

# GLOBAL COMPETITIVENESS IN PHARMACEUTICALS A EUROPEAN PERSPECTIVE\*

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## **I. Introduction**

Pharmaceuticals is a large, high-growth, globalised, and innovation intensive industry. Its products – drugs – are directed to satisfy consumer needs in an area – health care – which is vital for society. Health care and therapeutics are among the most relevant issues in the definition of the concepts of welfare and democracy in the new Century. Thus, the pharmaceutical industry is clearly a “strategic” sector for Europe.

Ever since the XIX Century, pharmaceuticals has been a stronghold of the European industry, and it still provides by far the largest contribution to the European trade balance in high-technology, R&D intensive sectors.

However, it is now a diffused perception that the European pharmaceutical industry is losing ground vis-à-vis the United States.

Against this background, the Report examines the competitive position of the European pharmaceutical companies and industries, and compares them with the pharmaceutical companies and industries in other parts of the world, particularly the US.

Over the last two decades, the industry has experienced some important structural changes, mainly driven by technological and institutional shocks that have affected all the stages of its value chain. In turn, this has led to changes in firms’ organisation and in market structure, within domestic markets, regionally, and globally.

On the one hand, the life sciences have transformed the prospects and the processes of drug discovery and development. On the other hand, the rise of healthcare and prescription drug spending has induced cost containment policies, which have affected the structure of demand in all the major national markets. In addition, increasingly stringent requirements for the approval of new drugs, together with the orientation of research towards increasingly complex pathologies, have implied

larger, more costly and internationally based clinical trials. Developments in legislation and in courts' interpretation of issues concerning intellectual property rights, as well as the increasing openness of domestic markets to foreign competition, have influenced patterns of industrial competition and the evolution of industry structure.

Jointly, these tendencies have implied a sharp increase in the resources needed to develop new drugs. Equally important, they have led to a redefinition of the nature and the complementarities between the fundamental sources of competitive advantages in this industry, namely R&D and innovative competencies, marketing and distribution capabilities.

The pharmaceutical industry today has to be understood as a system or network. Innovative activities, as well as production and commercialisation of drugs, rest on and involve, either directly or indirectly, a large variety of actors: different types of firms, other research organisations like universities and public and private research centers, financial institutions, regulatory authorities, governments, health care systems, consumers, physicians, etc. These actors are linked together through a web of different relationships, which include almost pure market transactions, "command and control" administrative rules, competition, collaboration, and all sorts of "intermediate forms".

This suggests that the competitiveness of the industry cannot be assessed by looking only at the individual firms, but also at the broader set of institutions, infrastructures, and policies that influence the actions of companies, and – even more important – at the dynamic interactions between these levels of analysis.

The picture is further complicated by the fact that the industry is populated by very different firms. In the first place, there are the multinational companies, which cover between 40 to 60% of most national markets in the advanced countries. These are fairly global firms. Although they do keep a good share of activities and sales in their own domestic, or at least continental markets, these companies operate across national or even continental borders, and they set divisions and

activities in other countries and regions as well. Often, their property is spread across different countries, particularly Europe and the US. These are highly R&D-intensive companies with large sunk costs both in R&D and in marketing and distribution assets.<sup>1</sup>

The industry is populated by two other types of firms. First, there are smaller companies which are specialised in the sales of non R&D-intensive drugs. They conduct mainly manufacturing and commercialisation activities, and do not invest in R&D. These are typically national companies which operate almost exclusively in their own markets. Since the past twenty years or so, another set of companies have populated this industry, notably the research intensive companies that have sprung off from the new opportunities opened up by the life sciences – the so-called New Biotechnology Firms (NBFs). These companies are specialised in the new biotechnologies, and their activities range from the discovery and development of new drug compounds to the development of new drug screening or research tools and technologies in fields like genomics, bioinformatics, etc.

Measuring competitiveness is always a difficult exercise, given the ambiguity with which this concept is sometimes used and the different possible interpretation that can be found in the literature. As a consequence, and given the complexity of the pharmaceutical industry in its relationships with the research, regulatory and healthcare systems, we introduce here a set of differentiated indicators, including various measures of value added, productivity, trade balance, world market shares and, above all, innovativeness. Jointly, these measures provide a fairly coherent and consistent indication about the dynamics of competitiveness and its determinants.

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<sup>1</sup> Manufacturing is not that important in this industry compared to R&D and commercialisation, which command the bulk of the investments.

The main finding of the Report is that indeed the European industry has been losing competitiveness as compared to the USA, although there are large differences and trends across European countries. As a whole, Europe is lagging behind in its ability to generate, organise, and sustain innovation processes that are increasingly expensive and organisationally complex. More specifically, the main results of the Report can be summarised as follows.

A. First, using Eurostat data we document that the European pharmaceutical industry is more labour intensive than the US or the Japanese industries. We find that the share of labour costs on the value of production in Europe is higher than in the US and Japan. The difference is sufficiently high to suggest that it cannot just stem from higher charges on labour costs in Europe. Moreover, the share of value added net of labour costs on total production value is much higher for the US and Japan. The US and Japanese industries rely more than Europe on "non-labour" inputs, such as capital or most likely R&D. The overall share of total value added on production value in the US and Japan is also higher than in Europe.

All these factors combined suggest that not only is the European industry labour intensive, but that the higher labour intensity is also associated with lower value added activities. While there are differences across European countries, our results are not inconsistent with the view that in the European pharmaceutical industry there is a less pronounced specialisation in R&D activities, and that there is a larger presence of non R&D-intensive firms which conduct fairly mundane activities.

We also find that while the European industry grew faster than the US and Japan in the 1980s, in the 1990s it has grown less than the US industry. This stems from a deceleration of the growth of the industry in Europe, and an acceleration of the US industry growth. We also employ traditional growth accounting techniques to Eurostat country level data to decompose the growth of the industry in the US, Japan, and the EU-15 countries. While employment growth has practically no contribution to the growth of production value in pharmaceuticals, we find that in the US (and Japan) the growth of the industry stems to a good extent from the

growth of its non-labour inputs. By contrast, these inputs contribute modestly to the growth of the industry in Europe, whose growth is accounted for largely by the unexplained residuals – viz. by factors that are independent of the growth of the measurable inputs.

One may be tempted to attribute this result to some form of unobserved technological change or externality. In fact, most of the technical change in this industry comes from specific investments in R&D, which are captured by the non-labour inputs in the value added figures for the industry. As a result, our interpretation about the weight of the residual in the European drug sector growth is that the growth of the industry in Europe is likely to depend to a good extent on factors other than R&D, capital or labour. Not only is this saying that the growth of the industry in Europe is more "erratic" than in the US or Japan, but also that the growth in capital or R&D translates less markedly into sales growth. The empirical evidences produced in Section V of this Report show that this is not independent of the effects of the regulatory regimes on industry structure, with the larger presence, in Europe, of firms and activities which are less dependent on internal R&D and innovation, and more on external inputs, such as licenses from international companies, pricing policies, or peculiarities of the public regulatory and health care systems or demand in individual European countries, etc.

B. Second, the Report focuses on the competitiveness of the European multinational corporations, particularly in comparisons with the US firms. These firms compete largely on new drug products based on substantial R&D investments. An important question is therefore whether the innovation- and R&D-based competitiveness of the European multinationals has worsened vis-à-vis their US or Japanese competitors. Our data indicate that the sales of major innovative products by the US multinationals have increased more significantly than those of the European multinationals in the 1990s. When we look at the number of the top selling new chemical entities (NCE) developed by the European and US firms, we find that the number of NCE developed by companies of either



regions is not substantially different. This suggests that the European multinationals are facing a comparative disadvantage in selling their new drugs. In fact, the US pharmaceutical market has grown from being roughly equal to the European market at the beginning of the 1990s to almost twice as much in very recent years. In particular, the restructuring of pharmaceutical demand and of the health care system, in the US, has translated into demand growth which has benefited mainly the US firms. In fact, in spite of their multinational nature, the bulk of the sales of the US and European firms is still in their own markets. It is therefore natural that the US firms have taken greater advantage of the growing demand in their own country. Indeed, we find that in this period the European multinationals as well have increased their market share in the US to take advantage of this opportunity. However differences in terms of market sizes and rates of growth does not rule out that differences in sales growth between European and US multinationals depend also on differences in the ability to discover and develop new drugs. In particular, we find that: a) in the 1990s US companies have gained a clear and growing leadership in terms of the sales generated by the New Chemical Entities (NCEs) launched on the market place; b) the portfolio of products held by the European multinationals tends to be older than that of the US firms. These evidences suggest that there may be some differences in research productivity in recent years as well.

C. Our third conclusion is that the relative position of the US as a locus of innovation in pharmaceuticals has increased over the past decade compared to Europe. One notable difference between Europe and the US in the 1990s is that while the US have continued the development of a new research-intensive industry in the life sciences, Europe has been unable to complete the process of vertical specialisation in the most innovative areas of the drug sector. Particularly, Europe has not really given rise to a full fledged industry of innovation specialist companies and technology suppliers like in the US. The US pioneered the rise of a new organisation of this industry, based on an effective division of labour between smaller and larger companies with different comparative advantages in the

“exploration” and “exploitation” of new innovation opportunities.<sup>2</sup> Since the very beginning of the new trend in the early 1980s, Europe has been less effective in encouraging the growth of new technology suppliers and innovation specialists. If anything, this is emphasised by the fact that the European drug multinationals have increasingly relied on sources of research capabilities and innovation located in the US, thereby reinforcing the difficulties in creating a European industry of technology suppliers. Likewise, we shall see in this Report that one important development in the industry in recent years has been the growth of new tools for drug discovery and testing (combinatorial chemistry techniques, genomics, highthroughput screening etc.). These tools can seriously enhance the efficiency of the research process in the industry. So far, however, the industry of new drug research tool producers is largely a US phenomenon. In principle, the fact that Europe has been unable to give rise to a full fledged industry of technology suppliers may not be considered as a critical problem for the competitiveness of the firms operating in the final markets. Competitiveness in sales depends on different factors from competitiveness in innovation. Moreover, in a globalised industry such as pharmaceuticals, companies may not need local technology suppliers, provided that the drug producers can tap the new technology sources in other markets. The question, however, is whether European drug companies can tap such international sources of technology. While this may not be a problem for the largest drug multinationals, the ability to do so by the large fringe of companies that operate in several European national markets is a totally different story. There is another, probably more important, twist to this issue. More than being critical for the growth of the downstream industry, the presence of a local industry of research-based firms and technology suppliers is critical because the industry is, by itself, a powerful source of growth. We shall note in the Report that the US biotechnology industry has given rise in the past two decades to a large number of new jobs, to at

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<sup>2</sup> See March, 1991.

least a dozen new world-class drug companies (e.g. Amgen, Chiron, Genzyme, and others), along with several new others in the new drug tool technologies (e.g. Incyte, Millennium), and it has produced a stream of revenues in the form of royalties from licenses or R&D contracts and collaborations.

D. The fourth conclusion that we want to highlight can be put very simply. The national European markets, especially in some Countries, are not competitive enough. We show this by using data on the variation in prices and market shares after patents expire. In some countries, which rely on administered prices, we find that prices and market shares do not vary substantially after patents expires. In competitive drug markets, price drops are a typical consequence of patent expiration and of entry by generic products, with a significant turnover in terms of market shares. We therefore conclude that there is too little market-based competition in the final markets in some of the European countries. This has contributed to nurture inefficient positions within the industry.

All in all, the Report claims that the competitiveness of the European pharmaceutical industry is negatively affected by the persistence of insufficient degrees of competition and institutional integration, still centred on domestic and fragmented markets and research systems. Four sets of variables are found to be relevant as sources of competitiveness and growth in pharmaceuticals: 1) The size and the structure of the biomedical education and research systems; 2) Some basic institutions governing labour markets for skilled researchers and managers, as well as corporate governance and finance; 3) Intellectual property rights and patent law; 4) The nature and intensity of competition on the final market.

The Report is organised as follows. In Sections II, III, and IV, a series of measures and indicators of the performance of the industry are developed. In section V we show that competition is an important determinant of competitiveness . In Section VI, the Report illustrates the role of some institutional variables. Section VII summarises our findings.

The data analysed in this Report come from OECD, Eurostat, the European Patent Office, IMS Health, and from PHID (PHarmaceutical Industry Database) at the University of Siena. The general approach is to combine two relevant perspectives in the analysis of competitiveness. On the one hand, the IMS, European Patent Office, and PHID data sets sustain a detailed analysis of industry dynamics and firm-level strategies, by location of corporate headquarters. On the other hand, the OECD and Eurostat data sets show production, trade, and R&D activities by country, regardless of the origin of the companies (OECD, Eurostat).

## II. Structural Indicators in the EU, USA, and Japan

Total expenditure on pharmaceuticals represents between 0.7 and 2.2% of GDP across OECD countries, with a mean at around 1.2%<sup>3</sup>. Demand for pharmaceuticals is highest in the US, Western Europe, and Japan. Prescription drug expenditures have grown significantly in the past 15 years (see Tables 1 and 2). First, data show the substantial growth of the US market during the Nineties. In particular, from 1995 to 1999, the US market had the highest percent annual growth rates, coming to account for approximately 40 percent of the total world market for ethical pharmaceuticals in 1999. Europe's share declined to less than 27 percent, while Japan's share in 1999 was nearly 16 percent. In general, total drug expenditures have been driven up by the introduction of new drug therapies, higher third-party coverage of drugs, the substitution of higher-priced new drugs for lower-priced-existing drugs, and, especially in the US, more aggressive marketing by manufacturers through direct-to-consumer advertising<sup>4</sup>.

**Table 1:  
Size of the Market in Pharmaceuticals, 1995-1999, US\$ billion**

Markets	1985	1989	1990	1995	1996	1997	1998	1999
World	79.1	153.3	165.8	280.3	290.8	296.1	304.7	337.2
Regional Shares	%	%	%	%	%	%	%	%
North America	28.1	34.0	32.4	31.2	33.0	35.9	38.1	40.2
Europe	22.0	31.0	26.5	29.6	30.7	28.8	29.1	26.7
A/A/A	23.4	30.0	35.1	32.4	29.2	27.5	25.0	26.4
Latin America	5.6	5.0	5.9	6.8	7.1	7.8	7.7	6.6

Source: IMS International

<sup>3</sup> See Jacobzone, 2000; OECD Health Data, 2000.

<sup>4</sup> GAO, 2000.

**Table 2:  
Largest Pharmaceutical Markets in the World, US\$ million**

Rank 1999	Country	1989		1994		1999	
		Rank	USD	Rank	USD	Rank	USD
1	USA	1	44789	1	75425	1	130069
2	Japan	2	30229	2	52568	2	53548
3	Germany	3	9984	4	16725	3	18500
4	France	4	9326	3	15152	4	17751
5	Italy	5	8260	5	8829	5	11332
6	UK	6	4526	6	6821	6	11029
7	Spain	8	3349	8	4710	7	6596
17	Belgium	13	1219	15	2162	17	2703
32	Russia	NA	NA	NA	NA	32	1033
18	Netherlands *	15	1087	16	2078	18	2391
19	Poland	NA	NA	27	1010	19	2260
20	Sweden	18	902	20	1418	20	2102
22	Switzerland	17	971	17	1619	22	1824
24	Austria	21	779	22	1382	24	1781
23	Portugal	24	667	23	1267	23	1805
25	Greece	28	512	26	1182	25	1423
31	Finland	25	579	33	715	31	1039
34	Denmark	33	417	34	679	34	913
40	Czech Republic	NA	NA	NA	477	40	748
38	Norway	37	354	NA	514	38	816

\* 1998 data for the Netherlands is based on estimated sales only.

The pharmaceutical industry is the fifth largest industrial sector in the EU, amounting to 3.5 per cent of the total manufacturing production (Eurostat). Moreover, the pharmaceutical sector provides a sizable, positive contribution to the EU trade balance (16,201 US\$ million in 1998). As can be seen in Tables 3 and 4, the EU as a whole is a net exporter of pharmaceutical products, with a positive

trade balance throughout the last decade. Between 1985 and 1998, the EU pharmaceutical sector has shown good trade performance compared to the US and Japan, with a trade balance that continued to rise. Even if the share of EU-15 exports to the US has increased, the rest of the world remains the main destination. Conversely, US exports are directed in a much larger proportion towards developed markets as compared to Europe<sup>5</sup>.

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<sup>5</sup> One is to warn however that trade data in the drug sector may reflect decisions to locate production and marketing activities by pharmaceutical multinationals.

**Table 3:****International trade of pharmaceutical products (US \$ million)**

	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998
<b>EXPORTS FROM EU-15 to:</b>														
Intra-EU-15	4458	6106	7687	8991	9530	12000	13511	16643	16376	19043	23679	25700	26329	30726
Switzerland & Norway	579	826	973	1069	1140	1498	1675	2082	2420	2471	3262	3263	3492	3935
Japan	407	640	889	1167	1177	1254	1449	1843	1906	2125	2227	2035	2009	1702
US	668	827	1006	1125	1246	1395	1710	2191	2291	2767	3636	4002	5282	7815
Rest of the world	3458	4190	4735	5228	5524	7201	7811	8875	9756	11016	13551	14725	16156	17175
Total world exports	9570	12589	15290	17580	18617	23347	26157	31634	32749	37421	46355	49725	53268	61353
Total extra-EU-15 exports	5112	6483	7603	8589	9087	11348	12646	14991	16373	18378	22676	24025	26939	30627
<b>IMPORTS TO EU-15 from:</b>														
Intra-EU-15	4517	6254	7806	9209	9989	12965	14928	17722	17121	20023	25307	26351	27127	31490
Extra-EU-15	2197	2916	3513	4031	4434	5663	6400	7706	8059	8719	10961	12344	12472	14426
Total world imports	6714	9170	11319	13240	14423	18628	21328	25428	25180	28742	36268	38695	39599	45916
<b>PHARMAC. TRADE BALANCE</b>														
Extra EU-15	2915	3567	4090	4558	4653	5685	6246	7285	8314	9659	11715	11681	14467	16201
Extra-EU-15 Export/Import ratio	2.33	2.22	2.16	2.13	2.05	2.00	1.98	1.94	2.03	2.11	2.07	1.95	2.16	2.12
<b>EXPORTS FROM US to:</b>														
EU-15	1162	1448	1459	1855	1686	1858	2070	2441	2508	2564	2811	3300	3819	4635
Switzerland & Norway	78	92	100	145	81	96	94	150	185	400	230	186	187	437
Japan	571	634	686	793	785	764	810	817	849	836	933	846	852	881
Rest of the world	979	1039	1103	1297	1108	1385	1635	1949	2204	2292	2459	2828	3179	3708
Total world exports	2790	3214	3348	4089	3660	4103	4609	5357	5747	6092	6433	7160	8037	9661
<b>IMPORTS TO THE US</b>														
Total world import	1718	2084	2498	3235	2117	2540	3092	3861	4198	4755	5605	7150	8737	10982
<b>PHARMAC. TRADE BALANCE</b>														
Trade balance	1072	1130	850	854	1543	1563	1517	1496	1549	1337	828	10	-700	-1321
Export/import ratio	1.62	1.54	1.34	1.26	1.73	1.62	1.49	1.39	1.37	1.28	1.15	1.00	0.92	0.88
<b>EXPORTS FROM JAPAN to:</b>														
EU 15	114	158	191	237	258	316	394	562	572	562	721	732	737	678
Switzerland & Norway	8	7	8	11	9	10	17	10	20	14	19	23	33	47
US	98	134	146	165	202	197	248	313	372	454	503	547	605	685
Rest of the world	171	215	244	303	299	354	431	485	514	525	602	587	577	505
Total world exports	391	513	589	717	768	877	1089	1370	1478	1556	1845	1889	1952	1915
<b>IMPORTS TO JAPAN</b>														
Total world import	1292	1724	2110	265+9	2732	2849	3313	3681	3947	4243	4917	4501	4242	3751
<b>PHARMAC. TRADE BALANCE</b>														
Trade balance	-901	-1211	-1521	-1942	-1964	-1972	-2224	-2311	-2469	-2687	-3072	-2612	-2290	-1836
Export/import ratio	0.30	0.30	0.28	0.27	0.28	0.31	0.33	0.37	0.37	0.37	0.38	0.42	0.46	0.51

Source: OECD World Trade Statistics, various issues. Note: Europe is EU-15 plus Switzerland and Norway.



