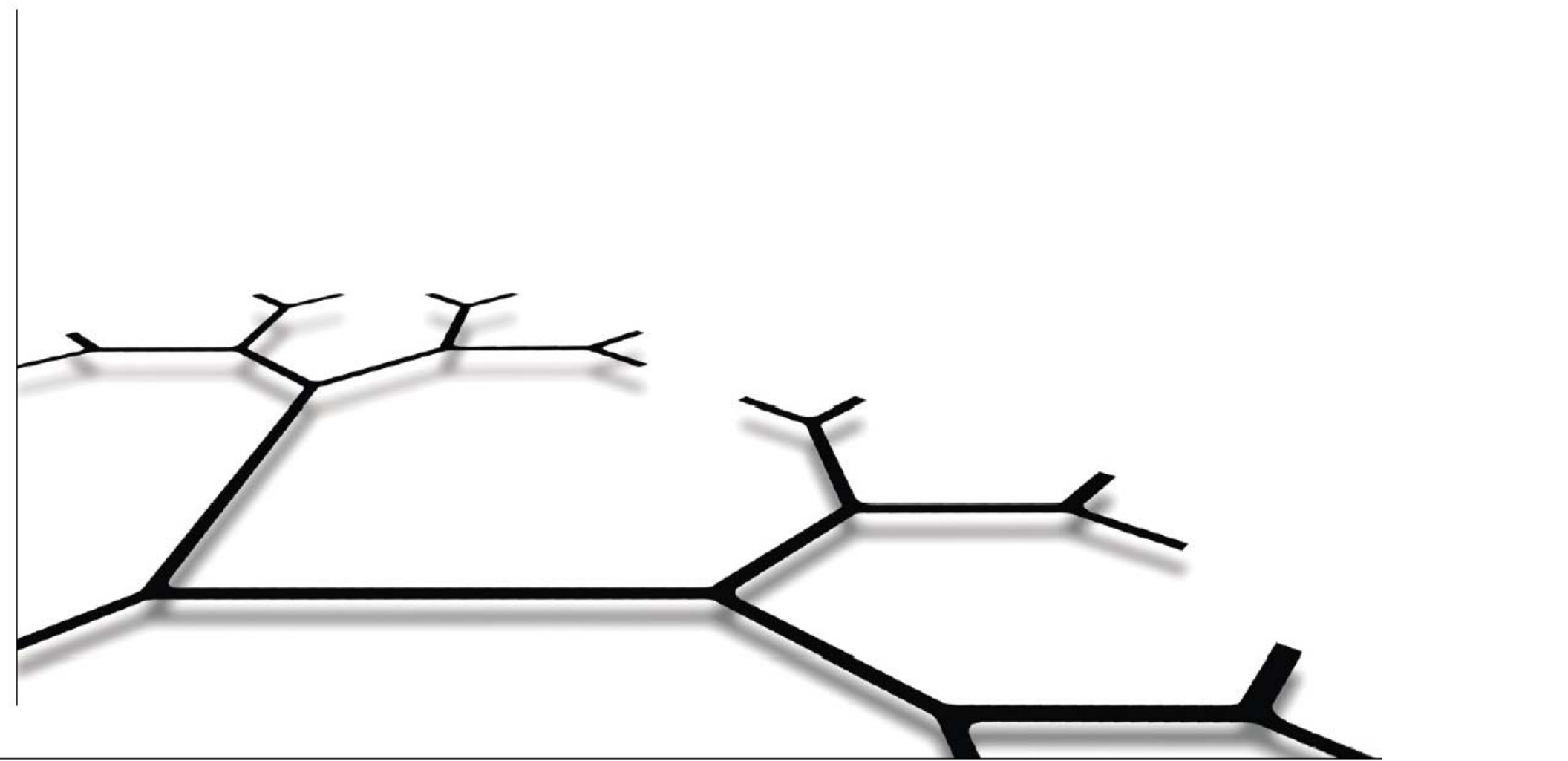


# Innovation, Regulation and Industrial Performances in Europe. Lessons for Pharmaceuticals

**M. Riccaboni & F. Pammolli**



# Capital Deepening and Productivity Slowdown

## Productivity Slowdown

- There is a large labour productivity gap between USA and EU-15 (65,4 per cent higher in USA in 2001).
- However, there has been a slowdown of pharmaceutical TFP worldwide in the last five years, and especially in the US.
- The US system suffers of an excessive capital intensity. The US capital intensity is a demonstration of the substantial amount of resources they are devoting to the pharmaceutical sector and that are at the basis of their competitiveness, but also a source of concern, because a prolonged disproportion of production factors may generate chains of diseconomies and negative externalities, both at the national and international level.

## EU-US Productivity Gap is Closing

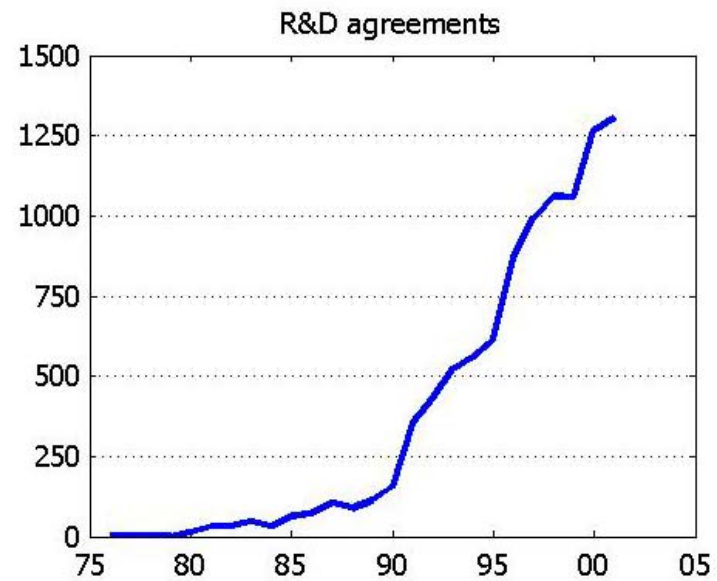
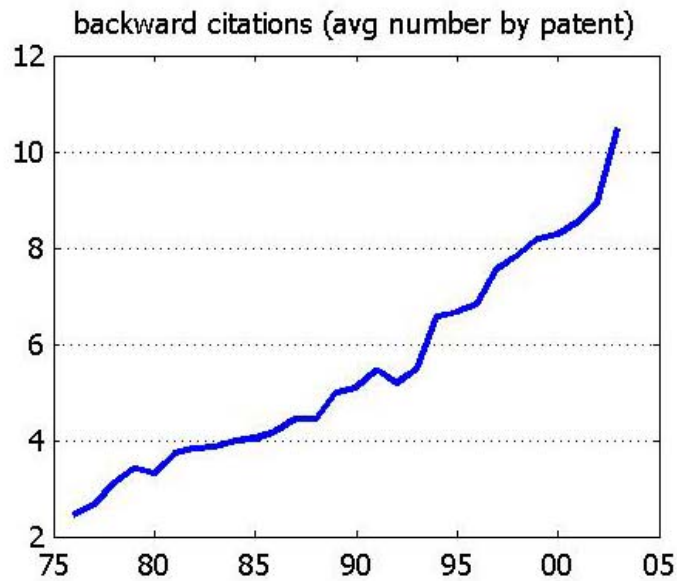
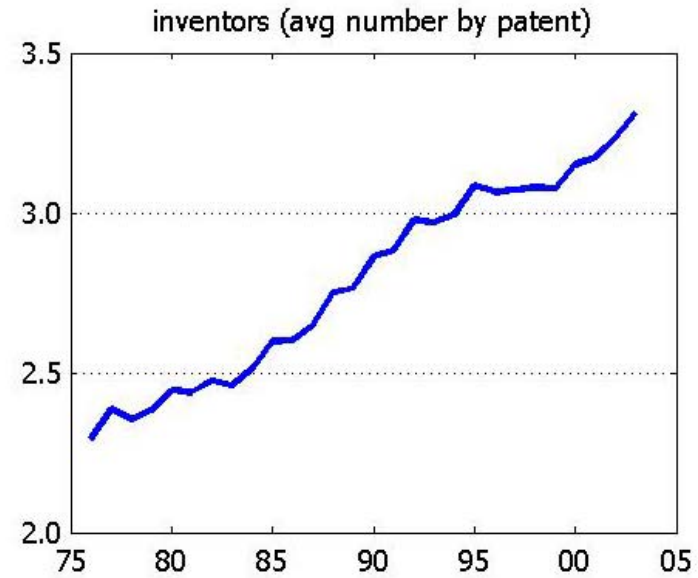
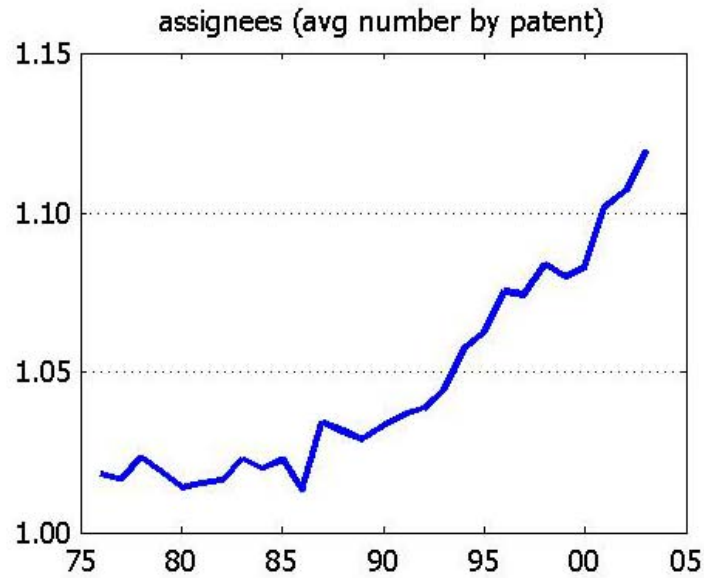
- Even if EU-15 remains less cost competitive than USA, its position improved substantially in the period 1995-2001, thanks to labour productivity increases and also to favourable dynamics in exchange rates.
- The good trend performance of EU-15 is explained mainly by the pharmaceutical sectors of the UK, Ireland, Sweden, Denmark, and Belgium. Capital intensity and labour productivity of these countries are much closer to the USA than the European average.
- Finally, it is worth noticing that Czech Republic and Poland have become more cost competitive than USA and EU-15 countries, thanks to their very low labour costs and rapidly increasing productivity.

