and the shortening of the time between licence application and approval by the administration as well as harmonisation to ensure greater price transparency.

The French drugs market is an administered market. The health sector accounts for 9.5 of GDP in France and in 2002 expenditure on pharmaceuticals amounted to € 25 billion, *i.e.* 18% of current health expenditure. Forty products, or 2% of those listed, account for half of the growth in the pharmaceutical industry's earnings in 1999. And the top fifty products account for 25% of total revenue from drugs.

The self-medication market amounts to 18% in Germany and 17% in the United Kingdom but only 10% in France.

While the generics market accounted for 50% of the market in the Netherlands, 40% in the United Kingdom, 44% in the United States and 33% in Germany, in France the share was 6% in 2000. Half of the listed drugs will soon no longer be protected by patents and the authorities are keen to promote the use of generics. A fiercer price war could lower the price of generic drugs to around 80% that of brand name drugs (cf. the United States). A study carried out by Xerfi in 2001 of the French generics market found that the generics sector was mainly covered by a dozen or so firms in France, all of which had relatively large marketing budgets. Revenue from sales of generics can be broken down as follows:

- Foreign groups: 59.1%;
- French groups: 32.4%;
- Independent laboratories: 8.5%.

French firms manufacturing generics give priority to brands other than INN brands. In all, some 50 firms supply the generics market in France. Developing the generics market is also becoming a priority as part of the effort to rein in increases in health expenditure; moreover, the right to substitute products also dates to 1999, the same year as the Innovation Act, demonstrating the strong encouragement given by government to the restructuring of the French pharmaceutical sector.

5.2 Market administration (G33 & G34)

Source: LEEM.

The French market is administered by:

- Retail sales and production permits;
- Set prices;
- A policy of setting reimbursement rates;
- Regulated distribution, with mapping of pharmacy locations and administered margin rates for wholesalers and retailers.

The price of each new drug arriving on the market is set in collaboration with the Economic Council for Health Products (CEPS) according to the objectives for expenditure on pharmaceuticals. The impact of health policy should be softened by the right given to firms in 2003 to set prices for innovative drugs freely. A drug may be sold on the market once it has been granted a sales permit (AMM) from the French authorities (AFSSAPS) or those at European level (EMEA). 632 permits of this type were issued in 2001 and the average time between the submission of an application to market a drug to its sale on the market is over 380 days. This delay is a handicap for pharmaceutical companies and a genuine source of loss of earnings.

5.3 Organisation of the national healthcare system (H35 & H36)

Sources: Régime Général français de Sécurité Sociale;
Département de la Santé (6th Report to Parliament, December 2002);
Farmaindustria, The pharmaceutical industry in figures, 2002 Edition.

In France, the price of reimbursable drugs is established through negotiations between the firms concerned and the interministerial committee (CEPS) or by Decree for a period of 5 years.

- The price of reimbursed drugs amounts to merely 66% of the price paid by the patient;
- Drug prices in France are equivalent to the average prices charged at the European level. The average rate of reimbursement for a drug was 74.8% in 2002. The difference between that figure and 66% is made up by personal supplementary health insurance schemes;
- Sales of reimbursable drugs amounted to € 15.1 billion in 2002, *i.e.* 52% of sales;
- The development of the generics market amounted to 14% of the reimbursable drugs market. The Social Security Funding Act of 2003 lays down a basic tariff for the reimbursement of generics and provides for the creation of generic drugs group.

5.4 Intermediaries and prescribers (I37)

Source: LEEM.

Further to the agreement reached in June 2002 with prescribers and health agencies, the negotiated price administration system is partly responsible for the emergence of a market for generics in France.

Through the price administration system, practitioners and health establishments are the main influences on the health system and the prescribing system. They consist of:

- 198 000 doctors;
- 40 500 dental surgeons;
- 22 500 pharmacies;
- The public hospital sector (1 726 establishments);
- The private hospital sector (1 280 establishments);
- Health insurance agencies.

The French prescribing system favours the development of the market for innovative products in that prescribers give priority to new products. The increase in consumption is linked to the increase in the number of prescribers, which has tripled over the past thirty years.

Table 5.1 Growth in the number of doctors in France (2002)

Year	Number of doctors (prescribers)
1970	70 000
1980	112 000
1990	173 000
2001	196 000

5.5 Consumers (J38 & J39)

In France, consumers neither pay nor decide and prescribing is structurally oriented towards innovative, and therefore the most expensive, products. The fairly routine replacement of old products with new products is one of the distinctive features of the French system.

The determinants of demand for drugs in France are as follows:

- High standard of living;
- Ageing population;
- Consumer habits of the new generations;
- The long-standing tradition of health protection which has created a well-established healthcare culture.

Individual income levels have little effect on demand and the French market would appear to be growing, indeed the French are the largest consumers of drugs in the world.

Table 5.2 Per capita spending on drugs and medicines in the OECD area (2000)

Country	Per capita expenditure
France	351
Japan	348
Belgium	321
United States	319
Italy	308
Germany	294
United Kingdom	233

Moreover, patients prefer to buy reimbursable drugs and have confidence in the system of pharmacovigilance which regularly checks drugs and medicines and which can withdraw any drug that proves to be ineffective. Drugs licensed for sale on the market are checked in accordance with strict procedures.

6. OUTLINE SUMMARY

In accordance with the objectives of the OECD Working Party on innovation policies in the biotechnology sector, and indeed of all the other participating countries, the previous chapters have described the public research system in this sector, the activity of the biotechnology industry, the exogenous and endogenous factors that influence demand and the development of the market, and last intervention by government and framework within which it acts.