**Table 4:**  
**Destination of pharmaceutical exports, percentages**

	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998
<b>EXTRA-EU EXPORTS FROM</b>														
EU-15 to:														
Switzerland & Norway	11.3	12.7	12.8	12.4	12.5	13.2	13.2	13.9	14.8	13.4	14.4	13.6	13.0	12.8
Japan	7.96	9.87	11.7	13.6	13.0	11.0	11.5	12.3	11.6	11.6	9.8	8.5	7.5	5.6
US	13.1	12.8	13.2	13.1	13.7	12.3	13.5	14.6	14.0	15.1	16.0	16.7	19.6	25.5
Rest of the world	67.6	64.6	62.3	60.9	60.8	63.5	61.8	59.2	59.6	59.9	59.8	61.3	60.0	56.1
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Extra-EU/Intra-EU exports	1.15	1.06	0.99	0.96	0.95	0.95	0.94	0.90	1.00	0.97	0.96	0.93	1.02	1.00
<b>EXPORTS FROM US to:</b>														
EU-15														
Switzerland & Norway	41.6	45.1	43.6	45.4	46.1	45.3	44.9	45.6	43.6	42.1	43.7	46.1	47.5	48.0
Japan	2.81	2.86	2.97	3.54	2.21	2.33	2.05	2.81	3.23	6.57	3.58	2.6	2.3	4.5
Rest of the world	20.5	19.7	20.5	19.4	21.5	18.6	17.6	15.3	14.8	13.7	14.5	11.8	10.6	9.1
Total	35.1	32.3	32.9	31.7	30.3	33.7	35.5	36.4	38.4	37.6	38.2	39.5	39.6	38.4
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100
<b>EXPORTS FROM JAPAN to:</b>														
EU 15														
Switzerland & Norway	29.2	30.7	32.4	33.1	33.6	36	36.1	41	38.7	36.1	39.1	38.8	37.8	35.4
US	1.96	1.37	1.39	1.58	1.15	1.13	1.53	0.72	1.36	0.93	1.01	1.2	1.7	2.5
Rest of the world	25.2	26.1	24.7	23.0	26.3	22.5	22.8	22.8	25.2	29.2	27.3	29.0	31.0	35.8
Total	43.7	41.8	41.5	42.3	38.9	40.3	39.5	35.4	34.8	33.8	32.6	31.1	29.5	26.4
Total	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Source: OECD World Trade Statistics, various issues. Note: Europe is EU-15 plus Switzerland and Norway.

In 1997, the industry employed in the EU-15 almost 475,000 people, up from slightly less than 400,000 in 1985. The share of pharmaceutical employment in total manufacturing in the EU-15 has increased from 1.52% in 1985 to 1.94% in 1997, compared to 0.94-1.27% in the US, and 0.91-0.98% in Japan<sup>6</sup>. The share of pharmaceutical value added in total manufacturing has increased in the same period from 2.24% to 3.35%, compared to 2.28-3.39% and 2.65-3.46% in the US and Japan, respectively.<sup>7</sup>

Trends in R&D spending for the period 1986-1995 are shown in Table 5. The amount spent on R&D increased in all the three regions. The US rank first in terms

<sup>6</sup> See EU Commission, 1997, and Panorama of EU Industry (CD-ROM), 2000.

<sup>7</sup> See also U.S.I.T.C., 1991 and 1999.

of both R&D spending and ratio of R&D to production, consolidating their supremacy during the Nineties. In 1995, the ratio of R&D to production for the US was 4 percentage points higher than Japan and 5.5 points higher than the EU.

Over the last fifteen years, both the value of production and employment have increased steadily in Europe, the USA and – to a lesser extent – in Japan (Figures 1 and 2).

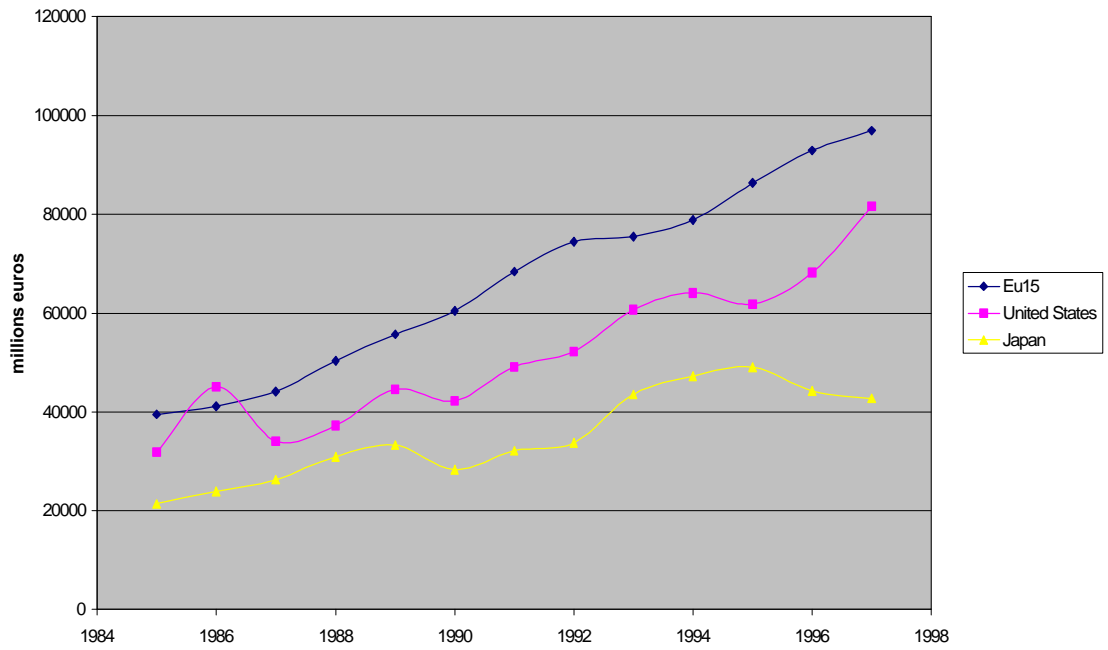
**Table 5:**

**R&D spending (millions of ECU)**

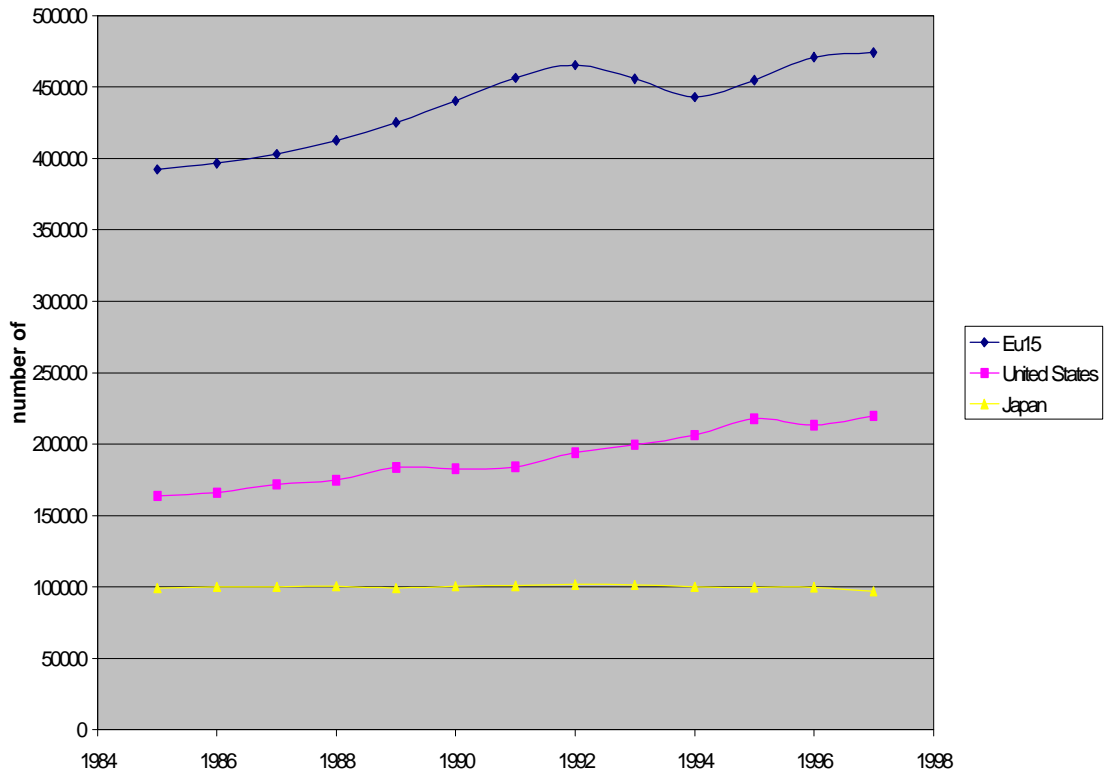
	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995
At current X-rate										
EU-15	3416	4034	4690	5352	6070	6474	6989	7181	7407	7708
United States	3954	3917	4436	5474	5357	6394	7163	8955	9329	9042
Japan	2073	2285	2748	3001	2810	3544	3918	4834	5216	5221
At PPP X-rate										
EU-15	3355	3969	4591	5252	6028	6365	6952	7231	7427	7701
United States	3621	4170	4891	5681	6418	7624	8703	9792	1037	1107
Japan	1480	1684	1907	2157	2493	2921	3209	3183	3257	3371
At current exchange rate, as a % of production										
EU-15	8.3	9.1	9.3	9.6	10.1	9.5	9.4	9.5	9.4	8.9
United States	11.3	11.5	11.9	12.3	12.7	13.0	13.7	14.8	14.6	14.4
Japan	8.7	8.7	8.9	9.0	10.0	11.0	11.6	11.1	11.1	10.3

Source: OECD, 1998 (for R&D expenses) and EU Commission, “Panorama of the EU industry” (for data on production).

**Figure 1:**  
**Production Value: EU-15, US, Japan**  
**(Nace 244)**



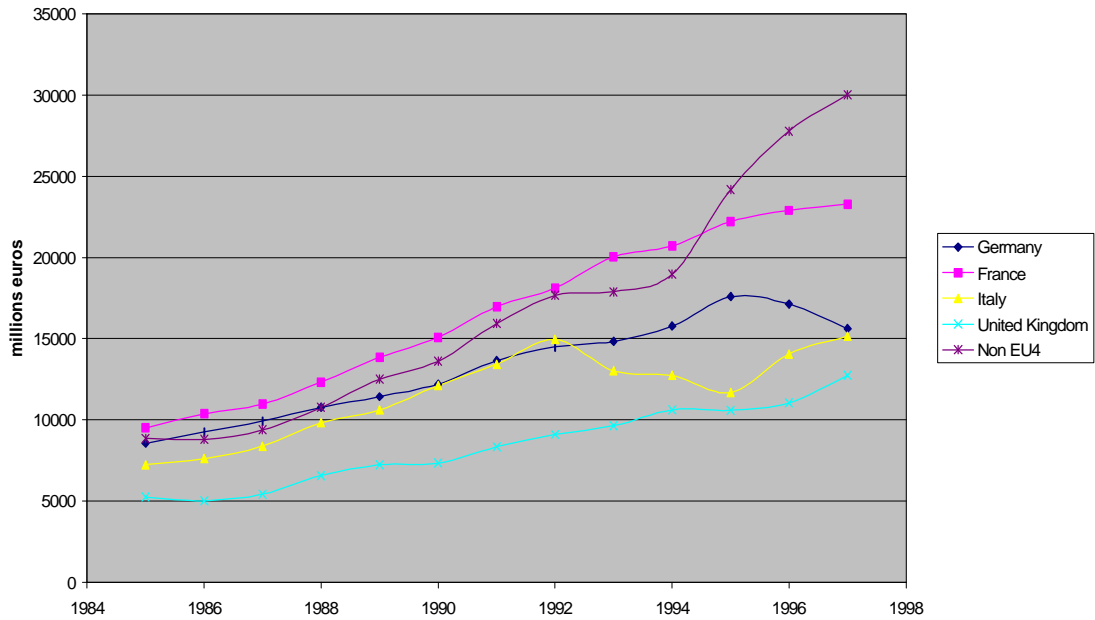
**Figure 2:**  
**Total Employment: EU-15, US, Japan**  
**(Nace 244)**



In the Nineties, significant differences and increasing divergence across European countries are observed, (Figures 3 and 4). The French industry shows a steady and considerable growth and the non EU-4 countries -especially Sweden, Ireland, Netherlands, and Denmark- literally take off, especially in the more recent years. Conversely, Italy declines sharply in the early Nineties, while Germany slows down in the last five years. With respect to its major competitors, Europe lags

behind the US (and also Japan) in terms of value added and according to different measures of productivity and competitiveness. Figures 1 and 2 show that both Production Value and Employment are higher in the EU-15 than in the US and Japan. Notably, the EU-15 employment in the industry has been roughly twice higher than the US during 1985-1997.

**Figure 3:**  
**Production Value: EU4 and non-EU4**  
**(Nace 244)**



**Figure 4:**  
**Total Employment: EU4 and non-EU4**  
**(Nace 244)**

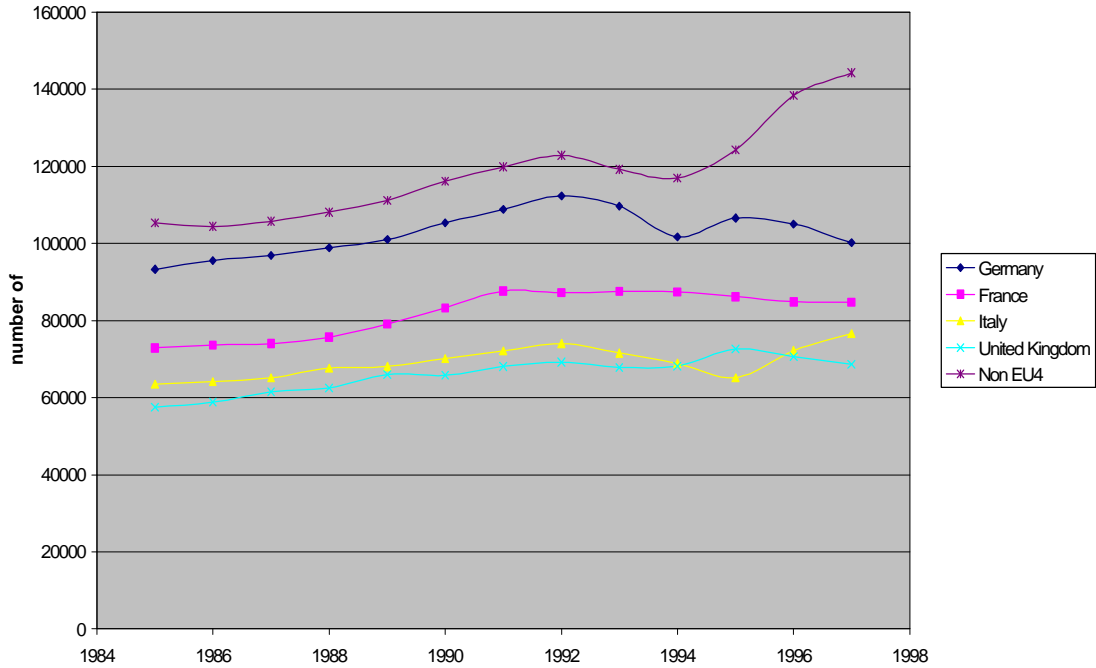


Table 6 reports the share of pharmaceutical labour costs on total production value in the EU-15, the US, and Japan, along with individual European countries. The Table also reports the share of the value of other "non-labour" inputs. The latter was computed by subtracting labour costs from the value added. Since value added is equal to labour compensation plus the compensation to other "internal" factors of production, we took this to be a measure of a bundle of inputs different from labour. Apart from physical capital, in the pharmaceutical industry this measure is likely to include R&D capital inputs. The Table also reports the share of total value added (which is the sum of the latter two shares) on the value of production. This provides a measure of the extent to which the industry relies on internally

generated inputs vis-à-vis inputs purchased from third parties. The shares in the Table are averages across 1992-1997 and 1986-1991.

**Table 6:**  
**Labour share and share of other non-labour inputs on production value**  
**(avg for 1992-1997 and 1986-1991)**

	1992-1997			1986-1991		
	Share of personnel costs	Share of non- labour inputs (*)	Share of value added	Share of personnel costs	Share of non- labour inputs (*)	Share of value added
EU-15	23.21%	16.58%	39.78%	24.92%	15.64%	40.56%
United States	13.50%	57.55%	71.05%	15.58%	55.32%	70.89%
Japan	12.57%	53.60%	66.17%	12.90%	53.31%	66.21%
Denmark	26.50%	26.99%	53.49%	26.99%	21.78%	48.77%
Germany	33.11%	9.36%	42.47%	31.81%	12.00%	43.81%
Spain	23.00%	14.33%	37.33%	27.73%	10.56%	38.29%
France	18.87%	14.00%	32.87%	20.18%	13.22%	33.39%
Ireland	10.69%	42.18%	52.87%	14.11%	33.06%	47.17%
Italy	22.74%	13.99%	36.73%	23.46%	13.50%	36.96%
Netherlands	18.43%	14.91%	33.33%	22.86%	11.18%	34.05%
Austria	23.17%	17.80%	40.97%	Na	Na	Na
Finland	26.44%	21.68%	48.12%	24.12%	25.14%	49.26%
Sweden	18.42%	30.59%	49.01%	Na	Na	Na
United Kingdom	21.69%	28.40%	50.09%	23.60%	30.23%	53.83%

Na = not available

Source: Our calculations from Eurostat data

(\*) Value of non labour inputs computed as total value added minus personnel costs.

The Table shows that the share of labour cost in Europe is higher than in the US and Japan, and this is stable across the two periods. This suggests that the European industry is more labour-intensive than the US or Japanese ones. One could argue that the higher share of labour cost in Europe may reflect higher labour cost charges. In fact, there is no reason why this should be so compared to Japan. Moreover, the other two shares in Table 6 show that not only do the US and Japan have a higher share of non-labour inputs, but also of value added as a whole. The difference is indeed substantial, with the US and Japanese firms showing a share of about 65-70% compared to 40% in Europe. This is suggestive of the presence in Europe of a relatively larger share of fringe companies that are specialised in low value added activities, like manufacturing and commercialisation of products licensed from other companies, or simply of low value added medical or medical-like substances.

These differences across the three regions prompted a deeper analysis of the factors

**Table 7:  
Decomposition of pharmaceutical growth -- contribution of labour, non-labour inputs and total factor productivity (TFP) (avg for 1992-1997 and 1986-1991)**

	1992-1997				1986-1991			
	Total growth	Labour	Non-labour inputs	TFP	Total growth	Labour	Non-labour inputs	TFP
EU-15	5.81%	0.14%	1.32%	4.35%	9.14%	0.62%	1.39%	7.13%
United States	8.44%	0.40%	4.84%	3.20%	7.18%	0.31%	4.43%	2.43%
Japan	4.71%	-0.08%	2.65%	2.15%	6.82%	0.04%	4.40%	2.39%
Denmark	6.43%	1.77%	1.90%	2.76%	8.72%	0.72%	4.54%	3.46%
Germany	2.25%	-0.49%	-0.74%	3.48%	7.74%	0.82%	0.89%	6.03%
Spain	3.16%	-0.23%	0.97%	2.42%	13.36%	0.56%	1.66%	11.14%
France	5.28%	-0.10%	1.30%	4.08%	9.61%	0.61%	1.43%	7.57%
Ireland	22.89%	1.64%	11.62%	9.63%	10.40%	1.11%	2.68%	6.61%
Italy	2.02%	0.22%	0.67%	1.12%	10.28%	0.49%	0.82%	8.98%
Netherlands	11.94%	0.46%	3.93%	7.54%	8.46%	0.26%	-0.45%	8.66%
Austria	1.93%	0.11%	0.94%	0.87%	Na	Na	Na	Na
Finland	6.95%	2.53%	0.12%	4.30%	10.32%	0.31%	4.26%	5.75%
Sweden	14.24%	0.80%	3.35%	10.09%	Na	Na	Na	Na
United Kingdom	7.04%	0.05%	1.72%	5.28%	7.72%	0.66%	2.55%	4.51%

Note: Contribution of labour and non-labour inputs was computed by the usual growth accounting procedure, notably  $g_S = w_L * g_L + w_K * g_K + residual$ , where  $w_L$  is the share of personnel costs on production value and  $w_K$  is the share of the value of non-labour inputs on production value. The value of non-labour input is the difference between value added and personnel costs;  $g_S$ ,  $g_L$ , and  $g_K$  are respectively the growth rates of production value, number of employees, and non-labour inputs. The residual, or  $TFP$ , is the difference between  $g_S$  and the first two terms of this expression. Computations based on Eurostat data.



that may drive the growth of the drug sector. Table 7 uses Eurostat data to decompose the growth in production value in the three areas during 1992-1997 and 1986-1991. We employed the typical growth accounting procedure, which divides the growth in sales into the part explained by the growth of its measureable inputs (typically labour and capital) – weighted by their cost shares – and the growth not explained by the growth in the inputs.<sup>8</sup> In our analysis, we distinguished between the growth in labour employment and the growth in the non-labour inputs defined as value added minus labour costs.

From Table 7 first notice that compared to the US and Japan, Europe fared the highest average growth in the value of pharmaceutical production during 1986-1991. By contrast, the average growth of the European industry declines in 1992-1997, while the US growth increases, and it overcomes the European rate. Second, in both periods the growth of production in Europe is accounted for largely by the residual total factor productivity (TFP). In the US and Japan, in both periods, production growth is explained mostly by the growth in the non-labour input, i.e. capital and R&D assets. This suggests that not only is the European industry more labour intensive, but it responds less substantially to growth in non-labour inputs like research or capital. The industry in Europe responds mainly to "exogenous" factors unrelated to the growth in these inputs.