# Gestation lags or fishing out?

# Private and Public Pharmaceutical R&D Expenditures (€million, PPP)

		1981-85		1986-90		1991-95		1996-02	
		€m	%*	€m	%*	€m	%*	€m	%*
<b>France</b>	private	543	5.32%	882	6.07%	1,736	8.43%	2,594	8,99%
	public	892	1.84%	1,436	2.11%	1,712	2.10%	2,388	2,25%
<b>Germany</b>	private	718	9.35%	1,168	10.85%	1,211	7.83%	2,096	11,46%
	public	224	0.38%	281	0.37%	1,800	1.32%	2,240	1,33%
<b>Sweden</b>	private	130	16.22%	264	20.90%	513	19.93%	1,087	21,89%
	public	216	2.42%	249	2.30%	299	2.40%	-	-
<b>Denmark</b>	private	53	9.35%	107	12.28%	196	14.46%	454	21,11%
	public	79	1.47%	109	1.80%	209	2.78%	254	2,50%
<b>Italy</b>	private	444	3.66%	783	5.20%	694	3.99%	610	2,83%
	public	-	-	260	0.46%	238	0.36%	181	0,23%
<b>Spain</b>	private	63	1.55%	143	2.60%	236	2.94%	402	3,89%
	public	13	0.09%	83	0.40%	120	0.37%	176	0,42%
<b>United Kingdom</b>	private	758	12.10%	1,494	16.04%	2,573	18.26%	4,095	26,77%
	public	-	-	-	-	1,424	2.15%	1,402	1,97%
<b>EU-15</b>	private	2,823	6.62%	4,995	8.21%	7,779	11.05%	11,131	12,61%
	public	686	0.72%	1,120	0.69%	4,521	1.20%	5,552	1,01%
<b>United States</b>	private	2,634	9.83%	4,995	11.22%	8,800	12.50%	11,987	13,58%
	public	6,399	4.53%	9,999	4.51%	14,272	3.79%	23,341	4,24%
<b>Canada</b>	private	-	-	134	4.70%	285	7.40%	557	12,20%
	public	181	0.86%	293	0.96%	409	0.98%	1,017	1,96%
<b>Japan</b>	private	1,318	6.49%	2,161	7.59%	3,431	9.51%	4,721	10,49%
	public	2,174	3.32%	2,944	3.17%	4,091	3.01%	4,990	2,89%

# Division of Innovative Labor in Pharmaceutical R&D



# Shares of USPTO-Granted Pharmaceutical Patents

	1974-1983			1984-1993			1994-2003		
	Assignee	Inventor	I-A	Assignee	Inventor	I-A	Assignee	Inventor	I-A
<b>France</b>	5.97%	6.05%	0.08%	5.39%	5.28%	-0.11%	5.71%	5.79%	0.08%
<b>Germany</b>	11.63%	11.57%	-0.06%	10.28%	10.45%	0.18%	7.13%	7.25%	0.12%
<b>Sweden</b>	0.81%	0.87%	0.06%	0.68%	0.67%	-0.01%	1.15%	1.09%	-0.06%
<b>Denmark</b>	0.31%	0.31%	0.00%	0.50%	0.54%	0.04%	0.82%	0.83%	0.01%
<b>Italy</b>	1.86%	2.05%	0.19%	2.29%	2.49%	0.21%	1.44%	1.76%	0.33%
<b>Spain</b>	0.12%	0.16%	0.04%	0.25%	0.29%	0.04%	0.30%	0.38%	0.08%
<b>UK</b>	5.53%	7.34%	1.82%	4.68%	6.41%	1.73%	3.86%	5.14%	1.28%
<b>Other EU-25</b>	2.02%	2.50%	0.48%	3.24%	3.08%	-0.16%	2.66%	2.54%	-0.12%
<b>EU-25</b>	28.26%	30.85%	2.59%	27.30%	29.22%	1.93%	23.07%	24.79%	1.72%
<b>USA</b>	59.02%	52.28%	-6.74%	55.16%	50.79%	-4.37%	60.06%	57.29%	-2.76%
<b>Canada</b>	0.74%	1.30%	0.56%	1.07%	1.39%	0.32%	2.53%	2.64%	0.11%
<b>Japan</b>	9.29%	9.44%	0.15%	13.41%	13.55%	0.13%	9.15%	9.32%	0.17%
<b>Switzerland</b>	1.60%	4.29%	2.69%	1.31%	2.91%	1.60%	1.35%	1.42%	0.08%
<b>Other</b>	1.10%	1.84%	0.74%	1.76%	2.14%	0.39%	3.85%	4.53%	0.68%
<b>Total</b>	100%	100%		100%	100%		100%	100%	