On the basis of this information, this section should provide answers to the initial questions posed by the Working Party:

- What are the barriers to the development and economic performance of biotechnologies (6.1)?
- What are the links between the degree of openness of a national innovation system and its performance? Would opening up the biotechnology economy improve the performance of the biotechnology industry (6.2)?
- What specific aspects of demand influence the innovation process in the pharmaceutical biotechnology sector, and what are the impacts on the output of innovative products (6.3)?
- To what extent do the framework for governmental action and innovation policies galvanise the innovation process? What improvements would enable policy actions to address the specific needs of the sector and encourage the innovation economy in the biotechnology sector (6.4)?

6.1 Opportunities for the pharmaceutical biotechnology economy

Current status of the driving force for innovation

In terms of scientific output, it would seem that the indicators of papers and patent applications in the areas of pharmacology and biology have declined over the past ten years, reflecting a decline in the productivity of research activity in these fields in France. Furthermore, the R&D effort is concentrated within industrial groups; biotechnology firms and small independent laboratories play merely a minor role.

While resident French firms file 6 900 patents a year, the pharmaceutical sector accounts for a only a small share of this total and the groups in the sector are more active in registering brand names.

Moreover, sources of financing for the biotechnology industry are generally starting to dry up. The industry is a major risk for investors who prefer to invest in downstream sectors, with the result that there is often no relaying of funding sources between the start-up phase and the development phases. Pharmaceutical groups also reduce their risk exposure in the same way, and at the same time have an international view of research which prompts them not to adopt a strategy that takes account of local considerations.

The pharmaceutical sector at the international level is evolving as a result of mega-mergers and acquisitions designed to concentrate activities. Groups are striving to establish a presence in all markets

and integrate R&D activities as a means of securing their future in those cases where they adopt an innovation-based development model.

The development of foreign subsidiaries into major players is likely to continue. The investments by foreign pharmaceutical companies in France have two objectives, namely to set up research structures and to gain access to the fourth largest market in the world whose prospects do not seem to have dimmed and which, in addition, offers access to the European market. Furthermore, the robustness of prescribing practices in the French market offers opportunities for innovative products which are the favoured choice of prescribers.

Lastly, a strategy based on innovation is not the only avenue chosen by firms in the sector, most of which have adopted a development model geared towards generic products.

Strength of the French pharmaceutical biotechnology economy

Like the independent laboratories, whose number has fallen to a third of the level twenty years ago, the development prospects for the French pharmaceutical industry could become a problem. The innovation-based approach adopted by the French pharmaceutical industry is not sufficient to maintain the current position of the industry. 2 000 people in France work in the area of pharmaceutical biotechnology, compared with 150 000 in the United States where innovation led to the creation of pharmaceutical biotechnology firms by as early as the late 1970s.

Given the weight of the partnerships between biotechnology firms and all firms in the pharmaceutical sector, the system needs to be revitalised. Although in policy terms the State has introduced incentives for firms to pool their research efforts, growth in strategic alliances is at a standstill due to the fewer number of firms in the pharmaceutical sector and because many of these firms have adopted a model based on brand development and aggressive marketing of generic products in a market which in France would seem to offer the potential for very high growth. Lastly, the systems put in place by the State to develop partnerships seem to be a very long way short of achieving their objective in that the development of strategic alliances by pharmaceutical biotechnology firms still remains limited (less than forty), excluding the incentive policies pursued by national technological innovation networks.

6.2 Opening up the system

The world market provides an outlet for French drugs and medication which French firms continue to export in large quantities. This world market favours firms which have adopted an international strategy, to the detriment of many pharmaceutical laboratories which failed to keep track of the expiry dates of patents or which continued to shelter behind French regulations.

Paradoxically, the strategic alliances that do exist are between pharmaceutical biotechnology firms and foreign firms. Nonetheless, firms are currently starting to become aware of these issues.

6.3 The role played by demand

Patients are passive actors in the French pharmaceutical economy. Demand is organised by practitioners. In addition, access to the distribution circuit, as well as being a necessity, is also restricted, which means that firms must establish a presence in the French market in order to be able to sell their products. The way in which the market is organised prompts foreign firms to develop a highly aggressive commercial and marketing policy.

6.4 Policy implications

There would appear to be a will to develop the downstream financing potential which was missing in the previous system. By as early as 2004, input from the CDC should make it possible to rapidly consolidate the viability of a dozen or so high-tech biotechnology firms. All that remains is to consider the effect of this policy in favour of investors.

To date, it is still not possible to assess the overall impact of this policy since 1999, although it must be said that the input of € 86 million a year by the State has brought about the following:

- Creation of 175 biotechnology firms over the past four years, 41 of which are now fully mature;
- Creation of over 870 R&D jobs in the sector in the short term;
- Over 400 patents or patent extensions.

Table 6.1 Impact of policies aimed at the creation innovative firms in the pharmaceutical biotechnology sector (optional)

1999	Competition and incubators	Networks	ANVAR	TOTAL
Number of projects supported	0	331	395	726
Number of biotechnology firms created or planned	148	3	27	178
Of which, number of pharmaceutical biotechnology firms created	32	3	n/d	35
Jobs created	654	440	430	1 524
Total cost to State	€ 32.5 million	€ 78 million	€ 88 million	€ 198.5 million
Average unit cost to State	€ 219 000	€ 234 000	€ 208 000	€ 219 000
Young firms assisted by Funds in 2002	28 in the life sciences	n/d	n/d	n/d
Patents/products expected in the medium term	12	219	198	429

Source: Ministry of Research, ANVAR.