Table 7 also highlights some specific patterns of individual European countries. Most notably, there is a fairly pronounced decline in the growth of production value between the two period in Germany, Italy, Spain, and partly in France. By contrast, the growth rates either increase or remain fairly high in the smaller European countries, and particularly in Denmark, Ireland, the Netherlands, and Sweden. In the UK, the growth rate in production values remains around 7% per year.

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<sup>8</sup> See for instance Jorgenson

Interestingly enough, in all the European countries, whether their growth is increasing or not, the weights of non-labour inputs vs TFP are always balanced towards the latter. That is, irrespective of their performance in the more recent years, these countries show the same pattern, notably that measurable inputs, and particularly the growth in R&D or capital, do not translate directly into production growth. The only exception is Ireland, which shows a remarkable annual growth (23%) in the 1992-1997 period. This is clearly related to the various peculiarities of the Irish economy which has started growing at bewildering rates during the past decade. It is also probably related to the well known pattern of domestic location of multinational corporations, lured by tax incentives. It is nonetheless interesting that not only is Irish pharmaceuticals growing at a very high rate, but this is the only European country where the contribution to growth by the non-labour input appears to be rather substantial. In short, Ireland seems to be the European country which resembles more closely the patterns observed for the US and Japan. Whether this is because US drug multinationals increasingly locate in Ireland or for other reasons is an issue that goes beyond the scope of this Report.<sup>9</sup>

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<sup>9</sup> Note that since we are using production value rather than sales as our measure for the growth of the industry, the patterns that we observe for Ireland, like for all the other countries, reflect genuine increase in production activities in the country, rather than, for instance, mere invoicing in Ireland by multinational corporations for tax purposes. Clearly, the increase in production in Ireland may reflect an increasing investment in the region by multinational firms rather than being growth by local companies.

### III. The European and US Multinationals: Comparative Performance

Large, diversified, multinational corporations play a crucial role in the drug industry. In this Section, we analyse some important indicators of performance, comparing the European and US largest companies.

Despite the high R&D intensity and the highly skewed distribution of product market sizes, the concentration of the pharmaceutical industry is low, albeit slightly increasing, mainly as a consequence of processes of M&A (see Table 8).

**Table 8:**  
**Market Concentration in Selected Countries, Corporate Groups**

	Corporate Groups			
	Top 10		Top 25	
	1994	1999	1994	1999
UNITED STATES *	52.82	47.87	81.50	84.51
JAPAN	38.38	37.25	64.18	63.65
SWITZERLAND *	49.90	51.57	71.62	75.58
AUSTRIA *	43.09	44.89	72.95	73.29
BELGIUM *	43.54	48.36	75.82	78.86
CZECH REPUBLIC *	48.79	44.64	69.46	69.09
DENMARK	58.01	53.22	85.33	84
FINLAND *	69.15	62.49	88.70	85.13
FRANCE	47.88	52.2	76.38	77.99
GERMANY *	34.97	38.35	61.79	64.9
GREECE	45.71	47.62	75.01	78.91
HUNGARY	65.34	58.91	86.83	86.48
IRELAND	48.82	50.17	77.01	77.62
ITALY *	44.18	44.68	70.06	73.19
LUXEMBOURG	44.04	51.15	73.14	76.46
NORWAY *	66.19	58.95	90.83	85.3
POLAND *	39.82	36.72	68.77	63.27
PORTUGAL	40.30	41.85	70.26	72.56
SLOVAK REPUBLIC *	55.86	49.45	76.65	75.24
SLOVENIA	81.35	72.6	94.23	92.05
SPAIN	39.47	40.27	67.12	69.8
SWEDEN *	68.02	56.87	88.22	82.49
UNITED KINGDOM *	48.04	49.13	71.53	71.39

Source: IMS International. \* Including hospital sales

The low concentration of the industry can be explained by some specific features of its competitive dynamics. First, the industry is composed by many therapeutic classes and by a wide range of technologies. Second, the successful introduction of a new drug within a given class is generally the first outcome of intense “races” to innovate, in which first mover advantages can be not long lasting. In general, any major innovation is followed, well before patent expiry and generic competition, by both product and process innovations by competitors, that can substantially erode the market power of the early innovator. Then, the expiration of the original patent marks a significant “market shock”, with generic firms and products expanding on the market. Third, the degree to which early innovators enjoy an advantage in introducing later major drugs within the same family of molecules tends to be limited<sup>10</sup>. This, jointly with the coexistence of several compounds or variations thereupon targeted to the same pathology, generally hinders the persistence of dominant positions in any individual market.

Data presented in Tables 9 and 10 show a marked process of globalisation within the industry. Table 9 covers the period from 1985 to 1998. The Table shows that in all the largest markets a significant reduction of the share controlled by local corporations. Data presented in Table 10 confirms this process of globalisation of the industry. Moreover, Table 10 shows the good performance of firms that belong to the core of the industry and are located in the US, UK, France, Switzerland, and Denmark. On the contrary, one can observe a declining pattern for German firms and the fall of Italy. Over the 1990s the US share of the world market has increased, driven by the growth of the internal market and by the control of a larger share of the European market. At the same time, Table 10 reveals that the European multinationals as well have increased their market share in the US<sup>11</sup>.

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<sup>10</sup> Sutton, 1998; Bottazzi, Dosi, Lippi, Pammolli, Riccaboni, 2000.

<sup>11</sup> For further details see Gambardella, Orsenigo, Pammolli, 2000.

As it is shown in Table 11, the headquarters of the largest pharmaceutical companies are located in Western Europe and the US, and Japan. Both in 1989 and in 1998, the top 10 pharmaceutical companies in terms of worldwide sales were headquartered in either the US or Western Europe. While no Japanese firms are among the top 10 companies, several Japanese firms fall in the next tier of top worldwide pharmaceutical sales<sup>12</sup>.

Table 11 confirms the good performance, as measured by market shares, of the largest European corporations in the last fifteen years. This result is robust, especially if one considers the lower size and rates of growth of the European market vis à vis the American one.

This result is not disconfirmed by data on the distribution of the 50 top selling new chemical entities launched, worldwide, in the two five-years periods 1985-1989 and 1995-1999 (see Table 12). Moreover, Table 13, which shows the R&D expenditures and the ratio R&D/sales for the top 10 pharmaceutical corporations, suggests that the R&D intensity of the largest pharmaceutical corporations is at least as high as that of their American counterparts.

However, two major qualifications must be introduced.

First, coming back to the 1989-1998 comparison of Table 11, it results that all European companies appearing in the top 10 ranking in 1999 have had to go through a significant merger or acquisition in order to remain in the top 10, which is not the case for their American counterparts.

Second, data presented in the second part of Table 12 indicate that the sales of major innovative products by the US multinationals have increased more significantly than those of the European multinationals in the 1990s. As it is well known, only a very small fraction of the patented compounds turns out to have significant therapeutic and economic value. Thus, New Chemical Entities (that is,

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<sup>12</sup> See USITC, 1999, p. 3-1; Gambardella, Orsenigo, Pammolli, 2000.

drugs whose active ingredients have not been previously approved for therapeutic use) provide the most relevant indication of competitiveness based on innovation capabilities. On this, it is important to notice that US companies have gained a clear and growing leadership in terms of the relevance, as measured by sales and geographical diffusion of New Chemical Entities (NCEs) launched on the market place<sup>13</sup>. As it is shown in Table 12, the share in terms of sales of NCEs launched by US corporations over the total sales generated by the first 50 NCEs on the market rises dramatically in the Nineties to reach almost 70%, while the share of Japan falls drastically. Both the Swiss and the Europe's share rises somewhat, with a significant increase of the UK and above all France, while Germany's share drops to 3%. In addition, Table 14 shows that in 1999 more than 80% of the total sales of the world top 15 drugs was originated by US companies, with a dramatic increase in the last decade and a corresponding sharp fall of Japanese and German corporations.

Finally, and this is an important point, the portfolio of products held by European multinationals tends to be older than that of the US firms, which suggests that there are differences in research productivity in recent years (see Table 15).

The evidence presented in this section can be interpreted by referring to two mechanisms.

On the one side, our results can be explained based on the evidences according to which an increasing fraction of major new drugs, diffused across the most important markets worldwide, has US origins, also thanks to the innovative output of some of the older "New Biotechnology Firms", like Amgen, Chiron, Biogen, Genzyme. In fact, the evidence presented in this section shows that US firms are now the dominant source of innovation and innovative drugs, with Europe lagging behind.

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<sup>13</sup> See Council on Competitiveness, 1998.

On the other side, especially as for the oligopolistic core of the industry, our results are explained by the strong differences in absolute sizes and in rates of growth of demand between Europe and the US. As we already pointed out, the US pharmaceutical market has grown from being roughly equal to the European market at the beginning of the 1990s to almost twice as much in very recent years. In our analysis, we are unable to distinguish whether the growth of the US market in the 1990s stems from higher prices or it is a genuine growth in demand. The size of the increase suggests that it cannot be just increases in prices (even though there can be some of it as well). In other words, the restructuring of pharmaceutical demand, and particularly of the health care system, in the US, has translated into demand growth, which has benefited mainly the US firms. In fact, in spite of their multinational nature, the bulk of the sales of the US and European firms is still in their own markets (see again Table 11a vs. 11b). It is therefore natural that the US firms have taken greater advantage of the growing demand in their own country.

**Table 9:  
Market Shares in Selected Countries, by Nationality of Corporation**

	1985	1989	1998	Change in share 1998-1989, percentage points
<b>USA</b>				
USA	74.7	69.59	63.32	-11.38
Japan	0	0.17	1.7	1.7
Switzerland	8.7	8.64	7.84	-0.86
EU-15	12.8	20.39	24.58	11.78
Others	3.8	1.21	2.56	-1.24
<b>JAPAN</b>				
Japan	76.4	79	78.36	1.96
USA	8.7	8.22	8.34	-0.36
Switzerland	3.3	3.56	3.55	0.25
EU-15	5.6	8.88	9.63	4.03
Others	6	0.34	0.12	-5.88
<b>GERMANY</b>				
Germany	56.6	55.03	45.06	-11.54
Others EU-15	12.8	15	19.67	6.87
USA	17.8	18.03	22.13	4.33
Japan	0.2	0.57	1.72	1.52
Switzerland	9.3	7.67	10.36	1.06
Others	3.3	3.7	1.06	-2.24
<b>UK</b>				
UK	33.4	42.73	24.45	-8.95
Others EU-15	17.2	19.03	23.75	6.55
USA	35.3	28.44	32.13	-3.17
Japan	0	0	0.94	0.94
Switzerland	7	6.48	7.26	0.26
Others	7.1	3.32	11.47	4.37
<b>FRANCE</b>				
France	51.6	48.46	36.86	-14.74
Others EU-15	20	23.72	29.25	9.25
USA	20.6	20.17	24.03	3.43
Japan	0	0.06	1	1
Switzerland	6.7	6.71	7.76	1.06
Others	1.1	0.88	1.1	0
<b>ITALY</b>				
Italy	39.6	42.43	25.76	-13.84
Others EU-15	27.8	27.34	32.36	4.56
USA	17.6	19.32	27.09	9.49
Japan	0	0.18	1.17	1.17
Switzerland	9.4	9.1	12.62	3.22
Others	5.6	1.63	1	-4.6
<b>SPAIN</b>				
Spain	37	30.68	24.8	-12.2
Others EU-15	32.6	38.14	39.98	7.38
USA	15.3	16.8	23.55	8.25
Japan	0.1	0.12	1.3	1.20
Switzerland	12.2	11.59	9.39	-2.81
Others	2.8	2.67	0.98	-1.82

Source: IMS International. \* Including hospital sales



**Table 10:**  
**Shares of Top100 Corporate Groups, by Nationality of Corporation, Major Markets**

Market	Nationality of Corporation*											
	USA	Japan	Switzerland	EU-15	Germany	UK	France	Italy	Sweden	Denmark	Netherlands	Belgium
<b>1985</b>												
World	34.2	13.1	7.7	24.8	9.6	9.2	2.8	1.3	0.6	0.2	0.5	0.6
North America	64.3	0.0	8.8	18.6	4.3	12.9	0.2	0.6	0.1	0.0	0.2	0.3
Europe	19.9	0.0	8.5	44.5	18.1	10.6	7.9	3.5	1.5	0.5	1.1	1.3
A/A/A	11.4	49.3	4.8	10.7	5.8	3.7	0.5	0.1	0.1	0.0	0.3	0.2
Latin America	34.4	0.0	11.1	22.9	14.8	4.5	2.2	0.5	0.1	0.0	0.6	0.2
<b>1989</b>												
World	31.2	15.7	10.1	24.7	9.6	7.4	3.2	2.1	1	0.4	0.5	0.5
North America	62	0.1	5.2	24.7	14	8.8	0.2	0.5	0.5	0.2	0.2	0.3
Europe	20.3	0.2	17.3	38.0	11.3	8.3	8.1	5.2	2.4	0.7	1	1
A/A/A	11.1	51.7	6.6	10.2	4	4.4	0.7	0.2	0.4	0.1	0.3	0.1
Latin America	30.9	0	15.9	22.8	5.7	12	3.3	1	0.2	0	0.6	0
<b>1998</b>												
World	36.0	11.0	8.0	28.8	10.0	9.0	4.4	0.6	2.8	0.7	0.6	0.6
North America	58.5	1.5	7.9	24.8	6.8	11.6	1.8	0.0	3.5	0.2	0.4	0.5
Europe	25.4	0.9	9.6	45.3	15.3	10.2	9.8	1.8	3.7	1.7	0.9	1.5
A/A/A	12.3	46.1	5.1	14.3	6.3	4.1	1.7	0.0	0.9	0.8	0.3	0.2
Latin America	28.6	0.2	11.9	27.8	16.1	5.8	4.1	0.1	0.7	0.0	1.0	0.0
<b>1999</b>												
World	39.0	11.1	7.7	27.8	7.3	11.9	6.1	0.5	-	0.7	0.6	0.6
North America	60.2	1.9	7.6	24.0	4.8	14.9	3.0	0	-	0.3	0.5	0.5
Europe	26.1	1.3	9.5	45.7	12.3	13.8	13.0	2.1	-	1.7	0.9	1.5
A/A/A	14.4	45.8	5.1	15.4	4.6	5.5	3.8	0	-	0.9	0.4	0.2
Latin America	29.6	0.2	11.7	26.7	12.1	6.6	6.7	0.2	-	0.1	0.9	0.1

\* Location of Headquarters. Source: IMS International

**Table 11a:**  
**Top 20 Pharmaceutical Corporations: Decomposition of Worldwide Sales: Major Geographical Markets, 1989**

	Crp.Nat.*	North America	Europe	Asia/Africa/Australia	Latin America					
1989										
1	MERCK&CO USA	4719	26568	563	11986	254	7267	154	1321	28
2	BRISTOL-MYERS SQB USA	4132	23635	572	10123	245	4917	119	2645	64
3	GLAXO UK	3662	168088	459	14904	407	3992	109	952	26
4	SMITHKLINE BEECHAM UK	3488	15591	447	13324	382	4674	134	1325	38
5	CIBA-GEIGY SWI	3382	13765	407	12310	364	5513	163	2232	66
6	AMERICAN HOME USA	3157	22888	725	5398	171	1515	48	1799	57
7	HOECHST FRG	2869	4303	15	16009	558	6455	225	1922	67
8	JOHNSON & JOHNSON USA	2742	17631	643	7266	265	1097	4	1453	53
9	BAYER FRG	2667	6347	238	11441	429	7494	281	1360	51
10	SANDOZ SWI	2520	8316	33	9853	391	5846	232	1184	47
11	LILLY USA	2460	18942	77	4034	164	615	25	1008	41
12	PFIZER USA	2363	12240	518	4844	205	5482	232	1039	44
13	ROCHE SWI	2248	8183	364	8565	381	3484	155	2225	99
14	SCHERING PLOUGH USA	1890	12039	637	3307	175	2306	122	1266	67
15	MAR MER DOW USA	1876	14689	783	2758	147	1238	66	93	05
16	UPJOHN USA	1816	12185	671	2433	134	2797	154	726	4
17	BOEHRINGER INGEL FRG	1766	4185	237	8565	485	3055	173	1854	105
18	WARNER-LAMBERT USA	1679	10007	596	4449	265	1629	97	705	42
19	CYANAMID USA	1662	7462	449	4869	293	3939	237	349	21
20	ABBOTT USA	1659	10817	652	2903	175	1476	89	1393	84

\* Location of Headquarters. Source: IMS International

**Table 11b:**  
**Top 20 Pharmaceutical Corporations: Decomposition of Worldwide Sales: Major**  
**Geographical Markets, 1998**

		Corp. Nat.*		North America		Europe		Asia/Africa/Australia		Latin America	
1998											
1	NOVARTIS	SWI	10724	4396,8	41	3764,1	35,1	1640,8	15,3	922,3	8,6
2	MERCK & CO	USA	10660	6182,8	58	3091,4	29	980,7	9,2	415,7	3,9
3	GLAXO WELLCOME	UK	10616	5361,1	50,5	3588,2	33,8	1157,1	10,9	509,6	4,8
4	PFIZER	USA	9928	6145,4	61,9	1935,9	19,5	1360,1	13,7	486,5	4,9
5	BRISTOL-MEYER SQB.	USA	9855	6366,3	64,6	1990,7	20,2	670,1	6,8	837,7	8,5
6	JOHNSON & JOHNSON	USA	9075	6298,1	69,4	1833,1	20,2	426,5	4,7	517,3	5,7
7	AMERICAN HOME	USA	7855	5082,2	64,7	1633,8	20,8	479,1	6,1	659,8	8,4
8	ROCHE	SWI	7712	2907,4	37,7	2930,5	38	933,1	12,1	933,1	12,1
9	SMITH BEECHAM	UK	7400	4181	56,5	2878,6	38,9	673,4	9,1	407	5,5
10	LILLY	USA	7398	5082,4	68,7	1516,6	20,5	458,6	6,2	340,3	4,6
11	ASTRA	SWE	6959	3590,8	51,6	2755,7	39,6	480,2	6,9	132,2	1,9
12	ABBOTT	USA	6383	4697,9	73,6	765,9	12	504,2	7,9	414,9	6,5
13	HOECHST	GER	6269	1749,1	27,9	2564,0	40,9	1247,5	19,9	702,1	11,2
14	SCHERING PLOUGH	USA	6191	4327,5	69,9	1002,9	16,2	359,1	5,8	501,5	8,1
15	WARNER-LAMBERT	USA	5998	4192,6	69,9	1253,6	20,9	311,9	5,2	239,9	4
16	BAYER	GER	5196	2234,3	43	1834,2	35,3	670,3	12,9	457,2	8,8
17	RHONE-POULENC	FRA	4611	1438,6	31,2	2360,8	51,2	474,9	10,3	331,9	7,2
18	PHARM. & UPIJOHN	USA	4547	1918,8	42,2	1841,5	40,5	536,5	11,8	250,1	5,5
19	ZENECA	UK	3793	1873,7	49,4	1384,4	36,5	390,7	10,3	140,3	3,7
20	BOEHRINGER INGEL	GER	3659	1053,8	28,8	1375,8	37,6	651,3	17,8	581,7	15,9

\* Location of Headquarters. Source: IMS International

**Table 12:  
Top 50 NCEs by Origin of Corporation\***

Nationality of the Main Producer Corporation *	Number of NCEs	
	1985-1989	1995-1999
USA	17	24
Japan	20	3
Switzerland	3	6
EU-15	10	16
UK	3	8
Germany	7	4
Netherlands	0	1
France	0	3

	Sales (%)	
	1985-1989	1995-1999
USA	41.49	69.12
Japan	37.33	3.92
Switzerland	2.91	7.78
EU-15	18.28	18.54
UK	6.53	9.38
Germany	11.75	3.33
Netherlands	0.00	0.80
France	0.00	5.03

\* Location of Headquarters. Source: IMS

**Table 13:**  
**Pharmaceutical R&D Expenditures, Top 10 Pharmaceutical Corporations, 1999**

World Ranking 1999	Company	Nationality*	Pharma R&D Expenditures (US\$m)	R&D as % of Sales
1	Merck&Co.	USA	1,821.1	11.9%
2	AstraZeneca	UK	2,183	17.1%
3	GlaxoWellcome	UK	1,927.5	14.6%
4	Pfizer	USA	NA	NA
5	Bristol Myers Squibb	USA	1,559	12.4%
6	Novartis	SWI	1,801.3	16.1%
7	Aventis	FRA	NA	NA
8	Johnson&Johnson	USA	1,400	16.4%
8	American Home Products	USA	1,389.9	15.6%
10	Roche	SWI	1,893.1	19.1%

\* Location of Headquarters. Source: Scrip League Tables.