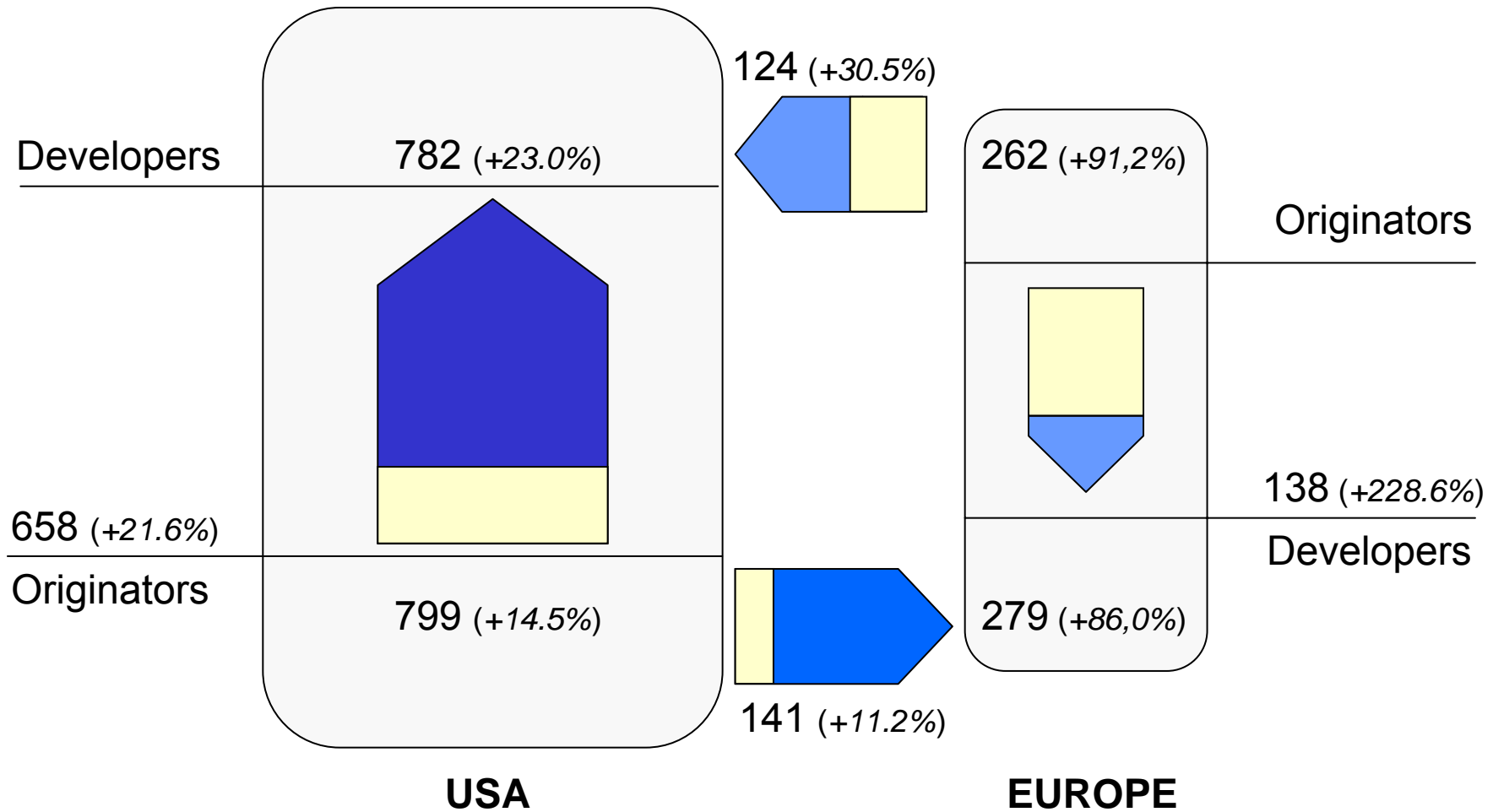
# Shares of USPTO Patent Citations

	1974-1983			1984-1993			1994-2003		
	Assignee	Inventor	I-A	Assignee	Inventor	I-A	Assignee	Inventor	I-A
<b>France</b>	5,11%	5,11%	0,00%	4,06%	4,14%	0,07%	4,23%	4,56%	0,33%
<b>Germany</b>	8,46%	8,23%	-0,23%	6,61%	6,75%	0,14%	4,90%	5,14%	0,24%
<b>Sweden</b>	1,28%	1,22%	-0,06%	0,82%	0,77%	-0,05%	1,05%	1,01%	-0,04%
<b>Denmark</b>	0,38%	0,39%	0,00%	0,50%	0,57%	0,07%	0,48%	0,47%	0,00%
<b>Italy</b>	1,04%	1,27%	0,23%	1,28%	1,40%	0,12%	0,89%	1,30%	0,41%
<b>Spain</b>	0,05%	0,07%	0,02%	0,11%	0,14%	0,03%	0,20%	0,24%	0,04%
<b>UK</b>	5,34%	6,94%	1,60%	3,66%	5,44%	1,78%	3,57%	4,61%	1,04%
<b>Other EU-25</b>	1,92%	2,28%	0,36%	2,38%	2,12%	-0,27%	2,16%	1,73%	-0,42%
<b>EU-25</b>	23,57%	25,50%	1,92%	19,43%	21,33%	1,90%	17,47%	19,06%	1,59%
<b>USA</b>	63,71%	59,33%	-4,38%	67,12%	63,52%	-3,60%	70,39%	68,13%	-2,26%
<b>Canada</b>	1,20%	1,69%	0,50%	1,31%	1,80%	0,49%	2,31%	2,38%	0,07%
<b>Japan</b>	9,26%	8,99%	-0,27%	9,55%	9,64%	0,09%	6,00%	6,07%	0,07%
<b>Switzerland</b>	1,24%	2,85%	1,61%	1,14%	2,00%	0,85%	1,19%	1,31%	0,12%
<b>Other</b>	1,02%	1,64%	0,62%	1,44%	1,70%	0,26%	2,64%	3,05%	0,41%
<b>Total</b>	100%	100%		100%	100%		100%	100%	

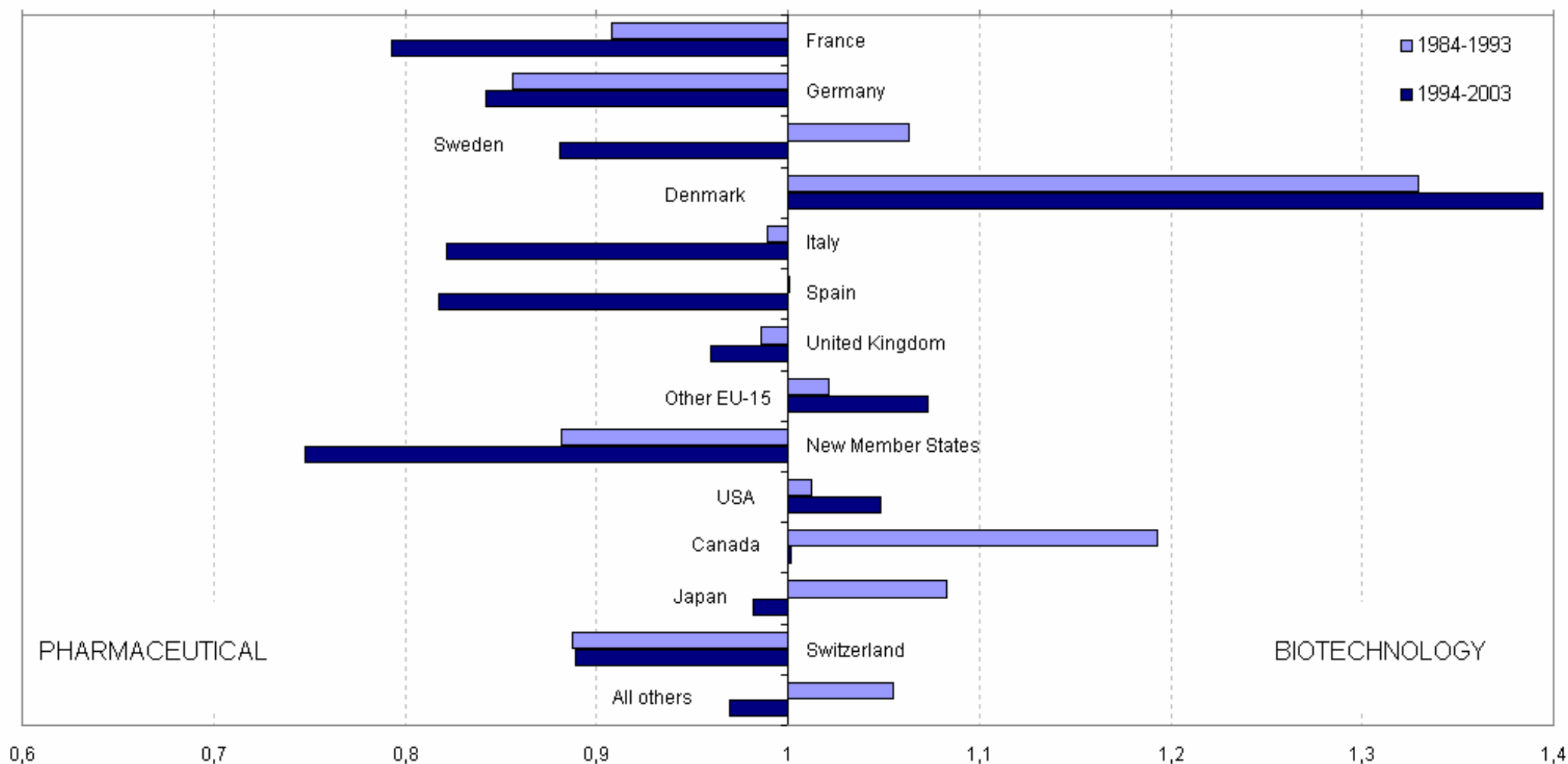
# The Internationalization of R&D Activities: Patent Citations

	1974-1983	1984-1993	1994-2003
<b>USA</b>			
Patent count	8,943	14,860	36,271
Number of citations <sup>1</sup>	6,680	40,332	201,510
Mean number of citations <i>of which.</i> <sup>2</sup>	0.75	2.71	5.56
US -> US	74.70%	73.00%	74.70%
US -> EU	18.29%	18.51%	18.82%
US -> JP	5.09%	7.06%	6.77%
<b>EU-25</b>			
Patent count	5,238	8,525	1,5904
Number of citations <sup>1</sup>	3,153	15,004	46,396
Mean number of citations <i>of which.</i> <sup>2</sup>	0.60	1.76	2.92
EU -> EU	55.25%	51.18%	43.64%
EU -> US	36.12%	38.83%	49.11%
EU -> JP	5.49%	7.96%	7.49%
<b>Japan</b>			
Patent count	1,582	3,845	5,678
Number of citations <sup>1</sup>	959	5,833	11,746
Mean number of citations <i>of which.</i> <sup>2</sup>	0.61	1.52	2.07
JP -> JP	40.88%	36.57%	35.96%
JP -> US	33.99%	37.68%	42.23%
JP -> EU	23.46%	23.90%	22.26%

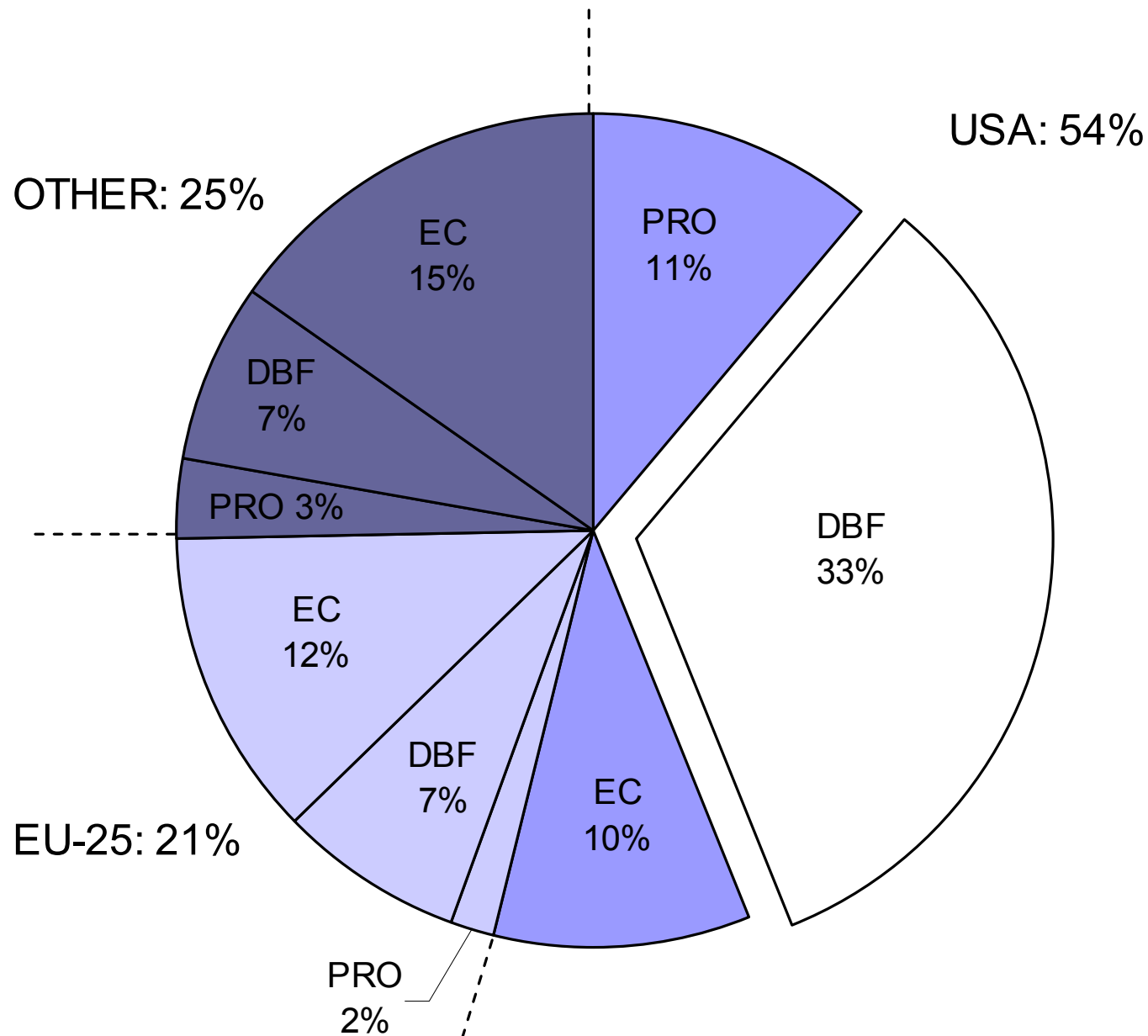
# Division of Innovative Labor Between the EU and the US