**Table 14:**  
**World Top 15 Drugs, by Origin of Main Producer Corporation**

Nationality of the Main Producer Corporation*	Total sales, \$ million, 1989	%	Total sales, \$ million, 1999	%
US	1697	47.94	11227	82.06
Japan	1173	33.14	460	3.36
Switzerland	0	-	835	6.10
EU-15	670	18.93	557	4.07
UK	243	6.86	557	4.07
Germany	427	12.06	0	-
France	0	-	0	-
Sweden	0	-	0	-
Other EU	0	-	0	-
Other non EU	0	-	0	-
Total	3540	100	13682	100

\* Location of Headquarters. Source: IMS

**Table 15:**  
**Recent Products' Contribution to Total Sales: Top 100 Global  
 Corporations<sup>\*</sup>, 1997**

% of Total 1997 sales from NCEs launched since 1988	
<b>USA</b>	32
<b>Japan</b>	29
<b>Switzerland</b>	14
<b>EU-15</b>	16

<sup>\*</sup> Location of Headquarters. Source: IMS

Source: IMS

## **IV. R&D and Innovation as Sources of Competitive Advantages**

### **IV.1 The Division of Innovative Labour in Pharmaceuticals**

There is little question that innovation constitutes one of the key sources of competitiveness in this industry and it is a major determinant of market structure<sup>14</sup> European companies, especially the big German and Swiss firms, have been major innovators in the industry ever since its inception. Following World War II, and also benefiting from the dramatic increase of support to of biomedical research and health care expenditure, US and, more recently, also British companies have progressively challenged the leadership of Continental Europe, establishing themselves as major innovators. However, the innovative core of the industry has been traditionally quite small and remarkably stable over time, with practically no entry until the mid-Seventies.

The emergence and stability of such innovative core was a consequence of the nature of pharmaceutical R&D, which – until the mid-Seventies – was based on the extensive exploration of chemical compounds and on incremental structural modifications of drug prototypes, organised around highly structured processes for carrying out mass screening programs. These processes involved large laboratories and highly disciplined internal organisational procedures, which became a source of first-mover advantages and of economies of scale in research. Through the evolution of the industry, the organisational capabilities developed to manage the processes of drug development and delivery – competencies in the management of large scale, expensive, clinical trials, the process of gaining regulatory approval as well as marketing and distribution – have acted as powerful barriers to entry in the industry. Around this core, a large fringe of firms has thrived through imitation and

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<sup>14</sup> See Gambardella, 1995; Sutton, 1998; Mataves, 1999; Henderson, Orsenigo, Pisano, 1999; Bottazzi, Dosi, Pammolli, Riccaboni, 2000.

generic competition after patent expiration as well as through production and marketing in local markets and product niches.

The advent of the so-called “molecular biology” revolution since the mid-Seventies has introduced drastic changes in the relevant knowledge base, in the processes of discovery and in the organisation of research, with the emergence of a new technological regime and new technological and organisational capabilities as a key source of competitive advantages<sup>15</sup>.

First, the “molecular biology” revolution has opened up new opportunities for the discovery and production of new drugs. At the same time, it has implied a radical shift in the knowledge base and in research procedures and methodologies, with the transition from quasi-random screening to “guided discovery” or discovery by design. Moreover, the importance of publicly generated scientific knowledge for industrial innovation has drastically increased<sup>16</sup>.

These changes have had major consequences on the organisation of research and on patterns of division of innovative labour. New technological opportunities have made it possible the entry of new firms, mainly specialised suppliers of specific techniques and intermediate products to larger companies. Established corporations have experienced complex processes of adaptation, absorbing the new knowledge base and adopting new, academic-like, forms of organisation of research, which rely crucially on the development of dense networks of collaboration with universities, public and private research centres and other companies, especially New Biotechnology Firms (NBFs)<sup>17</sup>. Yet, they continue to represent the inner core

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<sup>15</sup> See Orsenigo, 1989; Gambardella, 1995; Galambos, Sturchio, 1996; Orsenigo, Pammolli, Riccaboni, 2000; Drews, 2000.

<sup>16</sup> See Arora, Gambardella, 1994.

<sup>17</sup> See, among others, Arora and Gambardella, 1990, Powell et al., 1996; Orsenigo, Pammolli, Riccaboni, 2000.

of innovators in the industry. Only few of the new firms have succeeded in entering into such core. The – largely sunk – costs required for discovery and development have increased sharply and – as a consequence – barriers to entry have increased. Nowadays, an R&D project for a new drug is likely to last 8-12 years, with a cost in the range of US\$ 350-650 millions<sup>18</sup>. Moreover, molecular biology and the new general-purpose research technologies of combinatorial chemistry, highthroughput screening, and genomics, have increased firm-specific economies of scope related to knowledge spillovers across projects and research trajectories. Finally, large innovative corporations play a crucial integrative role across different bodies of knowledge as well as providing complementary assets in clinical development, regulatory affairs and distribution channels.

**Table 16:**  
**Shares in terms of Number of Patents, by Location of Inventors\***

Country	Pharma %			Biotech %		
	1978-1987	1988-1997	Total	1978-1987	1988-1997	Total
Canada	0.98	1.54	1.40	0.97	1.93	1.67
Switzerland	4.08	2.94	3.23	3.61	3.79	3.74
Germany	18.22	12.80	14.17	13.03	10.03	10.85
Denmark	0.59	0.80	0.75	1.43	2.35	2.10
Spain	0.18	0.45	0.38	0.14	0.40	0.32
France	7.38	9.69	9.11	7.18	6.98	7.04
Italy	2.85	3.24	3.14	1.06	1.75	1.56
Japan	15.02	13.64	13.99	22.21	17.06	18.47
Sweden	2.02	2.18	2.14	2.07	1.07	1.34
UK	8.59	7.73	7.95	7.12	7.85	7.65
USA	40.08	44.98	43.74	41.19	46.80	45.25
Total	100.00	100.00	100.00	100.00	100.00	100.00

\* Location of R&D Labs. Source: Our calculations on European Patent Office

<sup>18</sup> See Di Masi, 1991.



## IV.2 The US as an increasingly preferred location for invention?

This section provides some evidence on the geographical location of R&D laboratories within the industry, by means of patent data<sup>19</sup>.

All biotechnological and pharmaceutical European patents (EPO) for 1987-1996 were analysed. The total number of patents applied for between 1987-1996 that was found is 45,454. Patent micro-classes were created, to distinguish biotech from pharmaceuticals. Then, every patent was assigned to a given country of invention, by assigning to the country the share of the inventors in the patent that were located in the country. Thus, for instance, if a patent has ten inventors, two of which from Italy and the others from Germany, we assigned 0.2 to Italy and 0.8 to Germany. The vast majority of patents were produced by inventors located in only one country.

Table 16 shows that, both in traditional pharmaceuticals and in biotechnology, the share of patents by US inventors has increased in the 1990s compared to the 1980s.<sup>20</sup> The share of Japanese and German inventors has instead declined. France grows and overcomes the UK in pharmaceuticals, but not in biotechnology. Switzerland loses shares in pharmaceuticals, but grows slightly in biotechnology. In general, the relative positions of the US and the EU switch moving from biotech vs. pharmaceuticals. This suggests that the US have a comparative advantage in the newer biotech fields relative to more traditional pharmaceutical research.

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<sup>19</sup> As it is well known, measuring innovation is difficult and no single indicator usually yields a satisfactory picture. It is important to emphasise that in this Report R&D and patents are not used here as indicators of, respectively, innovative input and output, but as broad indicators of technological activities. See Griliches, 1990.

<sup>20</sup> EPO data might “overestimate” the patenting performance of Europe and “underestimate” that of the US. Here however we are comparing shares over time, and hence this problem may be less severe.

An equally informative picture is provided by the analysis of patent citations, by nationality of patent assignee. Patent citations provide a better measure of the technological and economic potential value of innovative activities than patent counts. Citations can in fact be used as a measure of the importance or impact of inventions and as a proxy of knowledge flows among patenting institutions. Widely cited patents tend to be “seminal” patents, i.e. key inventions on which further patent must refer to. Moreover, high citations rates have been shown to correlate with the economic value of patents. Thus, a high number of citations received by a given firm or country can be interpreted as a measure of the quality and relevance of its innovative activities<sup>21</sup>.

Data reported in Table 17 sharpen the results obtained by looking at patent counts. The US dominance is stronger both in pharmaceuticals and in biotechnology, and in both fields citations to US patents increased over the two periods. The share of citations to US patents is higher than the share of counts in the earlier Table, which suggests that on average US patents are relatively more important. By and large, the share of citations for the European countries is similar or lower than the share of counts. Only the UK shows a higher share for citations. Germany, France and Italy all show a lower share for citations than for counts. Among the 25 institutions which have the largest number of highly cited patents, 11 are American, 3 each are British, Swiss, German and French, one is Japanese and one Danish. Moreover, 4 are first generation biotechnology firms, and four are universities or public research centres.

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<sup>21</sup> Jaffe, Trajtenberg, Henderson, 1993; McMillan, Narin, Deeds, 2000.

**Table 17:**  
**Shares in terms of Patent Citations, by Nationality of Assignee\***

Country	Shares of Citations					
	Pharma %			Biotech %		
	1978-1988	1987-1997	Total	1978-1988	1987-1997	Total
Canada	1.21	1.55	1.45	0.83	1.65	1.32
Denmark	0.91	0.87	0.88	1.45	2.73	2.21
France	5.48	6.85	6.44	4.77	5.18	5.01
Germany	12.86	8.59	9.85	7.58	6.87	7.16
Italy	1.81	2.70	2.43	0.57	1.17	0.92
Japan	17.37	12.36	13.84	16.56	11.77	13.72
Spain	0.11	0.23	0.19	0.20	0.14	0.16
Sweden	2.42	1.88	2.04	1.63	1.21	1.38
Switzerland	4.02	2.98	3.29	4.17	5.12	4.73
UK	9.48	10.98	10.54	8.08	8.57	8.37
USA	44.33	51.02	49.04	54.16	55.61	55.02
Total	100.00	100.00	100.00	100.00	100.00	100.00

\* Corporate Headquarters. Source: Our calculations on European Patent Office. Data cleared from self-citations at the country and firm level. Source: European Patent Office-CESPRI database on European Patent Applications.

Table 18 gives information on the geographical location of inventive activities by the 30 selected firms. Table 17 shows that: a) On average, the inventive activities of the European and American firms are more internationalised as compared to Japanese corporations; b) When they do not invent in their own country, French and German companies invent in the US – note in particular the high share of biotech inventions in the US by German companies as compared to pharma patents; c) the UK, but also the Swiss companies, do relatively little research in their own country as compared to what they do in the US. Particularly, Swiss companies do a lot of their biotech research in the US; d) the US companies do few biotech patents in European laboratories, compared to the Europeans in the US (7.1% compared to generally higher than 10%).<sup>22</sup>

<sup>22</sup> See Gambardella, Orsenigo, Pammolli, 2000 for further details.

**Table 18:**  
**Top 30 Pharmaceutical Companies Worldwide -- Share of 1987-1996 European Patents**  
**Invented by Assignee from Country x in Region y**

Nationality of Assignee *	Region of invention									
	EU Biotech	EU Pharma	JP Biotech	JP Pharma	Other Biotech	Other Pharma	USA Biotech	USA Pharma	Total Biotech	Total Pharma
France (2)	86.6	84.8	0.0	0.0	0.9	0.6	12.4	14.6	100.0	100.0
Germ. (5)	80.4	95.2	0.2	1.0	1.5	1.2	17.8	2.6	100.0	100.0
Japan (4)	1.7	4.5	96.4	93.5	0.0	0.1	1.9	1.8	100.0	100.0
Sweden (1)	66.0	88.9	0.0	2.1	23.6	2.3	10.4	6.7	100.0	100.0
Switz. (2)	44.4	71.2	5.1	2.5	0.8	0.8	49.7	25.5	100.0	100.0
UK (2)	76.7	54.1	0.0	0.0	2.0	0.9	21.3	45.0	100.0	100.0
USA (14)	7.1	16.6	1.2	2.1	1.2	2.6	90.4	78.7	100.0	100.0
Total	36.7	51.7	8.7	7.4	1.5	1.6	53.1	39.2	100.0	100.0

\* Location of Headquarters. Source: Our calculations on European Patent Office

All in all, the evidence presented in this section shows that the relative position of the US as a locus of innovation has increased over the past decade compared to Europe. Moreover, our overall picture suggests that Europe's performance is comparatively worse in biotechnology.

The aggregate picture, however, stems from differentiated trends across individual European countries. It is also important to notice that the American leadership seem to derive less from the superiority of individual corporations vis-à-vis their European counterparts than from the presence of a larger number of innovative companies. This can be seen from the larger number of US companies within the top corporations, from the higher R&D intensity of the US industry as a whole and, indirectly, from the data examined in Section II. Moreover, the American advantage appears to be linked to the more pronounced role of the New Biotechnology Firms, and the universities as well, to research and innovative activities.

### **IV.3 Collaboration in Research, Markets for Technology, and Implications for Competitiveness**

As mentioned previously, the molecular biology revolution has entailed the adoption of new organisational forms of R&D, in particular a higher reliance on collaborations between firms, New Biotechnology Firms (NBFs) and universities.

The explosion of technological opportunities and the relevance of pure scientific, academic research for innovative activities associated with the advent of molecular biology, has meant that no individual firm can now be able to control and master internally all the knowledge required to discover and develop a new drug<sup>23</sup>.

Coupled with the establishment of property rights on such knowledge, all this has allowed the emergence and development of a vibrant market for technology. The ability to access and make efficient use of such network of collaborative relations and of the underlying market for technology has therefore become a crucial source of competitiveness.

Our analysis confirms that in the Nineties collaborations have increased in all the countries. In addition, we find that collaborations have increased in the phase of pre-clinical research relatively to the marketing stage<sup>24</sup>.

On this, Table 20, based on the PHID database at the University of Siena, unravels major differences in firms' research and licensing behaviour, focussing on seven major Countries (USA, UK, Switzerland, Germany, France, Italy, and Sweden) for 1992 to 1998.

The indicators presented in Table 20 are defined as the proportion of projects licensed in and out in a given phase of the R&D process, over the total number of projects developed in collaboration.

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<sup>23</sup> Powell et al., 1996.

<sup>24</sup> See Gambardella, Orsenigo, Pammolli, 2000.

More precisely,  $L_p/L$ ,  $L_{1-2}/L$ ,  $L_3/L$ ,  $L_r/L$  and  $L_m/L$ , indicate, respectively:

- the proportion of projects that were licensed-in in Preclinical ( $L_p/L$ ),
- the proportion of projects that were licensed-in Phase 1-2 of Clinical Research ( $L_{1-2}/L$ ),
- the proportion of projects that were licensed-in Phase 3 of Clinical Research ( $L_3/L$ ),
- the proportion of projects that were licensed-during the Registration Phase ( $L_r/L$ ), and, finally,
- the proportion of projects that were licensed-after commercialisation (Marketing:  $L_m/L$ ).

Other indicators are then considered:

- the ratio of licensed projects to in house projects ( $L/H$ ),
- the ratio of projects licensed in Preclinical to the projects developed in house ( $L_p/H_p$ ), and
- the ratio of licensed out projects in R&D to projects developed in house ( $L_O/H$ ).

In synthesis, Table 20 shows that US firms have consistently over time the highest propensity to collaborate in the pre-clinical phase, whereas collaboration in marketing remain significant in the European countries. Furthermore, US firms act more frequently as licensors (*Originators*) of new R&D projects as compared to the other European countries, which are typically licensees (*Developers*). Based on Table 20 it is possible to distinguish very clearly the behaviour of firms located in Countries like Italy and, to a lesser extent, Sweden, that have a high propensity to license-in in the latter phases of the R&D chain, from US, UK, and Swiss firms, that collaborate extensively also in the early stages of the R&D process.

Moreover, as it is shown in Table 19, the role of “Originators” of US (and Canadian) companies is linked to the disproportionate share of licences which involve – largely as licensors – NBFs, universities and other research centres as compared to the other major European countries (with the exception of the Netherlands, Denmark and Sweden), and Japan.

**Table 19:**  
**R&D Projects, by Country and Type of Institution, 1990-1999**

	Lead Pharma		DBFs		Univ./Inst.		R&D Projects	In-house	Originated	Developed
	Num.	Projects	Num.	Projects	Num.	Projects				
USA	82	1710	313	920	112	421	3051	27.43	26.78	45.79
Japan	137	1413	3	15	33	70	1498	37.12	21.16	41.72
Germany	37	716	17	30	7	8	754	27.19	21.09	51.72
United Kingdom	14	379	29	118	17	22	519	39.11	23.89	36.99
France	24	347	23	58	9	22	427	25.53	19.44	55.04
Switzerland	24	376	3	6	2	8	390	34.87	14.36	50.77
Italy	45	272	3	12	6	7	291	27.49	20.27	52.23
Spain	31	161	1	3	2	3	167	46.11	11.38	42.51
South Korea	46	154	0	0	2	4	158	16.46	4.43	79.11
Canada	7	16	32	95	8	13	124	20.16	33.06	46.77
Netherlands	10	49	8	46	2	2	97	9.28	30.93	59.79
Belgium	10	76	5	11	3	7	94	15.96	45.74	38.30
Denmark	3	32	5	36	2	2	70	31.43	37.14	31.43
Hungary	2	23	4	18	4	8	49	24.49	65.31	10.20
Israel	9	31	1	1	5	13	45	15.56	17.78	66.67
Australia	4	9	8	24	6	9	42	11.90	19.05	69.05
Argentina	18	36	0	0	0	0	36	2.78	-	97.22
Finland	4	20	1	3	0	0	23	21.74	26.09	52.17
Czech Rep.	5	9	1	1	1	10	20	50.00	15.00	35.00
Portugal	12	17	0	0	0	0	17	5.88	-	94.12
Sweden	2	5	5	11	1	1	17	11.76	47.06	41.18
Ireland	1	14	2	2	1	0	16	-	87.50	12.50
Others*	97	104	3	3	46	51	158	22.15	10.13	67.72
<b>Total</b>	<b>624</b>	<b>5969</b>	<b>467</b>	<b>1413</b>	<b>269</b>	<b>681</b>	<b>8063</b>	<b>-</b>	<b>-</b>	<b>-</b>

\*China, Russia, South Africa, Chile, Colombia, India, Austria, Brazil, Greece, Mexico, Indonesia, Morocco, Pakistan, Poland, Slovenia, Turkey, Croatia, Latvia, New Zealand, Taiwan, Uruguay, Malaysia, Monaco, Peru, Singapore, Slovak Republic, Venezuela, Bulgaria, Hong Kong, Jordan, Norway, Paraguay, Philippines, Ukraine. Source: PHID, University of Siena

**Table 20: Profiles of R&D Behaviour, Selected Countries, 1992-1998**

	N	H	L	L/H	L <sub>p</sub> /L	L <sub>1-2</sub> /L	L <sub>3</sub> /L	L <sub>r</sub> /L	L <sub>m</sub> /L	L <sub>p</sub> /H <sub>p</sub>	LO/H
USA											
1992	898	732	166	0.227	0.373	0.241	0.066	0.091	0.229	0.135	0.077
1993	1132	911	221	0.242	0.416	0.24	0.063	0.086	0.195	0.154	0.09
1994	1378	1104	274	0.248	0.453	0.219	0.058	0.078	0.193	0.176	0.096
1995	1834	1497	337	0.225	0.454	0.22	0.06	0.083	0.184	0.148	0.11
1996	2250	1832	418	0.186	0.474	0.206	0.074	0.086	0.16	0.152	0.123
1997	2257	1743	514	0.295	0.475	0.202	0.078	0.09	0.156	0.266	0.178
1998	2353	1763	590	0.336	0.489	0.206	0.069	0.087	0.148	0.244	0.255
Switzerland											
1992	216	184	32	0.301	0.176	0.196	0.039	0.098	0.491	0.038	0.106
1993	223	187	36	0.284	0.180	0.200	0.040	0.080	0.500	0.026	0.079
1994	248	205	43	0.251	0.173	0.195	0.021	0.086	0.525	0.034	0.076
1995	241	197	44	0.223	0.162	0.186	0.023	0.069	0.560	0.04	0.057
1996	235	192	43	0.223	0.181	0.204	0.045	0.045	0.525	0.036	0.050
1997	229	183	46	0.209	0.162	0.279	0.046	0.046	0.467	0.043	0.019
1998	226	176	50	0.192	0.138	0.333	0.055	0.055	0.419	0.051	0.016
UK											
1992	230	193	37	0.19	0.16	0.19	0.08	0.11	0.46	0.06	0.01
1993	488	217	41	0.18	0.17	0.17	0.05	0.10	0.51	0.07	0.01
1994	258	212	110	0.21	0.17	0.13	0.06	0.09	0.54	0.07	0.02
1995	334	275	150	0.21	0.27	0.12	0.07	0.08	0.46	0.06	0.02
1996	380	313	177	0.21	0.24	0.12	0.10	0.07	0.46	0.09	0.03
1997	442	362	211	0.20	0.34	0.10	0.09	0.07	0.40	0.13	0.05
1998	468	376	92	0.24	0.38	0.09	0.11	0.06	0.35	0.16	0.06
Germany											
1992	334	283	51	0.180	0.117	0.059	0.039	0.294	0.491	0.033	0.021
1993	381	321	60	0.187	0.150	0.066	0.050	0.266	0.468	0.046	0.018
1994	419	353	66	0.187	0.121	0.060	0.045	0.272	0.502	0.039	0.017
1995	461	361	100	0.277	0.130	0.060	0.060	0.230	0.52	0.065	0.027
1996	488	363	125	0.344	0.152	0.056	0.064	0.240	0.488	0.104	0.033
1997	476	339	137	0.404	0.167	0.065	0.065	0.226	0.477	0.139	0.038
1998	482	326	156	0.478	0.198	0.064	0.083	0.211	0.444	0.209	0.043
France											
1992	206	171	35	0.204	0.171	0.085	0.085	0.142	0.517	0.057	0.017
1993	234	193	41	0.212	0.195	0.073	0.073	0.121	0.538	0.073	0.015
1994	259	211	48	0.227	0.166	0.083	0.062	0.166	0.523	0.067	0.023
1995	287	230	57	0.247	0.175	0.052	0.070	0.210	0.493	0.084	0.021
1996	289	228	61	0.267	0.163	0.049	0.065	0.229	0.494	0.086	0.022
1997	264	199	65	0.326	0.138	0.046	0.061	0.215	0.540	0.096	0.030
1998	281	105	70	0.331	0.157	0.042	0.057	0.214	0.530	0.104	0.033
1998	295	207	88	0.425	0.284	0.079	0.045	0.170	0.420	0.247	0.063
Sweden											
1992	23	17	6	0.353	-	-	0.166	0.500	0.334	-	-
1993	28	21	7	0.333	-	-	0.142	0.428	0.430	-	-
1994	32	24	8	0.166	-	0.125	0.125	0.375	0.375	-	0.041
1995	34	25	9	0.360	-	0.111	0.111	0.333	0.445	-	0.040
1996	39	27	12	0.444	0.083	0.083	0.083	0.416	0.335	0.037	0.037
1997	48	31	17	0.548	0.117	0.294	0.059	0.294	0.236	0.064	0.032
1998	49	29	20	0.689	0.200	0.250	0.050	0.250	0.250	0.136	0.035
Italy											
1992	103	70	33	0.471	0.060	0.091	0.030	0.151	0.668	0.055	0.014
1993	125	83	42	0.336	0.048	0.071	0.023	0.214	0.644	0.048	0.012
1994	150	102	48	0.320	0.041	0.062	0.020	0.208	0.669	0.019	0.019
1995	168	111	57	0.513	0.035	0.052	0.070	0.193	0.650	0.018	0.025
1996	179	120	59	0.491	0.034	0.051	0.067	0.203	0.645	0.016	0.029
1997	187	121	66	0.545	0.060	0.045	0.060	0.197	0.938	0.080	0.035
1998	178	111	67	0.603	0.059	0.059	0.059	0.194	0.629	0.090	0.040

Source: PHID, University of Siena



This is an important point, as it suggests that one major difference between the US and Europe is really the presence in the US of an industry of technology suppliers, both new biotechnology firms and universities. In short, Europe and the US may not look too different if one looks individually at the large drug multinationals; but they do look different if one looks at the organisation of the industry. In the US there is not only a larger number of big innovative companies, but also a higher supply of new technologies and an extensive vertical specialisation between an industry that is specialised in the “exploration” of new technologies and innovation opportunities, and an industry that is specialised in their “exploitation”.<sup>25</sup>

As argued by several authors, this organisation of the industry can be highly conducive to innovation performance, as it exploits the comparative advantages of larger and smaller firms in the exploration and exploitation phases.<sup>26</sup>

Given this, the European research system need not only to be strengthened in terms of its ability to produce more and better research, but also to exploit its innovation potential by translating this potential into economic performance. For example, today the biotech industry in the US is said to account for 10% of the total US sales of pharmaceutical products, and to have produced more than a hundred thousands specialised jobs between 1984-1994 (on average seventy-five jobs per company)<sup>27</sup>. A recent study estimated that in California biotech companies linked to star scientists provided a sizable contribution in terms of new employment

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<sup>25</sup> See March, 1991.

<sup>26</sup> See for instance Arrow, 1983; Arora, Fosfuri, Gambardella, 2000; Arora, Gambardella, Pammolli, Riccaboni, 2000.

<sup>27</sup> See Scriabine, 1999.

opportunities<sup>28</sup>. In addition, over the past 10-20 years, some of the US biotech firms – e.g. Amgen, Centocor, Biogen, Chiron, Genentech, Genzyme, Immunex – have become leading producers both in the US and to a good extent abroad. These companies produce a fair number of products, some of which account for a few hundreds millions dollars in annual sales. At the same time, as we shall see below, biotech and similar companies selling drug research tools and technologies are a new important phenomenon of the US industry. Apart from providing new contributions in terms of industry growth, sales and employment, the rise of technology specialists in new areas witness the vitality of this process, and its potential for new economic spins. Finally, the intensive licensing out of technologies or products by the US biotech companies and related technology suppliers is likely to imply a steady flow of revenues in terms of royalty rates. This provides further accounts for the opportunities that can be created by the rise and growth of a dynamic and innovative industry.

In sum, the creation of an active European industry that thrives on innovation opportunities is likely to mean less for the fortunes and the competitiveness of the established European pharmaceutical companies. But it is likely to imply far more for the growth, the performance, and the vitality of the European pharmaceutical industry and environment as a whole.

In addition, Tables 19 and 20 confirm both the role of US firms as originators of new technologies and the importance of the market for technology within the US, as a powerful tool of transmission of knowledge across countries.

Although domestic sources of knowledge remain important, companies tend to get a large share of licences from the US, especially in the pre-clinical research phase, and much less so in downstream stages.

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<sup>28</sup> See Zucker, Darby, Armstrong, 1998.

This reinforces the point that the US feed both domestic and foreign companies, while European and Japanese firms tend to tap North American knowledge, much more than the other way around and even more than the domestic sources. As a result, rather than globalisation of research, we observe a process of concentration of research into North America.

Related important evidence comes from recent ongoing research on the relative performances of in-house vs. licensed in R&D projects<sup>29</sup>. Tables 21 and 22 show that licensed projects have a higher probability of success, and this is so for all the countries and phases of clinical trials. At the same time, US companies show a higher probability of success in all the phases of clinical trials. This stems from a higher probability of success of in-house projects, while the US probability of success from licensed projects is aligned with the probability of success from licensed projects of companies coming from any other country. To put it in a nutshell, participation to division of innovative labour and to markets for technology can allow companies to get access to external knowledge and to increase the productivity of their research. As a result, markets for technology can smooth the competitive differences across firms. While in-house development implies a different probability of success for companies from different nationality, in the case of licensed compounds the probability of success is not affected by the nationality of the firms. Internal differences in competitiveness, which depend on firm-specific capabilities, can be vanished by the fact that companies rely on common sources of technology, which they acquire from specialist technology suppliers.<sup>30</sup>

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<sup>29</sup> See Arora, Gambardella, Pammolli, Riccaboni, 2000. See also Pammolli, Riccaboni, Baio, 2000.

<sup>30</sup> See Arora, Gambardella, Pammolli, Riccaboni, 2000.

Coupled with the observation that US firms have higher propensity to using licenses than European or Japanese firms, these results bear some interesting implications for the analysis of competitive advantages in drug R&D<sup>31</sup>:

- i) US firms cumulate a higher ability of developing compounds in-house with a greater reliance on licenses, which is a more productive mode of innovating. Thus, the US competitiveness in drug innovation appears to be the “sum” of these two effects – better in-house capabilities and more effective use of the market for technology;
- ii) European firms lag behind their US counterparts in terms of their in-house capabilities and, moreover, of the extent of their use of the market for technology. Considering that licensed compounds have a higher probability of success, this implies that European companies should rely more on the market for technology, in order to partially compensate for their lower in-house capabilities.

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<sup>31</sup> See Arora, Gambardella, Pammolli, Riccaboni, 2000.

**Table 21:  
Licensing Agreements in R&D**

Out			In	
	Preclinical	300 (62.4%)	132 (27.4%)	49 (10.2%)
		USA	Europe	Japan
350 (73.4%)	USA	84.3%	50.0%	40.8%
96 (20.1%)	Europe	10.7%	41.7%	6.1%
31 (6,5%)	Japan	2.3%	4.5%	34.7%
	Clinical III	80 (45.5%)	57 (32.4%)	(2.1%)
		USA	Europe	Japan
98 (55.7%)	USA	67.5%	54.3%	33.3%
52 (29.5%)	Europe	27.5%	38.6%	20.5%
26 (14.8%)	Japan	5.0%	7.1%	46.2%
	Marketing	478 (29.3%)	820 (50.3%)	331 (20.4%)
		USA	Europe	Japan
503 (30.9%)	USA	42.3%	23.9%	31.7%
763 (46.8%)	Europe	38.1%	56.1%	36.6%
363 (22.3)	Japan	19.6%	20.0%	31.7%

Source: Our calculations from PHID, University of Siena

**Table 22:  
Success and Failure Rates of Licensed vs. In-House Drug Compounds (\*)**

	Preclinical/Clinical I			Clinical I/II			Clinical II/III		
	Failure	Success	Total	Failure	Success	Total	Failure	Success	Total
<b>Total</b>									
In-House	2038 (58.1)	1470 (41.9)	3508 (100)	355 (20.6)	1268 (79.4)	1623 (100)	428 (38.0)	698 (62.0)	1126 (100)
Licensed	192 (38.2)	311 (61.8)	503 (100)	36 (9.4)	348 (90.6)	384 (100)	49 (14.3)	293 (85.7)	342 (100)
<b>Total</b>	<b>2230 (55.6)</b>	<b>1781 (44.4)</b>	<b>4011 (100)</b>	<b>391 (19.5)</b>	<b>1616 (80.5)</b>	<b>2007 (100)</b>	<b>477 (32.5)</b>	<b>991 (67.5)</b>	<b>1468 (100)</b>
<b>US firms</b>									
In-House	849 (54.8)	700 (45.2)	1549 (100)	108 (17.0)	528 (83.0)	636 (100)	126 (33.2)	254 (66.8)	380 (100)
Licensed	129 (39.4)	198 (60.6)	327 (100)	21 (9.7)	195 (90.3)	216 (100)	22 (13.9)	136 (86.1)	158 (100)
<b>Total</b>	<b>978 (52.1)</b>	<b>898 (47.9)</b>	<b>1876 (100)</b>	<b>129 (15.1)</b>	<b>723 (84.9)</b>	<b>852 (100)</b>	<b>148 (27.5)</b>	<b>390 (72.5)</b>	<b>538 (100)</b>
<b>European firms</b>									
In-House	764 (61.6)	477 (28.4)	1241 (100)	176 (28.9)	433 (71.1)	609 (100)	189 (40.4)	279 (59.6)	468 (100)
Licensed	35 (36.8)	60 (63.2)	95 (100)	10 (11.9)	74 (88.1)	84 (100)	19 (20.1)	73 (79.9)	92 (100)
<b>Total</b>	<b>799 (59.8)</b>	<b>537 (40.2)</b>	<b>1336 (100)</b>	<b>186 (26.8)</b>	<b>507 (73.2)</b>	<b>693 (100)</b>	<b>208 (37.1)</b>	<b>352 (62.9)</b>	<b>560 (100)</b>
<b>Japanese firms</b>									
In-House	327 (61.8)	202 (28.2)	529 (100)	55 (19.0)	235 (81.0)	290 (100)	89 (39.9)	134 (60.1)	223 (100)
Licensed	8 (19.5)	33 (80.5)	41 (100)	3 (4.6)	62 (95.4)	65 (100)	8 (11.6)	61 (88.4)	69 (100)
<b>Total</b>	<b>335 (58.8)</b>	<b>235 (41.2)</b>	<b>570 (100)</b>	<b>58 (16.3)</b>	<b>297 (83.7)</b>	<b>355 (100)</b>	<b>97 (33.2)</b>	<b>195 (66.8)</b>	<b>292 (100)</b>

Source: Our calculations from PHID, University of Siena (\*) Drug compounds developed in-house vs acquired through licenses in Phase I, II, or III of clinical research by the top 100 pharmaceutical corporations, worldwide. Percentages in parenthesis are conditional probabilities of success and failure.

At the end of this section it is important to notice that the potential levelling effect of markets for technologies notwithstanding, the access to the network of collaborations and to the market for technology in pharmaceuticals is not unrestricted. Particularly, the network of collaborative relationships itself tends to consolidate and to become increasingly hierarchical. Indeed, the network has been expanding over time, mainly through the continuous entry of new, increasingly

specialised, US firms collaborating with large incumbents. Despite this growth, however, the network tends to consolidate around a rather stable core of companies. This core is composed by large incumbents and early entrants, who act as integrators of differentiated and strongly specialised fragments of knowledge. This suggests the existence of first-mover advantages even in the network of collaborations, which becomes increasingly difficult to enter as time goes by<sup>32</sup>.

#### **IV.4 Drug Research Tools: Another Largely US Phenomenon?**

The state of European competitiveness in pharmaceutical innovation is also reflected by the ability of the EU industry to develop and participate in the development of the new R&D tools and general-purpose technologies (GPTs) that have been introduced into the industry since the beginning of the Nineties. GPTs have enabled increasing levels of vertical specialisation and division of innovative labour in drug discovery, not differently from other high-tech industrial sectors<sup>33</sup>.

During the Nineties, a set of generic research technologies has been developed in biotechnology and pharmaceuticals, from polymerase chain reaction (PCR), to protein structure modelling, rapid computer based drug assay and testing, recombinant chemistry techniques, drug delivery systems, chemical separation and purification techniques that allow researchers to screen thousands of potentially promising compounds.

In short, the recent evolution of research strategies and heuristics in pharmaceutical R&D can be characterised by discerning between two main, coexisting search regimes. The first regime is based on biological hypotheses and molecules that tend to be specific to given fields of application (specialised technologies), while

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<sup>32</sup> See Orsenigo, Pammolli, Riccaboni, 1998 and 2000.

<sup>33</sup> See Helpman, 1998.

the second regime is characterised by the emergence of new generic tools (general purpose technologies).

In the case of specialised research hypotheses and molecules, the characterisation of biological targets and the corresponding design/experimentation of each new drug tends to require individual analysis. Lessons learned from the design and experimentation of one biological hypothesis/molecule cannot be immediately transferred to other biological domains, in order to develop other classes of drugs. Conversely, general purpose technologies are in principle applicable to multiple biological targets and diseases.

As for this Report, it is important to say that the two regimes are characterised by different investment and risk profiles. In particular, firms specialised in general-purpose research technologies have access to a larger market, both in terms of areas of application and partnering institutions. At the same time, they act in market segments that have significantly lower short-term risks, R&D costs, and capital requirements compared with those existing for integrated, product oriented, firms<sup>34</sup>. Aggregate data for the three major research technologies of combinatorial chemistry, genomics, and high throughput screening are presented in Figures 5 and 6. While the American dominance seems to be indisputable, in the last years European companies from the UK and, later on, from Germany, have entered the industry. In particular, German firms that have entered the industry have been moving away from the fully-integrated, expensive, and risky model of the first generation' NBFs. Instead, they have focussed on the development of business models based around the provision of technology services and intermediate outputs.

While these evidences could reveal a basis for a certain degree of technological specialisation of European start-ups in markets for technologies, the new drug

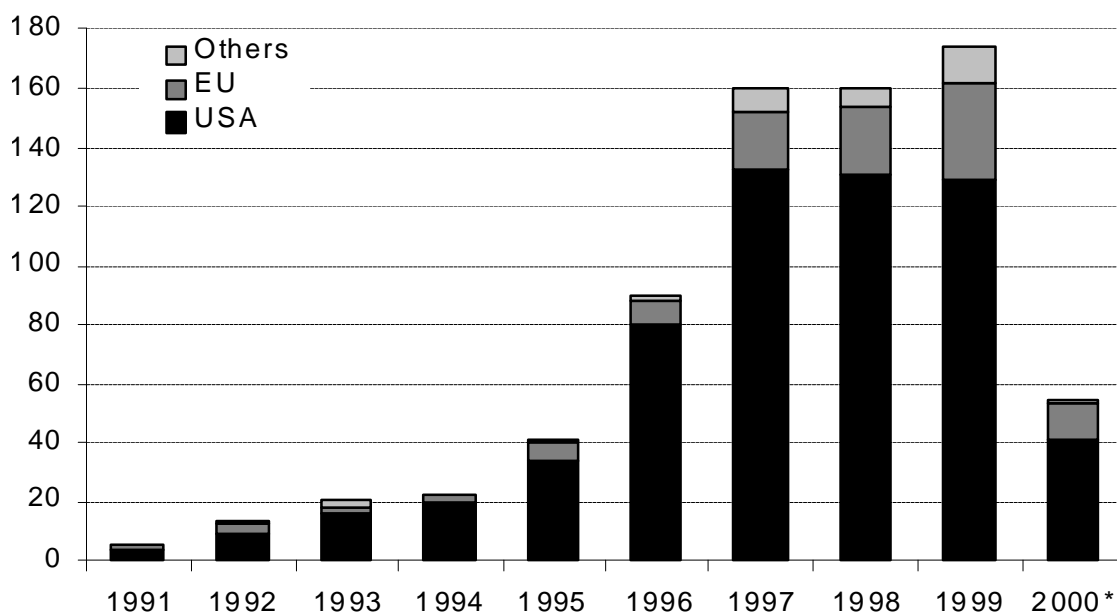
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<sup>34</sup> See Casper, Kettler, 2000.



discovery GPTs can quickly become commodities, with increasing levels of substitution and price competition<sup>35</sup>. For this reason, in order to evaluate the sustainability of any strategy of specialisation in the new GPTs, it is important to notice that “to grow, platform technology firms must move relatively quickly into new technologies or towards discovering their own targets for development using patented technology”<sup>36</sup>.

**Figure 5:**  
**Agreements in General Purpose Research Technologies**  
**(Combinatorial Chemistry, Genomics, Highthroughput Screening)**

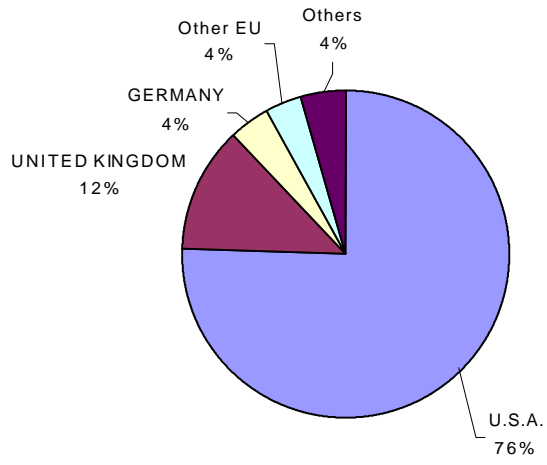


Source: PHID, University of Siena  
 \*First five months.

<sup>35</sup> See Arora, Fosfuri, Gambardella, 2000.

<sup>36</sup> See Casper, Kettler, 2000, p. 34.

**Figure 6:**  
**Agreements in General Purpose Research Technologies, Shares 1991-2000\***



Source: PHID, University of Siena  
\*First five months.

## V. The Role of Competition

Apart from leading drug multinationals, and some new biotech or technology-based companies, Europe fares a large number of low R&D intensive, “national”, small pharmaceutical companies. These operate exclusively in their protected domestic markets, and are characterised by low R&D and capital intensity, and poor innovative capabilities.

The presence of these firms suggests that patterns of competition in many European countries do not provide either a strong “carrot” or a strong “stick” (or neither), favouring the adoption of innovation- and international-oriented companies’ strategies. On the contrary, European regulated and fragmented environments allow for the survival of these producers.

It is well known that patterns of competition and firms behaviour in pharmaceuticals are influenced by institutional variables, like the structure of health care systems, price and product approval regulations, and legislation on property rights. How do these variables influence innovation and welfare is a difficult and controversial issue. The literature, however, seems to converge in arguing that competitive mechanisms associated with stringent regulatory environments for the approval of new drugs and competitive dynamics on the final markets tend to promote innovation in the pharmaceutical industry<sup>37</sup>.

On this, it is important to notice that the significant role of the EU notwithstanding, healthcare provision and legislation in Europe is the responsibility of individual member States. European national healthcare systems are hugely diversified in terms of the way they are organised and financed, ranging from national health schemes funded out of general taxes (the UK-Italy-Spain model), to mandated personal insurance with pluralist providers (the Germany-France-Netherlands

model). While “these variations reflect the different social values, ethics, and levels of wealth across Europe”<sup>38</sup>, they constitute an impediment to the creation of a unified European market, with all its implied consequences – economies of scale, higher competition, etc. Moreover, they are likely to contribute to generate inconsistencies, inefficient uses of resources, uneven standards of medical care, and distortions in the functioning of markets.

This Report does not review neither the specific barriers to integration that are still in place, nor the extensive EU legislation aimed at creating a single market in pharmaceuticals, with special reference to areas such as patent protection, biotechnology inventions, industrial manufacturing, product testing, market authorisations, labeling and advertising.