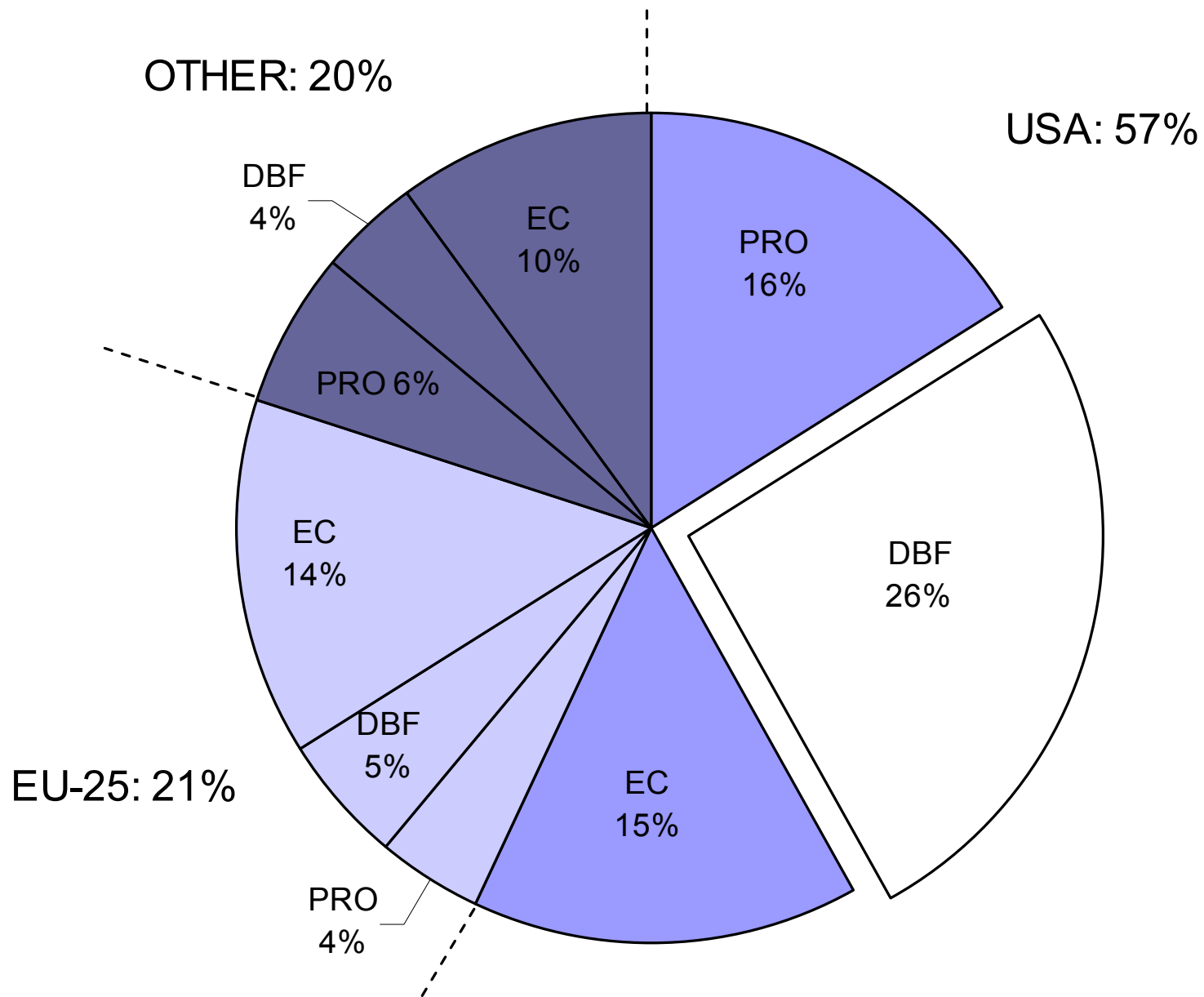
# Biotech/Pharma Specialization Index (1984-2003)



# R&D Projects Addressing Diseases Without Therapy



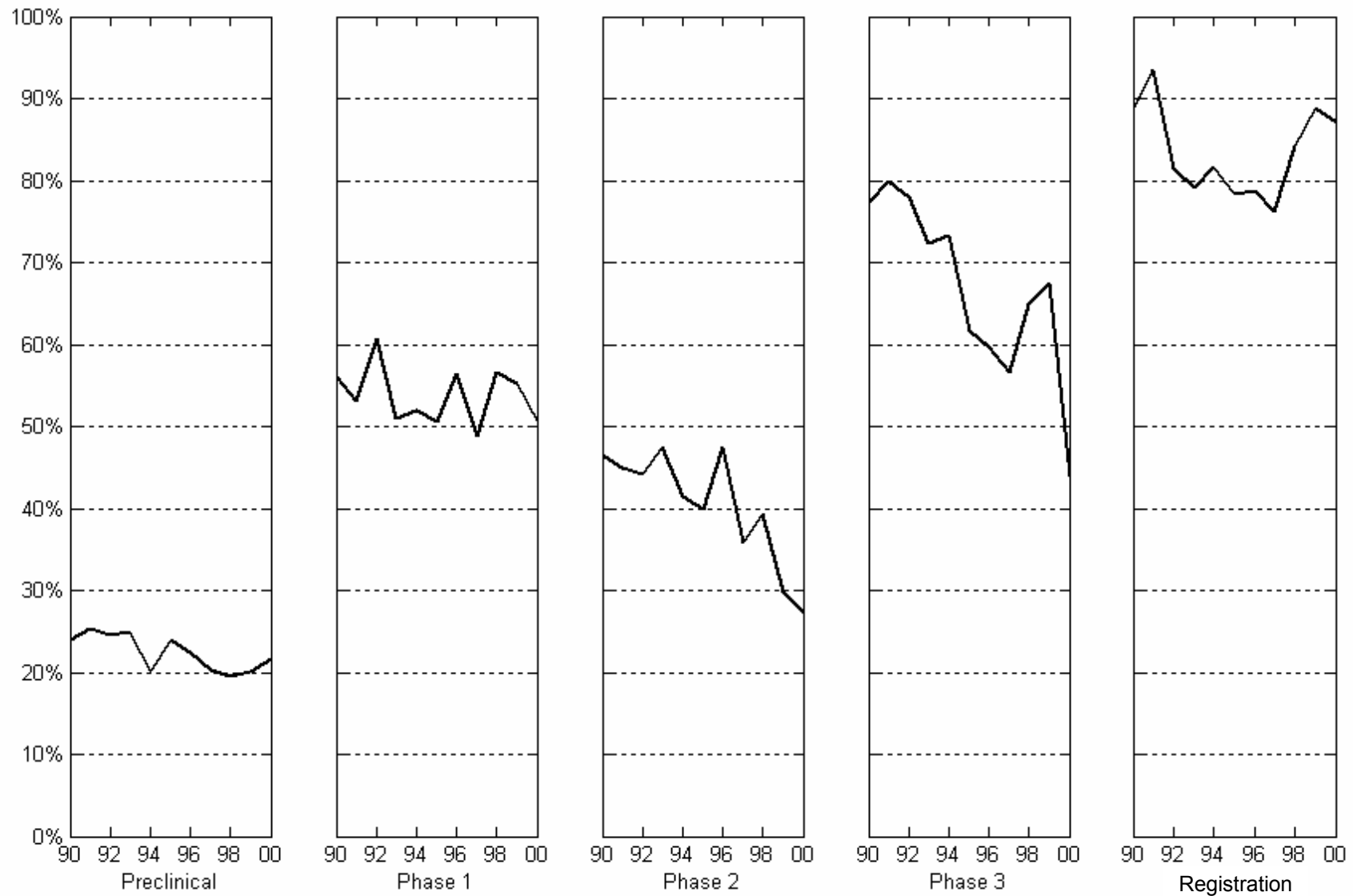
# R&D Projects Addressing African's Diseases



# Number of R&D Projects by Country and Latest Phase of Development

	1991-1996				1997-2004			
	Preclinical	Clinical	Market	Total	Preclinical	Clinical	Market	Total
<b>EU-25</b>	3550	2013	524	6087	2765	1562	306	4633
	<i>58,3</i>	<i>33,1</i>	<i>8,6</i>	<i>100</i>	<i>59,7</i>	<i>33,7</i>	<i>6,6</i>	<i>100</i>
<b>USA</b>	6189	2543	552	9284	4896	2164	379	7439
	<i>66,7</i>	<i>27,4</i>	<i>5,9</i>	<i>100</i>	<i>65,8</i>	<i>29,1</i>	<i>5,1</i>	<i>100</i>
<b>Japan</b>	1013	689	243	1945	496	481	133	1110
	<i>52,1</i>	<i>35,4</i>	<i>12,5</i>	<i>100</i>	<i>44,7</i>	<i>43,3</i>	<i>12</i>	<i>100</i>
<b>Others</b>	1716	776	222	2714	1409	655	147	2211
	<i>63,2</i>	<i>28,6</i>	<i>8,2</i>	<i>100</i>	<i>63,7</i>	<i>29,6</i>	<i>6,6</i>	<i>100</i>
<b>Total</b>	12,468	6,021	1,541	20,03	9,566	4,862	965	15,393
	<i>62,2</i>	<i>30,1</i>	<i>7,7</i>	<i>100</i>	<i>62,1</i>	<i>31,6</i>	<i>6,3</i>	<i>100</i>