Instead, based on specific empirical evidences, the Report focuses on some issues that are directly relevant for industrial competitiveness, seeking to identify a set of criteria against which the definition of specific measures by member States can be judged.

Given our interest on the low R&D intensive segment of the market, some features of the off-patent segment (more than 50 % of the market) have been addressed, by means of an extensive comparative analysis of industry structure and, moreover, the nature and intensity of competition preceding and following patent expiry. Five major markets, characterised by strong differences in terms of regulatory regimes and generic products penetration, were selected (USA, UK, France, Germany, Italy)<sup>39</sup>.

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<sup>37</sup> See Thomas, 1994; Danzon, 1996; Helms, 1996.

<sup>38</sup> EUI, 1999, p. 46.

<sup>39</sup> See Pammolli, Magazzini, Riccaboni, 2000.

The most important chemical entities whose patents expired from 1986 through 1997 have been selected, coming to a sample of more than 60 molecules per country (with the exception of Italy, for which only 20 molecules of known dates of patent expiry were available). A broad concept of market competition would involve the chemical entity and the market composed of therapeutic alternatives. For this Report a narrower context, the chemical entity market, is used because an Original drug directly competes with Multiple Source Drugs (MSDs) within a given chemical entity market<sup>40</sup>. In fact, the relevant data set includes information on all Original and Multiple Source drugs in a selected chemical entity, permitting inclusion of all drugs within a chemical entity (generic name)<sup>41</sup>.

Table 23 and Figures 7, 8, and 9 present some descriptive results of the analysis. While we not focus here on price comparisons across countries<sup>42</sup>, some relevant results for the analysis of patterns of industrial competitiveness can be outlined:

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<sup>40</sup> When substitution laws allow pharmacists to substitute multiple source drugs for the Original, substitution in the retail setting usually occurs within the same chemical entity, rather than among therapeutic alternatives. In addition, multiple source competition is primarily targeted at the Original rather than the therapeutic market. Therefore, effects of substitution among chemical entities within the broader therapeutically equivalent market are not taken into account. Price differentiation of one dosage form versus another for a specific product is not examined. Data are aggregated across all strengths, dosage forms, and packing sizes for all variables of each drug. Specific data for each manufacturer's sales in US dollars and number of units sold are pulled for each drug, strength, and dosage form.

<sup>41</sup> Data sources for the study include: the IMS Pharmacy and Hospital databases, information on patent expirations, and a self-administrated questionnaire used to collect primary data on drug entity characteristics. For the IMS International data sets, data for each manufacturer's sales in local currency, US dollars and number of units sold in five major countries (USA, UK, Germany, France, and Italy) were extracted. The data set includes quarterly data from the first quarter of 1986 through the fourth quarter of 1998.

<sup>42</sup> See Danzon, 1996.

- a) There are strong differences across countries in terms of extent of generic penetration (see Table 23) and intensity of competition after patent expiry. Systems that rely on free or semi-free prices and on competition-based mechanisms (USA and, since the exclusion of patented drugs from the reference pricing system in 1996, Germany; UK) do experience a significant degree of competition and mobility of market shares after patent expiry. On the contrary, systems that rely on price fixing (Italy, France) experience a significant degree of stability in firms market shares over time, irrespectively of patent expiry (See Figure 7).
- b) As it is shown by the boxplots representing the median (black bar) and the dispersion of price indexes relative to products based on any given molecule in the 24 quarters that follow patent expiry (see Figure 8), systems that rely more on competition are characterized by the introduction of low-price products. On the contrary, systems that rely on administered prices are unable to replicate the performance of private markets in the introduction of appropriate selective mechanisms and pressures on price levels. In fact, both a significant stability of prices over time and a lower variance of prices for products based on a given molecule at given points in time are observed.
- c) As it is shown in Figure 9, systems that rely on competition promote a clear distinction between firms that act as innovators and firms that act as imitators after patent expiry. To put it in a nutshell, Original products can enjoy premium prices and exclusivity profits under patent protection, and face fierce price competition after patent expiry. On the contrary, systems that rely on administered prices nurture strategies of pre-emptive brand proliferation and horizontal differentiation by imitative brand name products well before patent expiry (as an extreme case, see the data on the Italian market in Figure 9).

All in all, these findings give support to the view that, irrespectively of any difference in terms of existing financial sources and organisational solutions, the European environment should be characterised by a larger diffusion of innovative

management methods<sup>43</sup>, and by higher levels of market-based competition, to begin with, in the off-patent segment of the market.

As for industrial policy and competitiveness issues, an increased market competition in the off-patent segment of the market can contribute to foster efficiency and to design adequate incentives to innovate within the European environment, promoting patterns of industrial restructuring and selection and, moreover, allowing higher prices and returns on investment for innovative products that are still on patent<sup>44</sup>.

Incidentally, a stronger reliance on competition mechanisms would induce a restructuring of vertical relationships within distribution channels, targeting drug distribution costs as an important area for productivity gains. In many European countries, distribution margins for wholesalers and pharmacists are still fixed by law, in general as a fraction of the final price. A higher reliance on competition-based mechanisms and regulatory strategies could enable the introduction of a higher degree of competition within distribution systems. In particular, together with a higher reliance on negotiation procedures targeted to wholesalers and pharmacists, the diffusion of cost-effective ways of dispensing drugs could be encouraged, relying on mail-order pharmacies and on the potential gains in productivity that are associated with the new Information and Communication Technologies (ICTs).

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<sup>43</sup> See GAO, 2000.

<sup>44</sup> See also Jacobzone, 2000.

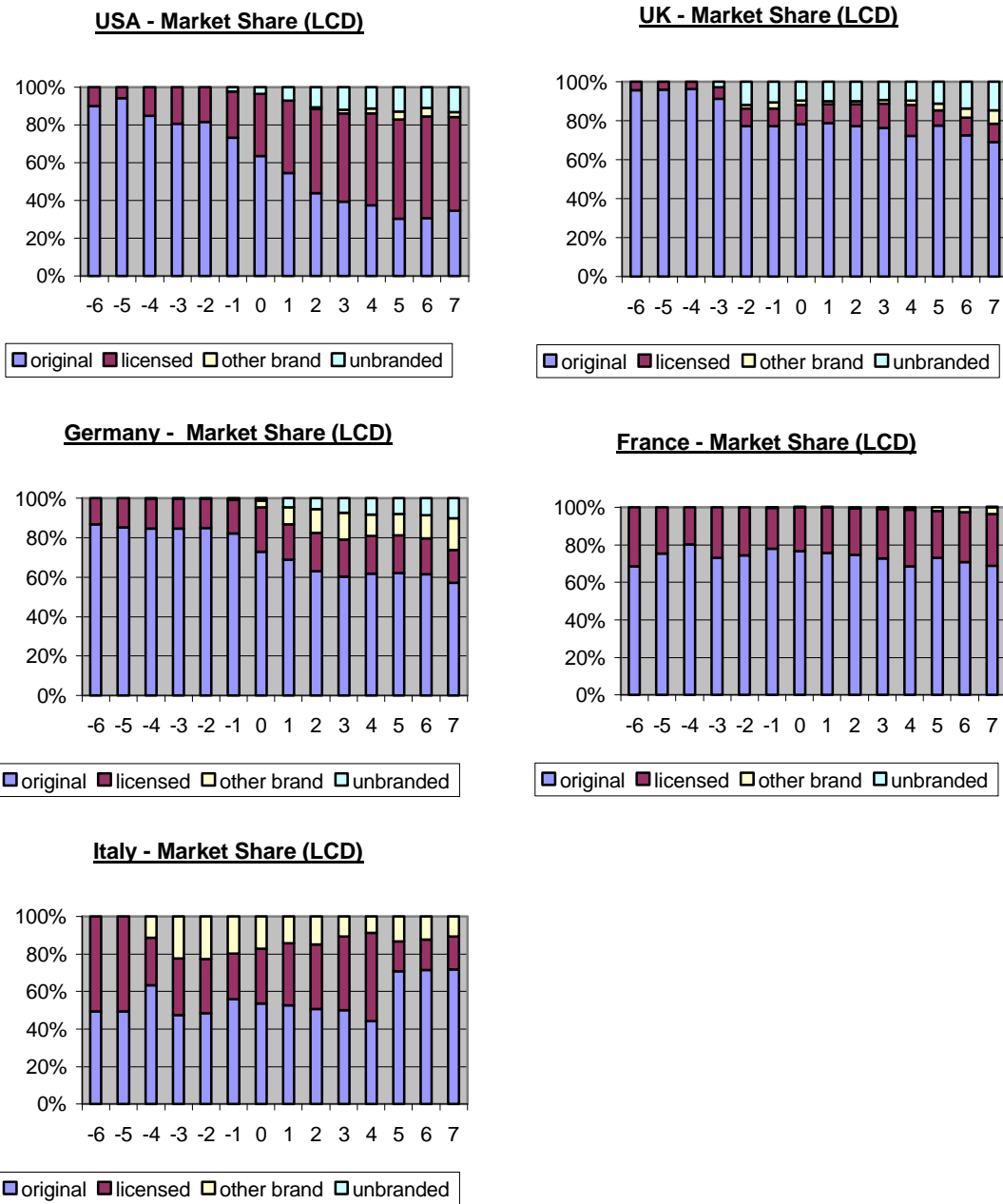
**Table 23:**  
**Shares of National Markets, by Segments (Local Currencies)**

UK	1995	%	1996	%	1997	%	1998	%	1999	%
Total	3079925	100.0	3418347	100.0	3717642	100.0	4020721	100.0	4393304	100.0
Original Brands	2054281	66.7	2244111	65.6	2354743	63.3	2479768	61.7	2710701	61.7
Licensed Brands	295382	9.6	352663	10.3	443882	11.9	543888	13.5	637844	14.5
Patent NA	224990	7.3	234525	6.9	242357	6.5	243468	6.1	254009	5.8
Unbranded	505273	16.4	587048	17.2	676660	18.2	753597	18.7	790751	18.0
Germany										
Total	16153087	100.0	17303736	100.0	17373555	100.0	18715431	100.0	20700206	100.0
Original Brands	6616472	41.0	7115339	41.1	7345085	42.3	8247688	44.1	9370111	45.3
Licensed Brands	2521735	15.6	2792930	16.1	2822032	16.2	3093478	16.5	3475739	16.8
Patent NA	3059322	18.9	3201668	18.5	3082150	17.7	3164577	16.9	3243271	15.7
Unbranded	3955558	24.5	4193800	24.2	4124288	23.7	4209689	22.5	4611084	22.3
France										
Total	54116334	100.0	56464471	100.0	59441833	100.0	63165381	100.0	66307342	100.0
Original Brands	30946406	57.2	31833518	56.4	32922120	55.4	35489372	56.2	37887996	57.1
Licensed Brands	10521138	19.4	11596251	20.5	12812585	21.6	13695996	21.7	14338627	21.6
Patent NA	9007638	16.6	9129428	16.2	9325357	15.7	9297699	14.7	9137431	13.8
Unbranded	3641153	6.7	3905274	6.9	4381770	7.4	4682315	7.4	4943288	7.5
Italy										
Total	9458883	100.0	10467499	100.0	11344110	100.0	12224672	100.0	13539132	100.0
Original Brands	4503552	47.6	5018454	47.9	5470191	48.2	5850940	47.9	6566792	48.5
Licensed Brands	2627876	27.8	2859136	27.3	3155605	27.8	3507939	28.7	3934993	29.1
Other Brands	1287527	13.6	1485288	14.2	1603394	14.1	1717773	14.1	1883483	13.9
Patent NA	985623	10.4	1044362	10.0	1042953	9.2	1069730	8.8	1070524	7.9
Unbranded	54304	0.6	60259	0.6	71966	0.6	78291	0.6	83340	0.6

Source: IMS International



**Figure 7:  
Market Shares after Patent Expiry, Selected Countries**

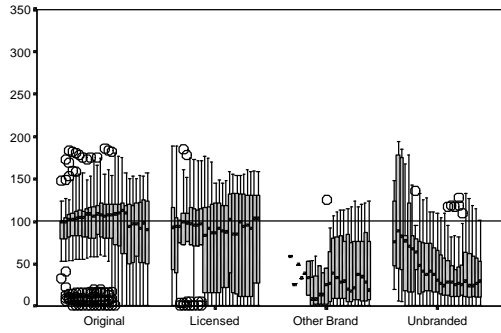


Source: Pammolli, Magazzini, Riccaboni, 2000

**Figure 8:**  
**Price Indexes after Patent Expiry, Selected Countries**

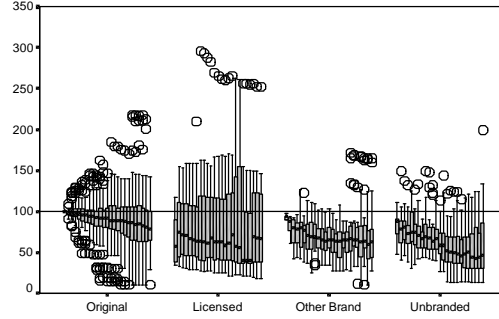
USA: price indexes

based on Original price at time 0



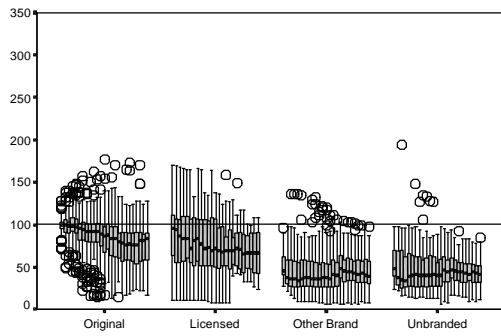
UK: price indexes

based on Original price at time 0



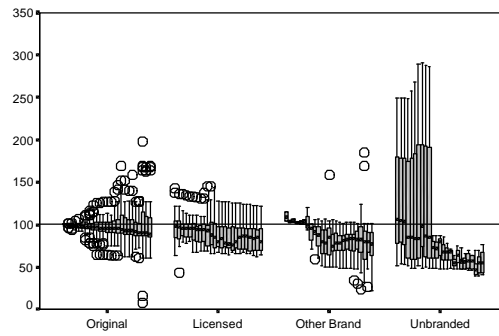
Germany: price indexes

base on Original price at time 0



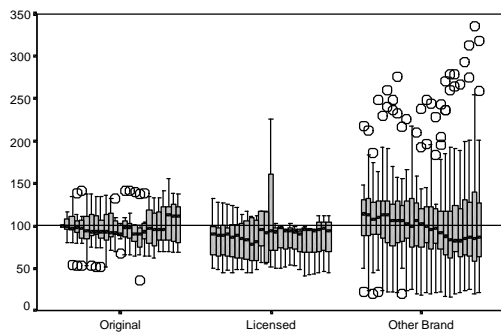
France: price indexes

based on Original price at time 0

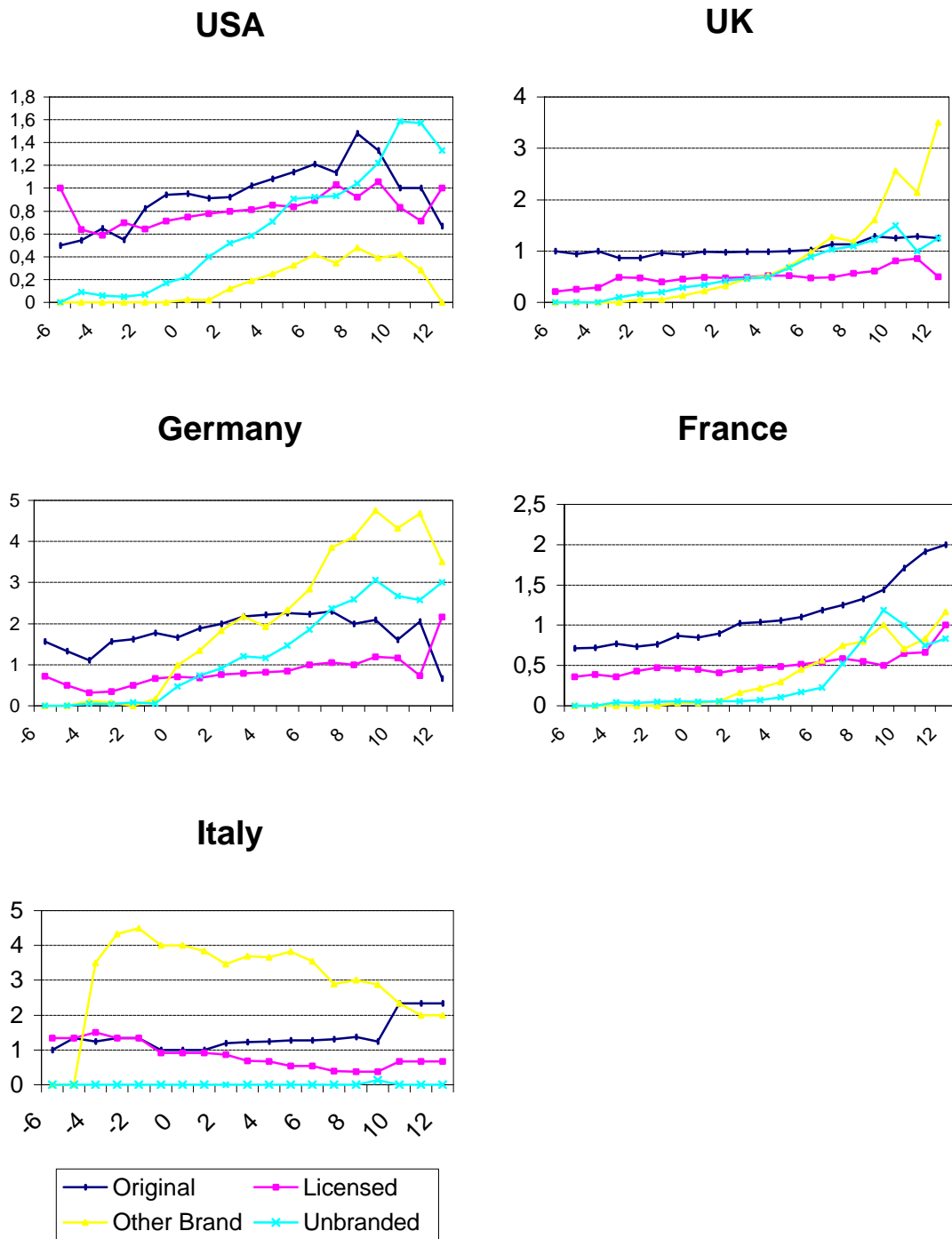


Italy: price indexes

based on Original price at time 0



**Figure 9:  
Number of Products per Molecule, Selected Countries**



Source: Pammolli, Magazzini, Riccaboni, 2000

## **VI. Institutional Determinants of Industrial Competitiveness**

The evidences discussed so far show, among other things, that North America has become the main locus of innovation in pharmaceuticals, to which European companies turn to get knowledge. This may have different implications, and one may even suggest different readings of this phenomenon.

For example, it could be argued that the situation is indeed worrisome, in spite of the fact that the competitiveness of the European industry in sales has not worsened as much as its competitiveness in innovation. Advocates of this view could argue that it's only because of the time needed to bring new drugs to the final market that Europe's competitiveness has not deteriorated severely over the past decade. In fact, the analysis of the dynamics on the R&D side reveals that the gap with the US is becoming large, especially in biotechnology and in the most innovative, globalised, profitable, and best selling drugs, i.e. at the frontier of innovation.

By contrast, one could argue that the problem may be not so severe for the larger European companies, as long as the more internationalised European drug companies succeed in tapping the US knowledge and get into the sources of new products and technological competencies overseas.

In any case, as suggested by our earlier discussion on this point, the problem is severe for the competitiveness of the European environment as a whole.

In particular, the observed concentration of research and innovation in the USA is worrying because Europe risks to be relegated into the fringe of the industry, surviving and even thriving through imitation, generics, marketing, but giving up a large share of the value added and becoming dependent on the USA for the development of new products.

Most notably, the inability to develop an industry of technology specialists, coupled with the persistence of a fringe of national firms which – especially in some European countries – are not innovative and protected from competition, can

ultimately give rise to a system which may lose significant opportunities for growth as well as for promoting qualified, research-based employment.

As always in the case of sectoral and national systems of innovation<sup>45</sup>, several factors have interacted to produce trends like the ones we are assessing here, and these factors have acted at different levels. Thus, especially if one examines these issues in terms of long run trends and perspectives, one cannot underestimate the role of structural policies in education, science and technology, regulation, labour, patent law, taxation; the institutional settings, in terms of legal and financial institutions, professional bodies, intermediating institutions, corporate governance rules; the industry; companies within the industry.

According to this Report, four sets of variables are particularly relevant in the specific context of the pharmaceutical industry: 1) The size and structure of the biomedical education and research systems; 2) Some basic institutions governing labour markets for skilled researchers and managers, as well as corporate governance and finance; 3) Intellectual property rights and patent law; 4) The nature and intensity of competition on the final market. In the sections that follow we shall analyse each of these issues in turn.

## **VI.1 Education and Research in Biomedical Innovation Systems**

There is little question that the sheer amount of resources devoted to biomedical research in the USA in the post-war era goes a long way to explain the American leadership in life sciences.

Both qualitative and quantitative evidence suggests that this spending has had a significant effect on the productivity of those large US firms that were able to take

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<sup>45</sup> See Nelson, 1993, 1996; Mowery, Rosenberg, 1993; Zysman, 1994; Mowery, 1997; Pavitt, 1998; Dosi, 1999;

advantage of it<sup>46</sup>. Public funding of biomedical research also increased dramatically in Europe in the post-war period, but total spending did not even approach American levels. As a consequence, and despite the existence of centres of absolute excellence, the overall quantity and quality of scientific research lagged behind in Europe. In turn, this created a vicious circle, with a significant drain of human and financial resources from Europe to the USA, which has contributed to further strengthen the American advantage.

Jointly with the levels of funding, other factors are likely to have played an important role. In fact, the institutional structure of biomedical research evolved quite differently in Continental Europe as opposed to the USA (and partly to the UK). First, the structure of the funding system and the strategies of the funding agencies are crucially important. In the USA, most of the funding is administered through the NIH, with: a) a substantial integration between the production of biological knowledge on the nature and mechanisms of human diseases, clinical research, medical practice, and the discovery and development of new therapeutic treatments; b) a significant support towards basic or fundamental science in universities and public research centres, widely disseminated through publication in the refereed literature. Moreover, the American system is characterised by a variety of sources of funding and selection mechanisms, which complement the role of the NIH and act – always starting from scientific excellence – according to different allocative principles<sup>47</sup>. All in all, the US research system achieves efficiency through competition among research units. At the same time, it allows diversity to be explored and institutional flexibility to be achieved.

In Europe, funding has tended to be administered mainly at the national level, with strongly differentiated approaches and wide differences across countries. This is

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<sup>46</sup> See Ward, Dranove, 1995; Cockburn, Henderson, 1996.

<sup>47</sup> See Braun, 1994; Mowery, 1998; Stokes, 1997, and Guston in Branscomb, Keller, 1998.

likely to have hindered the development of a critical mass, especially in smaller countries. In many cases, resources have either been spread among a large number of “small” laboratories, or they have been excessively concentrated in the few available centres of excellence. Funding coming from the various European programmes has only partially changed the situation<sup>48</sup>. The absolute size and the higher degree of integration of the American research system, as opposed to the fragmented collection of national systems in Europe constitutes a fundamental difference.

Moreover, biomedical research in Europe has been less integrated with teaching. At the same time, within medical schools in Continental Europe, medical research has had a somewhat marginal role as compared to patient care, inducing a hiatus between clinical practice and training in molecular biology .

The relevance of the research-teaching nexus in favouring high quality scientific research and its integration with industrial research can hardly be underrated. In particular, the diffusion of molecular biology into general training in many European countries is a relatively recent phenomenon as compared to the USA and it has only recently become a standard part of the curriculum of pharmacologists, pathologists and medical consultants. Research has tended to be confined into highly specialised laboratories in universities and especially in public research centres, with little interaction with teaching, medical practice, and industrial research.

Also for these reasons, large European companies have been in general more sluggish in adopting molecular biology as compared to their American competitors. Particularly, the European firms have remained for a longer time more closely linked to the cognitive and organisational procedures that governed research when chemistry constituted the main knowledge base.

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<sup>48</sup> Pavitt, 1998.

This has produced a vicious circle that has made the entry of the new biotechnology companies more difficult. In the first place, there is evidence showing that rates of formation of new start-ups are strongly correlated with the strength of University and public research institutes in the underlying sciences<sup>49</sup>. Moreover, given the delay in the adoption of molecular biology by the large companies in Europe, new prospective start-ups lacked an essential source of survival and growth, through the establishment of collaborative agreements. In the absence of such competencies, the large European companies turned to the American scientific and technological base to tap and absorb the new requisite competencies during their catching-up process. Indeed, the evidence produced in this Report, as well as several studies, show that large European multinationals have tended to establish agreements with research centres and biotech companies in the USA rather than in Europe<sup>50</sup>. Finally, given the fast rates of progress of the scientific and technical knowledge, European start-ups would be often pre-empted by American companies.

In sum, the organisational structure and the internal institutional diversity of the public research system in the USA has promoted (both in terms of incentives and in terms of organisational capabilities) the commercial exploitation of academic research, mainly through the formation of new, specialised companies. The flexibility of the American academic system, the high mobility of the scientific labour market and, in general, the social, institutional and legal context that made it relatively straightforward for leading academic scientists to become involved with commercial firms, have been major factors in the development of the new industry<sup>51</sup>.

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<sup>49</sup> See Zucker, Darby, Brewer, 1997

<sup>50</sup> See Orsenigo, Pammolli, Riccaboni, 2000.

<sup>51</sup> See Powell et al., 1996.



The willingness to exploit the results of academic research commercially also distinguishes the US environment from Europe. This willingness has been strengthened since the late 1970s and the passage of the Bayh-Dole Act, and the resulting role of universities as seedbeds of entrepreneurship has also been extremely important in the take-off the biotechnology industry<sup>52</sup>.

In contrast, links between the academy and industry – particularly the ability to freely exchange personnel – have been weaker in Europe. Indeed, the efforts of several European governments were targeted to the strengthening of industry-University collaboration. Thus, one observes a mushrooming of initiatives all across Europe aiming at establishing stronger links between industry and universities and to encourage a more entrepreneurial attitude by universities, rather than the mobility of personnel or the ease for university researchers to establish or participate in companies.

At the same time, policies have been targeted mainly to the set-up of specific organisational devices to manage technology transfer, like science and technology parks or other agencies for technology transfer. These initiatives have taken a wide variety of forms and show a mixed record in their performance and it has been only in very recent times that symptoms of the diffusion of a different attitude have emerged. In some cases, the presence of intermediary institutions has paradoxically increased the distance between University and industry, introducing an additional layer in the relationship instead of creating flexible mechanisms that are not burdened by all sorts of bureaucratic structures and requirements.

The US experience would then suggest that a flexible environment whereby academic researchers can more easily move into the development of companies is more conducive to the raise of new research-based firms and to the corresponding technology-based industry. Yet, the US system is not immune from an important

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<sup>52</sup> See Mowery, 1998.

shortcoming. As Paul David and Partha Dasgupta have argued, this system can seriously undermine the norms and rules of “open science”<sup>53</sup> The latter implies that the scientific community – unlike the community of profit-seeking technologists that operate in firms – diffuse their discoveries through publications and the like. The system of open science has for many years been an important determinant of the diffusion of knowledge in industry, and therefore ultimately of industrial growth. As the academic system turns to become far more secretive than in the past, this virtuous circle can be severely hampered. In the US life sciences and biotechnology industry, the “privatisation” of knowledge has already become a serious issue.

The desirable situation is probably an intermediate one between the US and European system. To identify the specific features of an institutional mechanism that would enjoy the advantages of both systems, while minimising their penalties, is an issue that is beyond the scope of this Report. Our goal here is to point out that while the US system can have interesting implications for the growth of a technology-based industry, the European system is more likely to be able to preserve the norms of openness in scientific research which would then nurture the very same technology activities that can give rise to the growth of industries and firms. Yet, we also note that while the US should take in serious consideration the contamination of academic norms, which can be produced by an excessive reliance on exclusive licensing agreements between universities and firms, Europe should care about the excessive ties, bureaucracy, and hierarchies of its scientific institutions, both at the national and the European levels.

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<sup>53</sup> See Dasgupta, David, 1994.

## **VI.2 Financial Markets, Corporate Governance, and Labour Markets for Skilled Researchers and Managers.**

It is often mentioned that the take-off of biotechnology – and more generally – of pharmaceuticals in the US, both through the large established corporations and the new biotechnology firms (NBFs), owes much to some specific institutions and attitudes that are typical of the American environment and much less developed in Europe. These factors have to do with the structure of financial markets, corporate governance, and labour markets for skilled researchers and managers. The development of venture capital, for example, rests critically on the nature of ownership and contract law typical of the US, which can be used to create sophisticated legal structures used to support risky new ventures.

An important feature of the American institutional environment, which has favoured the development of NBFs and the fast restructuring of big pharmaceutical corporations, is the existence of an active labour market for scientists, technicians, and managerial experts within biotechnology. For example one firm fails or decided to shed competencies in one area, employees must be able to obtain similar employment without severe loss of salary or status. Top executives at start-up firms typically come from large pharmaceutical companies or University research laboratories. These often senior scientists/managers would hesitate in making the move to a start-up if the career risk of doing so were large.

Furthermore, innovation is dependent on the flow of knowledge between University labs, start-up research firms, and large pharmaceutical firms. While joint research projects, strategic alliances, and so forth, facilitate this exchange of knowledge, these “network externalities” are also supported by the rapid movement of scientists and technicians across firms. Thus, if the labour market did not support extensive lateral career mobility across firms, these network externalities would be difficult to sustain.

In Europe, the organisation of labour and company law, combined with the organisational strategies of most large companies, constrains the development of

US-style active labour markets, and make it harder for companies to “hire and fire” personnel or rapidly cut non-performing assets.

Moreover, though there is often some lateral movement across firms very early in a person’s career, the vast majority of European employees build their own careers within one firm. Correspondingly, the structure of decision-making, remuneration, and career-paths within firms differ fundamentally from common practice within the United States or United Kingdom. Career paths tend to be well specified, incremental, and based on rank hierarchies.

This structure of large company organisation works quite well in industries dependent on long-term investment strategies in relatively stable technologies, characterised by the diffusion of deep skills throughout the firm. In particular, it encourages the creation of tacit organisational knowledge throughout the firm that enhances flexibility. However, this system creates fundamental obstacles to the creation of high-risk technology start-up firms. The risk of a «jumping ship» from an established large company (or – though there is less research in this area – a prestigious University professorship) to a start-up firm is extremely high<sup>54</sup>

More generally, successful research in high-technology firms requires the recruitment of scientists with highly specialised knowledge<sup>55</sup>.

In the US, this problem is partially dealt with through a market-based system of financial institutions and through very strong financial incentives, typically stocks options. In Europe, this area is undergoing extensive change during the late 1990s, but during the 1980s the organisation of the European financial markets and property rights law made stock-based financial systems difficult to implement.

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<sup>54</sup> See Soskice, 1997; Casper, Kettler, 2000.

<sup>55</sup> Audretsch, Stephan, 1996; Powell et al., 1996; Zucker, Darby, Brewer, 1997.

It is commonly believed that lack of venture capital has restricted the start-up activity of biotechnology firms in Europe. There is little question that venture capital played a key role in facilitating the creation of NBFs and of a market for technology in the USA.

There are important institutional reasons why the venture capital market is so large in the US. First, very substantial private legal competencies exist and, due to the «enabling» nature of ownership and contract law, sophisticated legal structures can be used to support risky new ventures. These include the high-powered performance incentives for managers and scientists discussed above. Second, and probably most important, in the United States the ownership of firms is primarily financial in structure, and rooted in large capital markets (e.g. NASDAQ, NYSE). Conversely, in many European countries, the lack of developed capital markets for technology firms create important barriers for prospective venture capitalists.

The forms of corporate governance and the structure of labour and financial markets are therefore likely to have hindered the process of adaptation of the European industry to the technological and institutional shocks. However, direct empirical evidence on these issues is not massive. Moreover, the relevance of these factors might turn out to be somewhat exaggerated. In fact, the observed difference in performance among some European countries may have more to do with differences in institutional settings, drug price regulation mechanisms, the nature of the scientific system, and the like. This suggests that differences in the nature of corporate governance and in the structure of labour and financial markets may have been important but not decisive factors in shaping the patterns of adaptation.

Similarly, as far as venture capital is concerned, there appear to have been in Europe many other sources of funds (usually through government programs) available to prospective start-ups. In addition, although venture capital played a critical role in the founding of US biotechnology firms, collaborations between the new firms and the larger established corporations provided a potentially even more

important source of capital. This raises the question: could prospective European start-ups turn to established pharmaceutical firms as a source of capital?

As noted earlier, European large corporations have collaborated relatively more with US biotechnology firms. Even in the absence of other institutional barriers to entrepreneurial ventures, start-ups in Europe might have been crowded out by the large number of US based firms anxious to trade non-US marketing rights for capital. Given the number of US NBFs in search of capital, European firms interested in commercialising biotechnology had little incentive to invest in local biotechnology firms.

As a partial support to this interpretation, in several European countries various initiatives by both domestic and foreign investors to launch venture capital funds were attempted in the Nineties, with mixed success so far and often ending up investing in new foreign biotechnology companies. Conversely, foreign venture capital firms have funded some of the few experiences of successful European NBFs.

All in all, the slow development of venture capital in Europe seems to depend less on the lack of investors and funds than on the paucity of supply of promising start-ups based on solid scientific research.

### **VI.3 Protection of Intellectual Property Rights**

It is widely acknowledged that patents are a fundamental incentive to innovative activities in pharmaceuticals and biotechnology<sup>56</sup>.

Both the U.S and the majority of the European countries have provided relatively strong patent protection in pharmaceuticals. In contrast, in Japan and in Italy, until (respectively) 1976 and 1978, patent law did not offer protection for pharmaceutical products: only process technologies could be patented. As a result,

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<sup>56</sup> Mansfield, 1998; McMillan, Narin, Deeds, 2000;

Japanese and Italian (as well as Spanish) firms have tended to avoid product R&D and to concentrate instead on finding novel processes for making existing molecules.

Similarly, the establishment of clearly defined property rights also played a major role in making possible the explosion of new biotechnology firms in the USA, since the new firms had few complementary assets that would have enabled them to appropriate returns from the new science in the absence of strong patent rights. In the USA, a tight appropriability regime in the biotechnology industry emerged quite quickly, for example through the Bayh-Dole Act in 1980 and through the granting of very broad claims on patents<sup>57</sup>. In Europe, the scope for broad claims on patents is greatly reduced and usually process rather than product patents are granted.

A draft directive from the Commission that strengthens the protection offered to biotechnology was recently approved by the European Parliament. Still, considerable controversy surrounds this issue. It is indeed worth stressing that too strong an appropriability regime may not be unambiguously beneficial, especially as it concerns publicly funded research. Increasingly, in the USA doubts are voiced by economists, lawyers and industry analysts that the diffusion of an excessively permissive attitude towards the granting of broad claims on patents might actually slow down the process of diffusion and circulation of knowledge and hence the future rate of technological advance. However, it is also important to notice that the rationale for stronger protection to intellectual property in biomedical research is not based, according to this Report, on the traditional argument that the concession of broad property rights is an incentive to the production of knowledge. Rather, the argument is based on the assumption that property rights would favour the creation of markets for technology and hence a faster and more ordered diffusion and use of

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<sup>57</sup> Merges, Nelson, 1994.

knowledge<sup>58</sup>. This argument is however controversial and complex, and cannot be simply accepted at face value in general. Particularly, as we noted earlier, the increasing privatization of scientific knowledge is a problem of the US research system<sup>59</sup>.

#### **VI.4 Degrees and Forms of Competition on the Final Market**

Since regulation and public intervention in pharmaceuticals pursue multiple goals, which relate to both health and industrial policy, the history of the market regulatory regimes is characterized by a set of highly differentiated trajectories and patterns.

Before the “managed care” revolution, in the US pharmaceutical companies’ returns from product innovation were protected by the low bargaining power of buyers. Moreover, unlike most European countries (with the exception of Germany and the Netherlands) and Japan, drug prices in the US have been unregulated by government intervention.

Until the mid-1980s the overwhelming majority of drugs were marketed directly to physicians, who largely made the key purchasing decisions by deciding which drug to prescribe. Both the payers and the ultimate customers – patients – had little bargaining power, even in those instances where multiple drugs were available for the same condition. Because insurance companies generally did not cover prescription drugs (in 1960, only 4% of prescription drug expenditures were funded by third-party payers), they did not provide a major source of pricing leverage. Pharmaceutical companies were afforded a relatively high degree of pricing flexibility. This pricing flexibility, in turn, contributed to the profitability of investments in drug R&D.

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<sup>58</sup> See Arora, Fosfuri, Gambardella, 2000.

<sup>59</sup> See Merges, Nelson, 1994; Eisenberg, 1996; Mowery, 1998.



When the rising costs of prescription drugs benefits have driven employers, insurers, and managed care plans to adopt new measures of cost containment<sup>60</sup>, a differentiated set of techniques has been developed by the new buyers groups (HMOs, PBMs, insurance companies), which relies extensively on private funds and market-based techniques, allowing processes of corporate adaptation and restructuring in marketing and distribution channels and, moreover, stimulating competition and, indirectly, incentivating innovation.

Historically, drug prices were also relatively high in other countries that did not have strong government intervention in prices, such as Germany and the Netherlands. In the UK, price regulation was framed as voluntary co-operation between the pharmaceutical industry and the Ministry of Health, under the Pharmaceutical Price Regulation Scheme (PPRS). This scheme left companies to set their own prices, but a global profit margin with each firm was negotiated, which was designed to assure each of them an appropriate rate of return on capital investment including research, in the UK. The allowed rate of rate return was negotiated directly and was set higher for export oriented firms. In general, this scheme tended to favour both British and foreign R&D intensive companies, which operated directly in the UK. Conversely, it tended to penalise weak, imitative firms as well as those foreign competitors (primarily, the Germans) trying to enter the British market without direct innovative effort in loco<sup>61</sup>. In Japan, the Ministry of Health and Welfare used to set the prices of all drugs, using suggestions from the manufacturer based on the drug's efficacy and the prices of comparable products. Once fixed, however, the price was not been allowed to change over the life of the drug<sup>62</sup>. Thus, whereas in many competitive contexts prices began to fall as a

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<sup>60</sup> US Senate, 1993; GAO, 2000.

<sup>61</sup> Burstall, 1985, Thomas, 1994.

<sup>62</sup> Mitchell, Roehl and Slattery, 1995.

product matured, for a long time this was not the case in Japan. Given that manufacturing costs often fall with cumulative experience, old drugs thus probably offered the highest profit margins to many Japanese companies, further curtailing the incentive to introduce innovative drugs.

The procedures for the approval of drugs have also played an important role. For example, there is now widespread recognition that the introduction of the Kefauver- Harris Amendments in 1962 in the USA had a significant impact in inducing a deep transformation of the US pharmaceutical industry, particularly through raising the cost and complexity of R&D. Partly as a result many US firms were forced to upgrade their scientific capability. The adoption of tight scientific procedures in clinical trials might also have pushed to develop earlier and stronger relationships with the new emerging biomedical community. Similarly, Britain appears to have actively encouraged a "harsher" competitive environment. Since the early 1960s, the British system encouraged the entry of highly skilled foreign pharmaceutical firms and a stringent regulatory environment also facilitated a more rapid trend towards the adoption by British companies of institutional practices typical of the American and Swiss companies: in particular, product strategies based on high priced patented molecules, strong linkages with universities and aggressive marketing strategies focused on local doctors. The resulting change in the competitive environment in the home market induced British firms to pursue strategies aiming less to the fragmentation of innovative efforts into numerous minor products than to the concentration on few important products that could diffuse widely into the global market. By the 1970s, the ensuing transformations of British firms had led to their increasing expansion into the world markets<sup>63</sup>.

Conversely, the less successful performance of other national pharmaceutical industries (like Italy and Japan) reflects much weaker competitive pressures in domestic markets. In these countries, the combination of patent laws, policies

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<sup>63</sup> Thomas, 1994.

surrounding licensing and comarketing agreements, and drug pricing and reimbursement regimes, produced a “soft” regulatory regime whereby firms had little incentive to develop world-class product development capabilities, and in general they concentrated on finding novel processes for making existing foreign or domestically-originated molecules. Moreover, in these countries, firms were usually protected from foreign competition and simultaneously had strong incentives to license products that had been approved overseas. Under this regime the predominant technology strategy for pharmaceutical companies often became the identification of promising foreign products to license-in.

On this, it is important to say that in the recent years, under the pressure of increasing fiscal constraints, some European countries complemented their price fixing procedures with interventions on levels of reimbursement, delistings, price cuts. While, according to the available evidences, these measures have tended to realize, at best, short-term savings and, in any case, they have not affected rates of growth of expenditure on pharmaceuticals, these measures have introduced new distortions in the final markets<sup>64</sup>.

At the same time, in some European countries – albeit in different forms and speed – regulatory schemes have been changing towards an increasing reliance on market based mechanisms. This trend is important. However, firms’ strategic orientations and organisational attitudes change slowly and tend to persist for long periods of time. Equally, the development of competencies and innovative capabilities is a long, cumulative and difficult process that does not respond immediately and smoothly to economic incentives.

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<sup>64</sup> See Jacobzone, 2000.

## **VII. Conclusions**

### **VII.1. Summary of the main results and issues**

The main results of this Report can be summarized as follows.