# The Probability of Success of R&D Projects



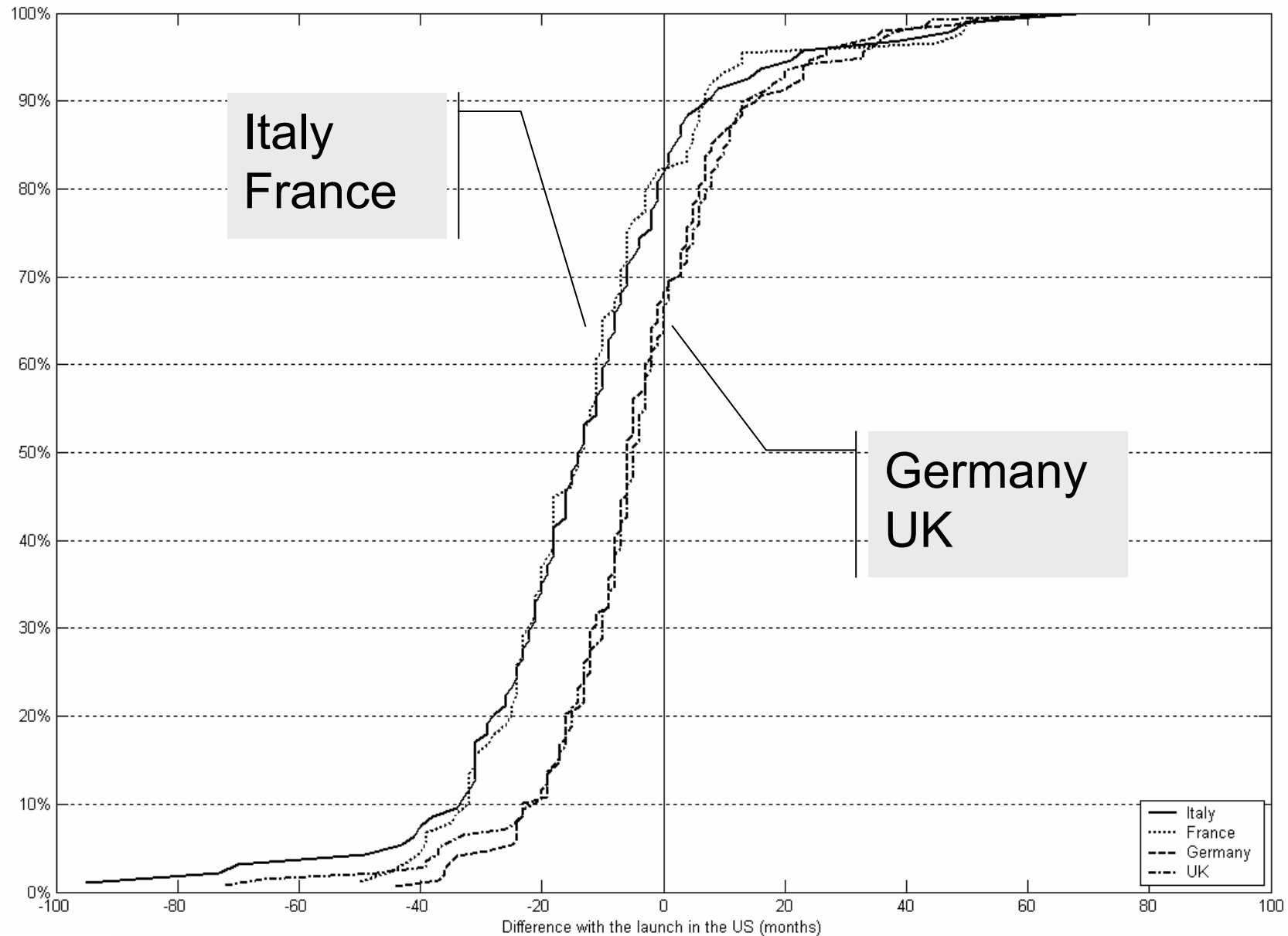
# Number of Investigational Drugs and Drug Approvals in the US



# Number of NCEs Launched Worldwide, by Nationality of R&D Corporation

		1994	1995	1996	1997	1998	1999	2000	2001	2002
USA	Num	12	14	14	19	22	17	14	18	13
	%	28,6	31,1	31,8	37,3	50	37	35,9	48,6	36,1
EU-15	Num	9	13	18	18	11	14	14	5	10
	%	21,4	28,9	40,9	35,3	25	30,4	35,9	13,5	27,8
Japan	Num	18	10	6	9	5	10	7	5	10
	%	42,9	22,2	13,6	17,6	11,4	21,7	17,9	13,5	27,8
Other	Num	3	8	7	5	6	5	4	9	3
	%	7,1	17,8	13,7	9,8	13,6	10,9	10,3	24,4	8,3
Total		42	45	45	51	44	46	39	37	36

# Introduction Lags with Respect to the USA



# License-in Agreements by Phase of Signing

Stage at signing	US & Canada			Europe			Japan			Others		
	Count	% US & Canada	% Europe	Count	% US & Canada	% Europe	Count	% US & Canada	% Europe	Count	% US & Canada	% Europe
From start	77	5,3%	5,3%	50	3,6%	3,6%	8	1,5%	1,5%	8	2,0%	2,0%
Preclinical	594	41,0%	46,3%	370	26,4%	30,0%	122	23,4%	25,0%	59	14,6%	16,6%
Clinical I	166	11,4%	57,7%	134	9,6%	39,5%	46	8,8%	33,8%	17	4,2%	20,8%
Clinical II	183	12,6%	70,3%	178	12,7%	52,2%	76	14,6%	48,4%	59	14,6%	35,5%
Clinical III	116	8,0%	78,3%	172	12,3%	64,5%	74	14,2%	62,6%	51	12,7%	48,1%
PreReg.	59	4,1%	82,4%	100	7,1%	71,6%	47	9,0%	71,6%	35	8,7%	56,8%
Registration	11	0,8%	83,2%	12	0,9%	72,5%	8	1,5%	73,1%	11	2,7%	59,6%
Market	244	16,8%	100%	386	27,5%	100%	140	26,9%	100%	163	40,4%	100%

# Increasing Complexity of R&D Efforts

	Potential Entry	Actual Entry	Intensity %	Avg Success Rate
<b>Etiology</b>				
Monofactorial etiology	237,688	1,756	0.74	21.67
Unknown etiology	41,562	451	1.09	20.35
Multifactorial etiology	464,428	7,279	1.57	17.22
<b>Chronicity</b>				
Acute	245,713	1,839	0.75	19.89
Chronic	495,875	7,625	1.54	17.58
<b>Outcome</b>				
Not lethal	210,199	1,630	0.78	21.00
Maybe lethal	398,708	5,118	1.28	17.62
Always lethal	134,771	2,738	2.03	16.51
<b>Damage</b>				
No organ damage	291,618	2,117	0.73	24.51
Organ damage	452,060	7,369	1.63	16.33
<b>Complication</b>				
No complications	100,089	496	0.50	26.21
Complications	643,589	8,990	1.40	17.49
<b>Diffusion</b>				
Rare	175,338	1,206	0.69	36.20
Widespread	568,340	8,280	1.46	16.96