- a) In the 1990s the European industry has grown less than the US industry. This stems from a deceleration of the growth of the industry in Europe, and an acceleration of the US industry growth. The restructuring of pharmaceutical demand, and particularly of the health care system, in the US, seems to have translated into demand growth, which has benefited mainly the US firms. Moreover, in the US (and Japan) the growth of the industry stems to a good extent from the growth of its non-labour inputs. By contrast, these inputs contribute modestly to the growth of the industry in Europe, whose growth is accounted for largely by the unexplained residuals – viz. by factors that are independent of the growth of the measurable inputs. Our analysis shows that, plausibly, the growth of the industry in Europe depends to a good extent on factors other than R&D, capital or labour. Not only is this saying that the growth of the industry in Europe is more “erratic” than in the US or Japan, but also that the growth in capital or R&D translates less markedly into sales growth. This is probably not independent of our earlier remarks about the larger presence in the European pharmaceutical sector of firms or activities which are less dependent on internal R&D and innovation, and more on external inputs such as licenses from international companies, pricing policies or peculiarities of the public health care systems or demand in individual European countries, etc.
- b) These trends take place within a context of marked globalisation of the pharmaceutical industry. Protection on local markets diminishes and penetration from foreign companies increases in each domestic market.

The shares of US, British, French and Danish largest corporate groups increases in all regions, whereas Germany and Italy lose ground. Market shares of domestic corporations fall everywhere in domestic markets;

- c) Our data indicate that the sales of major innovative products by the US multinationals have increased more significantly than those of the European multinationals in the 1990s. Moreover, European big corporations seem to lag somewhat behind in their ability to produce and above all sell, new, innovative, best selling drugs. However, when we look at the number of the top selling new chemical entities (NCE) developed by the European and US firms, we find that the difference is not as big as the difference in sales. This might indicate that the European firms are facing a comparative disadvantage in selling their new drugs. All in all, the observed differences in sales growth between European and US largest multinationals during the Nineties do not seem to depend only on differences in the ability to develop new breakthrough drugs, but also on the observed difference in demand growth between the two areas.
- d) Data confirm that the 1990s have shown an acceleration of the competitiveness of the US pharmaceutical industry as a whole in the innovation-intensive segment of the industry. First, the leading US firms have a higher share of turnover based on recent products compared to the European firms. Second, the US: i) have a higher share of patents in the new biotech fields compared to “classical” pharmaceuticals; ii) are a preferred destination of research by the European companies as well. This latter point is important. It suggests that the leading European companies may reinforce the US advantage in biotech, as they nurture US rather than European scientific base and biotech companies. This is an indication of the existence of path-dependent effects, or first-mover advantages – i.e. biotech started in the US, and this may produce persisting advantages over time. Not only the Swiss and UK companies have in their portfolios a high

share of biotech patents invented in the US, but French and, to some extent, German, companies license in biotech patents generated in the US as well.

- e) The competitive advantage of the US companies in innovation relies both on higher internal capabilities and on a higher reliance on collaboration, especially in the pre-clinical stages of research and development. However, the US companies have: i) higher probability of success during phases I, II, and III of the clinical trials when the new compounds have been developed in-house; ii) a higher share of licensed compounds. Moreover, we found that: iii) the probability of success does not differ among US and European companies when the compounds are licensed. This finding suggests that the US exhibit a more pronounced division of labour in the drug innovation process between large companies on the one hand and small biotech/specialised firms as well as scientific institutions on the other.
- f) The US advantage and the emergence of a process of deteriorating competitiveness in Europe have been emphasised and deepened by the advent of the molecular biology revolution. The competitiveness of the US system seems to be largely related to the extensive exploration of new technological opportunities. In fact, one notable difference between Europe and the US in the 1990s is that while the US have become the centre of world basic research in life sciences and have continued the development of a new research-intensive industry in this field, Europe has been unable to develop and attract research and to complete the process of vertical specialisation in the most innovative areas of the drug sector. Particularly, Europe has not really given rise to a full fledged industry of innovation specialist companies and technology suppliers like in the US. In principle, the fact that Europe has been unable to give rise to a full fledged industry of technology suppliers is not a critical problem for the competitiveness of the firms operating in the final drug markets. We argued earlier that

competitiveness in sales may depend on different factors from competitiveness in innovation. Moreover, in a globalised industry such as this, companies may not need local technology suppliers, provided that the drug producers can tap the new technology sources in other markets. The question however is whether all the European drug companies can tap such international sources of technology. In addition, this Report shows that the presence of a local industry of research-based firms and technology suppliers is critical because the industry is by itself a powerful source of growth. Other factors appear to be linked to country-specific variables, primarily, the level of funding of fundamental scientific research and the structure of the biomedical research systems; the degree and the forms of competition on the market for drugs. Furthermore, other institutional factors are likely to have played an important role, even if here the evidence is less compelling: some basic institutions governing labour markets for skilled researchers and managers, company organisation and finance; the levels of patent protection;

- g) The above findings are consistent with other features of the European environment, linked to the “institutional shock” created by cost-containment policies in a context of fragmented institutions and rules. In particular, this Report shows that there is too little competition in some European countries and that this lack of competition tends to nurture inefficient positions within the industry. Price fixing mechanisms tend to protect local firms in domestic markets, allowing for the survival of infra-marginal companies in some European countries. These are highly labour intensive companies. What is important is not that they specialise in marketing. This might not be too serious a problem, if companies could take advantage of an effective division of labour with innovators located elsewhere - and possibly in Europe. On the contrary, local, marketing-specialised companies might even be able to exploit their specific knowledge of local markets as an important competitive asset. However, -

absent the implicit protection afforded by price regulation mechanisms- the benefits of such division of labour can only be reaped through much higher efficiency than it is shown by the vast majority of these companies, as data on productivity demonstrate. Moreover, if the declining trend of the share of marketing agreements vis-à-vis research agreements persists over time, many European companies might be relegated into the fringe of the world industry. In any case, a deteriorating innovative performance is likely to imply lower growth, lower welfare, and lower independence of European countries.

## **VII.2 Global Competitiveness in Pharmaceuticals. An Interpretative Framework**

To begin with, it is important to recognise that over the past decade significant progresses have been made both within individual countries and at the European level towards the introduction of stronger competition, the strengthening and the re-organisation of the research base, the creation of capital markets, etc..

Some large European corporations appear to have caught-up with their American competitors, also through strategies of external growth. In more recent years, an encouraging dynamism is observed in countries like Germany, France, the Netherlands, Sweden and Denmark, as the rate of creation of NBFs is concerned. These changes are not yet reflected in the data on competitiveness, but certainly represent a motive for optimism.

Moreover, the decline in European competitiveness in pharmaceuticals and biotechnology is not a homogeneous phenomenon, but it actually results from largely heterogeneous performances of individual firms and countries. To a considerable extent, the European problem derives from the deterioration of the German and Italian performance. Conversely, the cases of the UK, Denmark but also Sweden and Ireland, have to be considered as success stories.



This consideration is even more important, as soon as it is recognised that behind these different cases, there are extremely varied motivations and policies. For example, there is no doubt that the successes of France and Ireland derive from radically different approaches. Moreover, recent developments in German biotechnology would suggest that local institutional frameworks can be successfully modified and adapted to the requirements of the technological regimes, without changing their fundamental character.

Thus, a definite and too detailed policy prescription fitting all European countries might be misleading. However, the results of this report suggest some broad, but clear, policy implications:

#### *A. Upgrading basic scientific research*

First, to the extent that the decline of European competitiveness is linked to a deteriorating innovative performance, especially in the new, leading edge technologies, efforts should be primarily devoted to the strengthening of innovative capabilities. In turn, this implies a fundamental upgrading of basic scientific research.

The crucial importance of the availability of a strong research base can hardly be underrated, in that it is the basic pre-condition for strong technological competencies, industrial dynamism, and also for the efficacy of other policy initiatives aiming at inducing institutional and cultural changes. While it might be true that the European performance in science is comparatively better than the technological and industrial performance, still the gap with the USA is very large. Moreover, whilst the American research system (including Canada) is an integrated system, highly differentiated and pluralistic within a common framework, European science is composed of fragmented and relatively small national systems. Indeed, European research teams tend to collaborate comparatively more with US groups and there is little question that North America constitutes the main attractor of human and financial resources from all over the world, including Europe. Since the dynamics (and the economics and sociology) of scientific research is

characterised by strong path-dependent effects and first-mover advantages, success breeds further success and divergence tends to increase rather than decrease.

Strengthening the research base implies not only increased funding, but also introducing important changes in the organisation of research systems: for example and primarily:

- Realise a closer integration between teaching and research in biomedical sciences;
- Promote an integrated environment, in which a set of differentiated sources of funding, which act according to alternative allocative mechanisms and principles, and compete for supporting absolute scientific excellence;
- Realise the constitution – on these principles – of an integrated European – as opposed to a collection of small national or even sub-national – research system.

#### *B. Favouring the integration between scientific and industrial research*

The results of the report show also that Europe has been facing severe difficulties in exploiting scientific research for industrial purposes. On the one side, this and other complementary analyses<sup>65</sup> reveal that the American pharmaceutical industry was able to gain extraordinary benefits from its research base, because of the fluid nature of the boundary between public and private institutions in the field. As mentioned previously, the relative European weakness in pharmaceuticals, biotechnology, and biomedical sciences is likely to depend, primarily – on the smaller scale, the lower quality and the organisation of scientific research itself. These considerations notwithstanding, measures can be taken to improve the interaction between industry and basic research, both at the level of large corporations and through the creation of new science-based firms. As previously

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<sup>65</sup> Henderson, Orsenigo, Pisano, 1999; National Research Council, 2000.

mentioned in the report, this has been indeed the main focus of several policy actions taken by governments and local authority throughout Europe. However, these policies have mainly aimed at building bridges between University and industry and to developing financial and infrastructural facilities like venture capital, science parks, etc. In practice, these measures – important as they are – appear to reflect a conceptualisation of the innovative process based on some version of the so-called linear model and – as a consequence – to emphasise the aspect of the transfer of knowledge. Recognising the interactive nature of the processes of innovation in biomedical and pharmaceutical research<sup>66</sup>, more emphasis should be given instead to the problem of a more direct integration of different agents and fragments of knowledge. Thus, measures should be taken to favour the development of more direct linkages between universities and industry, through the integration of research and teaching and the development of markets for technology.

### *C. Strengthening industrial R&D*

Firms remain the main locus and engine of industrial innovation. Thus, strengthening their technological capabilities appears as a crucial priority for European competitiveness. The results of this report indicate that rather than an insufficient investment in R&D, European companies lag behind their American counterparts primarily in terms of their capabilities to organise research according to the principles dictated by the new technological regime. Moreover, the persistence of a large fringe of non-innovative companies, which survive in domestic markets through marketing based strategies and through implicit protection, still characterises many European countries.

Thus, European firms should improve their in-house research capabilities, also using in a much more systematic and efficient ways networks of collaborative

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<sup>66</sup> See Stokes, 1997; Galambos, Sturchio, 1998.

relations with universities and NBFs and the market for technology. A major result of the report is that division of labour could help in reducing the competitive differences due to different in-house capabilities. In other words, a division of innovative labour would enable drug companies which are behind the leading US ones in organisational capabilities, and innovation, to catch up. Similarly, the markets for technology and division of labour can support firms specialised in marketing, provided they are able to improve their efficiency. However, leadership in modern pharmaceutical R&D requires the development of adequate integrative capabilities, i.e. of competencies in co-ordinating decentralised research activities and in identifying and exploiting complementarities and economies of scope.

#### *D. Strengthening market-based competition within an integrated environment*

Besides the already mentioned problems related to insufficient connections with science, excessive diversification and delays in adopting the new organisational principles of pharmaceutical R&S, other factors contribute to explain why fewer European corporations have adapted successfully to the molecular biology revolution and why such process is taking place more slowly than in the USA. These factors have to do with the general principles of organisation of corporate governance, financial markets, markets for skilled labour.

More specifically, this Report shows that the decline of European competitiveness in pharmaceuticals is linked to the persistence of a fragmented market and, at the same time, to major “non-market” and bureaucratic failures in public intervention and price regulation attempting

In this respect, strengthening competition at the European level constitutes a fundamental pre-requisite for inducing more innovation-oriented strategies and higher efficiency of less innovative firms. On the one hand, strong levels of patent protection for the segment of the in-patent products should be guaranteed and enforced. On the other hand, National Health Authorities, should converge on a higher reliance on innovative management methods and on competitive mechanisms, moving away from schemes excessively based on administrative

decisions and bureaucratic structures/rules in the regulation of the market. The off patent segment of the market and the distribution system could constitute two important test-beds for such a deregulation pattern for pharmaceuticals.

Two general principles could help the achievement of a higher level of integration of the market. First, a higher variety of schemes and sources for the financing of healthcare and pharmaceuticals could be promoted in all European Countries. Second, Governments could fix reasonable levels of patients' copayment<sup>67</sup> through the introduction of schemes analogous to incentive-based, open formularies, so that competition on the final market can be stimulated in ways that fully preserve equity and, moreover, national health policy goals and solutions<sup>68</sup>.

At the end of this Section, it is important to notice that the movement towards a regulatory environment based on an integrated set of market-based mechanisms will become even more crucial with the accession of Central and Eastern European Countries (CEECs). In principle, the Enlargement to CEECs can contribute significantly to the competitiveness of the European Industry. In order for this goal to be realised, however, an integrated regulatory and competitive environment has to be quickly designed and implemented. In particular, in the absence of a higher reliance on market-based competitive mechanisms, the Enlargement could very easily lead to amplify the existing distortions. This is particularly true given the financial pressure that the new Member States will experience and the tensions that would necessarily emerge between cost containment issues and the principle of a free movement of goods<sup>69</sup>.

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<sup>67</sup> See Newhouse, 1993.

<sup>68</sup> See Jacobzone, 2000.

<sup>69</sup> Incidentally, it is important to notice that, given the fact that it is unprecedented in its scale and the relative starting position of the candidates vis à vis existing members, in the case of pharmaceuticals the Enlargement will certainly require some transitory measure, for example, in the form of a

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derogation to the principle of free movement of goods associated with a systems of rebates for patented drugs covered by each National Healthcare System.

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## More information on Enterprise DG

Additional useful information on the work of Commissioner Erkki Liikanen and the Enterprise Directorate-General is available through printed publications and on the web.

### **Commissioner Erkki Liikanen, responsible for Enterprise and the Information Society:**

[http://europa.eu.int/comm/commissioners/liikanen/index\\_en.htm](http://europa.eu.int/comm/commissioners/liikanen/index_en.htm)

### **Enterprise DG on the web:**

[http://europa.eu.int/comm/dgs/enterprise/index\\_en.htm](http://europa.eu.int/comm/dgs/enterprise/index_en.htm)

### **Enterprise DG work programme:**

[http://europa.eu.int/comm/dgs/enterprise/work\\_programme\\_2001.htm](http://europa.eu.int/comm/dgs/enterprise/work_programme_2001.htm)

### **Enterprise DG's printed publications:**

<http://europa.eu.int/comm/enterprise/library/index.htm>

**Enterprise Europe** is a free-of-charge newsletter published quarterly in the 11 Community languages by the Enterprise Directorate-General. It covers the whole range of Enterprise DG's work, announcing new initiatives as well as providing practical information.

<http://europa.eu.int/comm/enterprise/library/enterprise-europe/index.htm>

**CORDIS focus** is published twice a month in English, French, German, Italian and Spanish. It provides a review of the main developments in all aspects of European Union research and innovation activities, covering general policy developments, programme implementation, calls for tenders and results, events, legislative activities, and much more.

<http://www.cordis.lu/focus/en/src/focus.htm>

**Innovation & Technology Transfer** is published six times a year in English, French, German, Italian and Spanish by the European Commission's Innovation Programme, which aims to promote innovation at Community level and encourages SME participation under FP5. The emphasis is on timely news relevant to these objectives and in-depth 'case studies' of successful projects.

<http://www.cordis.lu/itt/itt-en/home.html>

**Euroabstracts** is published six times a year in English by the 'Innovation and SMEs' programme, part of the European Commission's Fifth Research Framework Programme. The Innovation and SMEs programme promotes innovation and encourages the participation of small and medium-sized enterprises (SMEs) in the Framework Programme.

<http://www.cordis.lu/euroabstracts/en/home.html>

**European Trend Chart on Innovation newsletter.** The Trend Chart project develops practical tools for innovation policy makers in Europe. It pursues the collection, regular updating and analysis of information on innovation policies at national and Community level. The newsletter is published quarterly in English, French and German. Further reports and studies are available on the web site <http://trendchart.cordis.lu/Reports/>

Reports, studies etc.

The Enterprise Directorate-General regularly publishes reports and studies on its various areas of activity. Here is a selection of recent publications.

**Global Competitiveness in Pharmaceuticals – A European Perspective. Enterprise Papers No 1, 2001.** Luxembourg (Eur-Op), 2001. 108 pages (EN). Catalogue No NB-37-01-162-EN-C

**Building an innovative economy in Europe.** Luxembourg (Eur-Op), 2001. 67 pages (EN). € 11.50. Catalogue No NB-NA-17-043-EN-C

**Innovation policy in a knowledge-based economy.** Luxembourg (Eur-Op), 2000. pages (EN). Catalogue No NB-NA-17-023-EN-C

**European innovative enterprises : lessons from successful applications of research results to dynamic markets.** Luxembourg (Eur-Op), 2000. pages (EN). Catalogue No NB-BA-17-024-EN-C

**Promoting innovation management techniques in Europe.** Luxembourg (Eur-Op), 2000. pages (EN). Catalogue No NB-NA-17-022-EN-C

**Getting more innovation from public research.** Luxembourg (Eur-Op), 2000. 99 pages (EN). Catalogue No NB-NA-17-026-EN-C

**Creating an entrepreneurial Europe. The activities of the European Union for small and medium-sized enterprises (SMEs) – 2000 edition.** Luxembourg (Eur-Op), 2001. 150 pages (available in all Community languages). Catalogue No NB-27-00-992-\*\*-C

**The intangible economy: impact and policy issues.** Luxembourg (Eur-Op), 2001. 59 pages (EN). € 20. Catalogue No NB-31-00-772-EN-C

**The European observatory for SMEs - Sixth Report.** Luxembourg (Eur-Op), 2000. 432 pages (DE, EN, FR) € 53. Catalogue No CT-22-99-200-\*\*-C

**The European observatory for SMEs - Sixth Report. Summary.** Luxembourg (Eur-Op), 2000. 22 pages (available in all Community languages). Catalogue No CT-22-99-208\*\*\*-C

**European competitiveness report 2000.** Luxembourg (Eur-Op), 2000. 119 pages (EN). € 9. Catalogue No NB-31-00-918-EN-C

**Report on the implementation of the action plan to promote entrepreneurship and competitiveness.** Brussels (European Commission), 2000, 2 vol. (Vol. I available in all Community languages, Vol. II in DE, EN, FR).

**Industrial aspects of the information society: business networks and the knowledge-driven economy: an empirical study carried out in Europe and Canada.** Luxembourg (Eur-Op), 2000. 81 pages (EN). € 43. Catalogue No CO-25-99-253-EN-C

**Methodologies for benchmarking framework conditions.** Luxembourg (Eur-Op), 2000. 17 pages (EN). Catalogue No NB-31-00-780-EN-C

**The role of information and communications technologies in growth and competitiveness.** Luxembourg (Eur-Op), 2000. 17 pages (EN). Catalogue No CO-26-99-449-EN-C



## Guides

**ATEX guidelines. Guidelines on the application of Directive 94/9/EC of 23 March 1994 on the approximation of the laws of the Member States concerning equipment and protective systems intended for use in potentially explosive atmospheres.** Luxembourg (Eur-Op), 2001. 118 pages (EN). Catalogue No CO-22-99-014-\*\*-C

**Guide to the implementation of directives based on the new approach and the global approach.** Luxembourg (Eur-Op), 2000. 112 pages (DE, FR, EN). Catalogue No CO-22-99-014-\*\*-C

**Useful facts in relation to the personal protective equipment directive 89/686/EEC, 1999 edition.** Luxembourg (Eur-Op), 2000. 145 pages (EN). Catalogue No CO-21-99-020-EN-C

**Electrical and mechanical engineering directory, 2000 edition.** Luxembourg (Eur-Op), 2000. 133 pages (EN). Catalogue No CO-24-99-275-EN-C

**Cosmetlex: The rules governing cosmetic products in the European Union.** Luxembourg (Eur-Op), 2000, 3 vol. (EN). vol. 1: Cosmetics legislation, 74 pages, € 14.50; vol. 2: Methods of analysis, 187 pages € 31; vol. 3: Guidelines, 84 pages, € 16.

vol. 1 catalogue No NB-26-99-958-EN-C

vol. 2 catalogue No NB-26-99-966-EN-C

vol. 3 catalogue No NB-26-99-974-EN-C

On-line version: <http://pharmacos.eudra.org/cosmetic/index.htm>

**Eudralex: The rules governing medicinal products in the European Union.** Luxembourg (Eur-Op), 1998-, (DE, EN, ES, FR, IT), priced.

Medicinal products for human use, vols 1, 2a, 2b, 3

Medicinal products for human and veterinary use, vol 4

Veterinary medicinal practice, vols 5, 6a, 6b, 7a, 7b (8 and 9 not yet published).

On-line version: <http://pharmacos.eudra.org/eudralex/index.htm>

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