# Number of Scientific Publications (Medline) by Scientists in Developing Countries

		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
<b>China</b>	no.	1939	2345	2932	3826	4592	7834	9848	12631	16862	21467
	%	1,04	1,11	1,35	1,68	1,95	2,97	3,56	4,38	5,54	6,57
<b>India</b>	no.	2378	2660	2714	3059	3508	4160	4911	5481	6210	6902
	%	1,28	1,26	1,25	1,35	1,49	1,58	1,77	1,90	2,04	2,11
<b>Israel</b>	no.	3286	3341	3652	3763	3970	4509	4612	4781	5121	5402
	%	1,76	1,58	1,69	1,66	1,68	1,71	1,67	1,66	1,68	1,65
<b>Russia</b>	no.	498	793	1042	1694	1769	2610	2674	2754	2940	2130
	%	0,27	0,38	0,48	0,75	0,75	0,99	0,97	0,95	0,97	0,65
<b>S. Africa</b>	no.	764	743	801	846	875	994	1058	999	1066	1140
	%	0,41	0,35	0,37	0,37	0,37	0,38	0,38	0,35	0,35	0,35
<b>Brasil</b>	no.	613	669	805	827	874	842	869	1104	1306	714
	%	0,33	0,32	0,37	0,36	0,37	0,32	0,31	0,38	0,43	0,22
<b>EU-25</b>	no.	60420	66386	69004	72869	77444	86610	93264	97675	100716	108315
	%	32,40	31,49	31,85	32,06	32,80	32,86	33,70	33,84	33,09	33,15
<b>US</b>	no.	92216	108179	109312	111318	113287	122881	126094	129324	135563	145314
	%	49,45	51,31	50,45	48,97	47,99	46,63	45,56	44,80	44,54	44,48
<b>Japan</b>	no.	24379	25731	26414	29105	29756	33108	33448	33930	34586	35316
	%	13,07	12,20	12,19	12,80	12,60	12,56	12,08	11,75	11,36	10,81
<b>Total</b>		186493	210847	216676	227307	236075	263548	276778	288679	304370	326700

# Number of Pharmaceutical Patents Filed in the US by Assignees and Inventors in Developing Countries

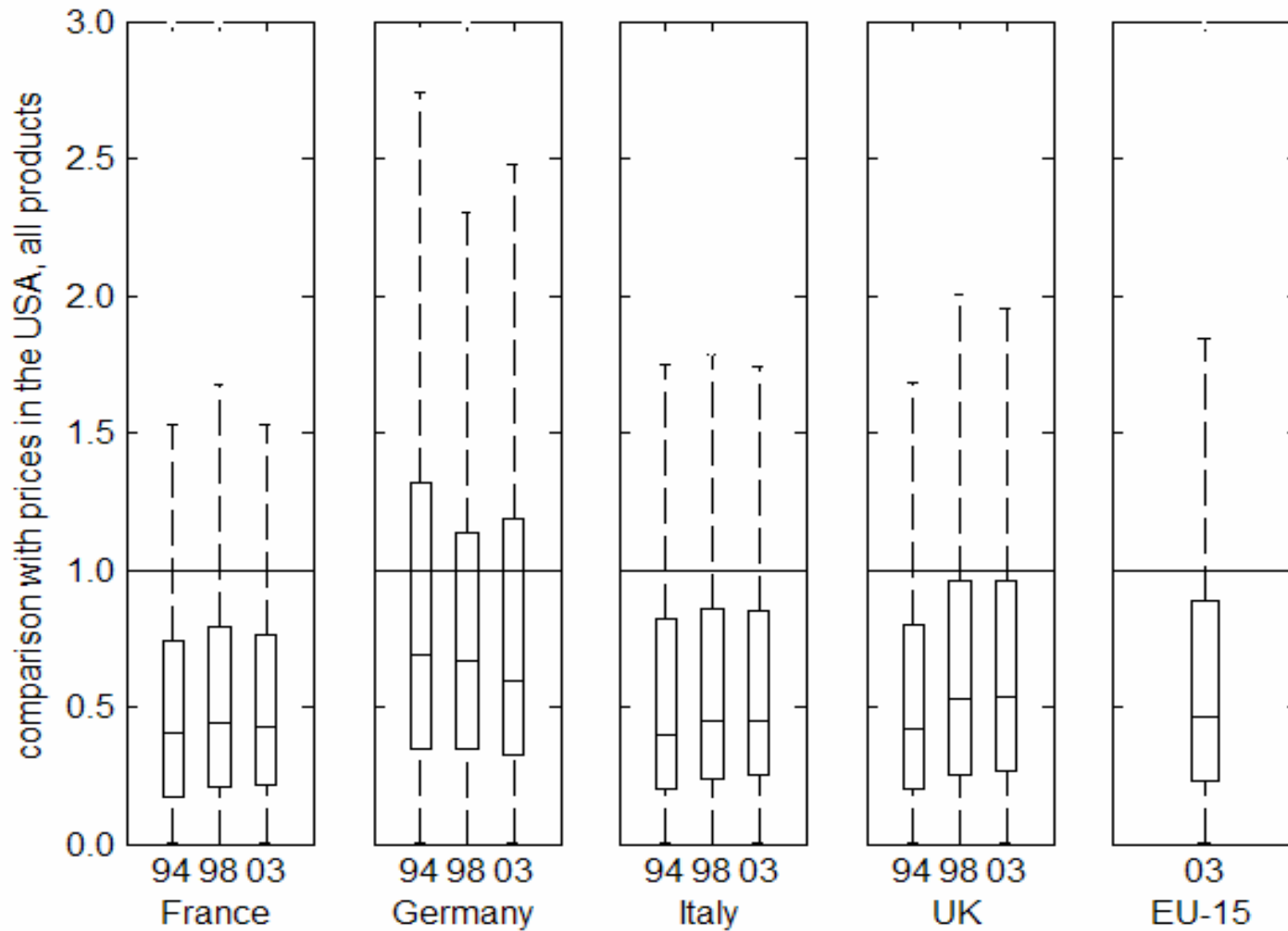
	Assignee			Inventor			I-A		
	2000	2005	growth	2000	2005	growth	2000	2005	growth
Israel	461	778	68,8%	742	1,184	59,6%	281	406	44,5%
India	71	333	369,0%	230	554	140,9%	159	221	39,0%
China	34	96	182,4%	127	286	125,2%	93	190	104,3%
South Africa	29	42	44,8%	92	122	32,6%	63	80	27,0%
Russia	21	36	71,4%	96	181	88,5%	75	145	93,3%
Brazil	10	30	200,0%	62	126	103,2%	52	96	84,6%

# Number of Pharmaceutical Patents Filed in Developing Countries

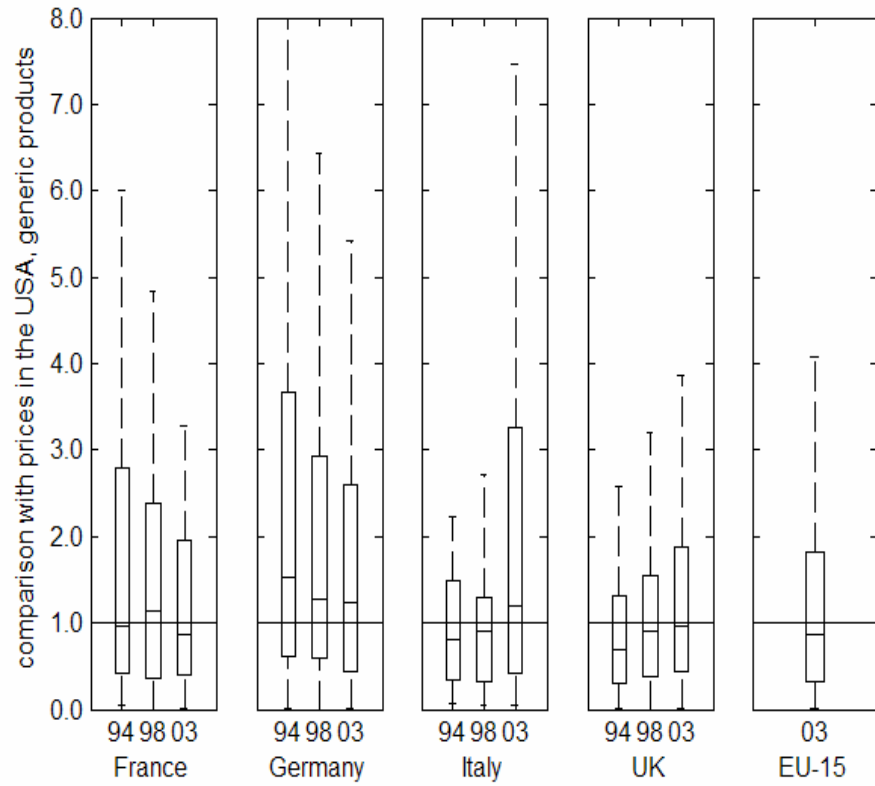
	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004
China	133	324	338	516	778	2284	2537	1820	2898	4826
	-	143,6	4,3	52,7	50,8	193,6	11,1	-28,3	59,2	66,5
Russia	1091	896	1569	1624	1944	1624	1084	1719	2259	2126
	-	-17,9	75,1	3,5	19,7	-16,5	-33,3	58,6	31,4	-5,9
Brasil	83	145	380	759	2452	3590	2584	2502	1931	3265
	-	74,7	162,1	99,7	223,1	46,4	-28,0	-3,2	-22,8	69,1
South Africa	1392	1635	1640	1706	1604	631	548	1463	1663	1828
	-	17,5	0,3	4,0	-6,0	-60,7	-13,2	167,0	13,7	9,9
Israel	1037	1012	599	839	1079	887	1425	1468	814	902
	-	-2,4	-40,8	40,1	28,6	-17,8	60,7	3,0	-44,6	10,8
India	69	84	201	114	195	213	202	226	325	-
	-	21,7	139,3	-43,3	71,1	9,2	-5,2	11,9	43,8	-

# Price Regulation, Market Contestability, Turnover and Incentives to Innovation

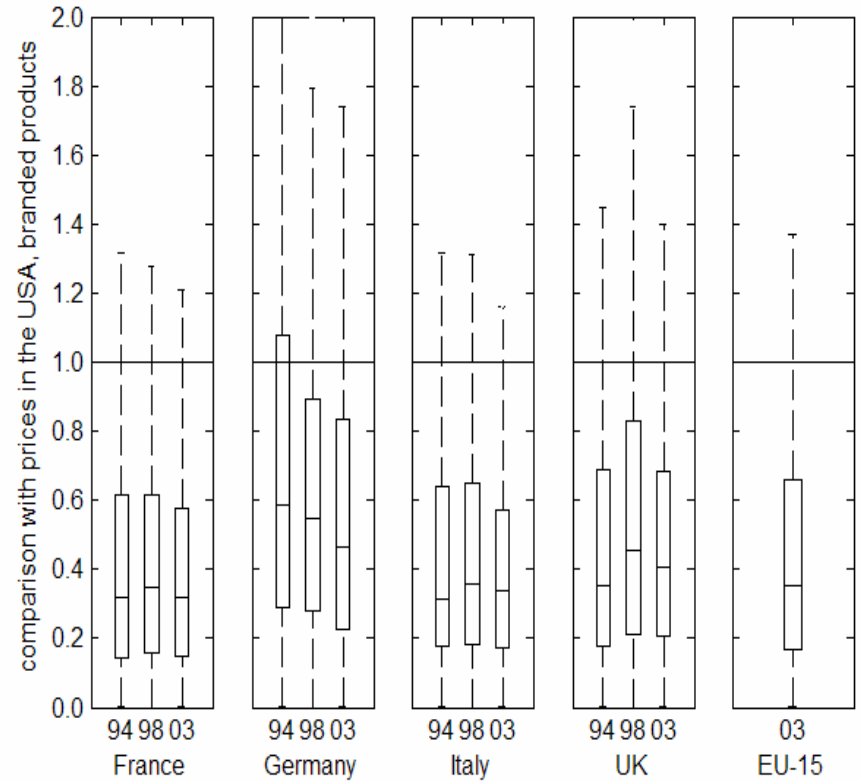
# Price Comparison Between the US and Europe



# Generics vs Branded Drugs



Generics



Branded

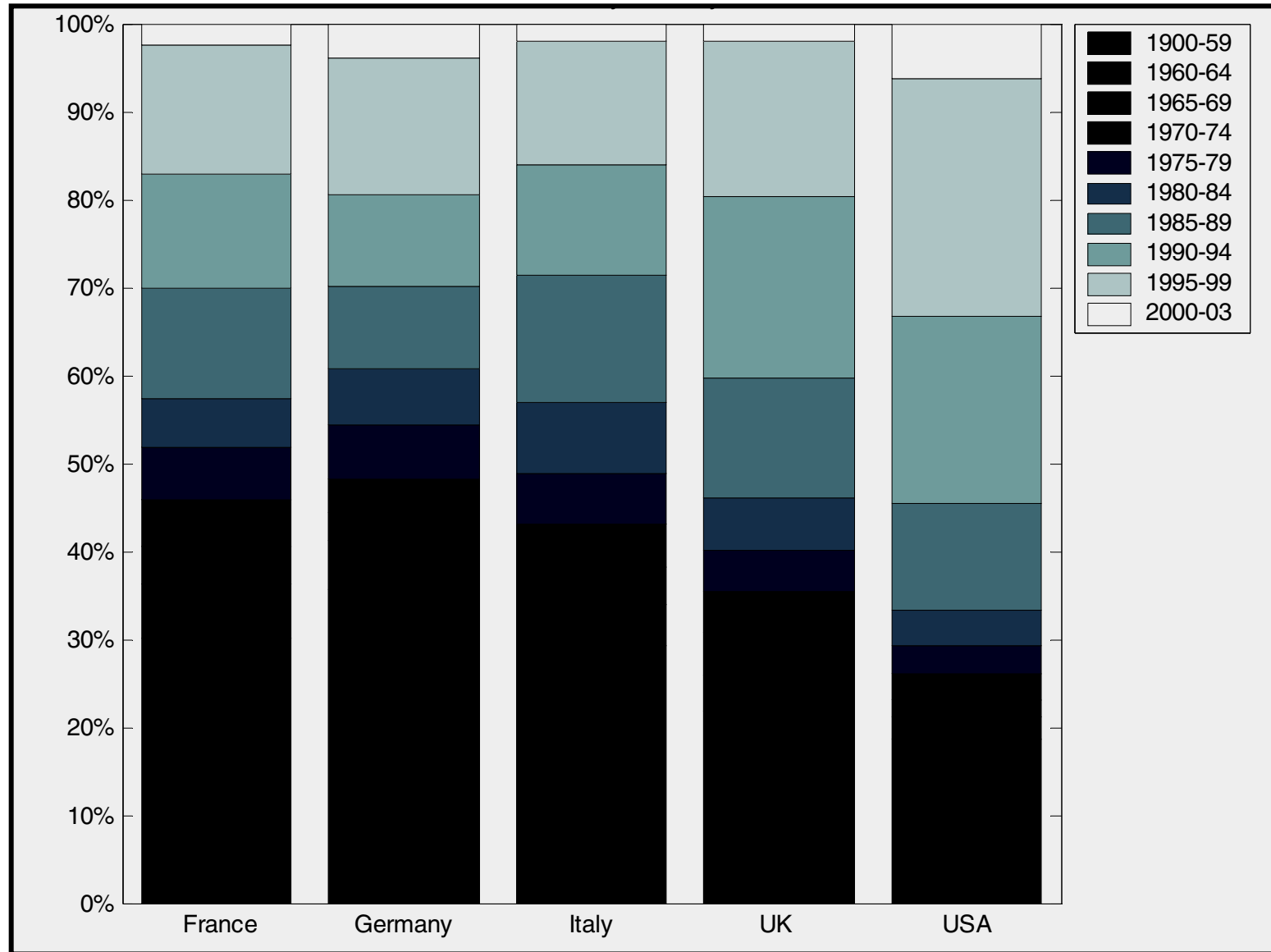
# Generic Penetration (1994-2003)

Country	1994	1998	2003
	% of total sales		
France	1,01	1,02	5,45
Germany	5,51	5,42	9,83
Italy	0,92	0,90	2,48
UK	8,74	10,37	17,03
EU-15	3,44	3,77	7,93
USA	7,57	6,15	6,88

Country	% of total volumes (standard unit)		
	1994	1998	2003
France	2,52	2,54	11,12
Germany	9,33	11,01	19,27
Italy	1,20	1,17	4,85
UK	28,05	31,28	33,79
EU-15	8,75	10,17	15,91
USA	27,14	34,68	42,16

# Share of Sales by Products' Launch Date



# Price Regulation and Incentives to Innovation

