



**COMPARATIVE STATISTICS FOR  
THE UK, EUROPEAN AND US  
BIOTECHNOLOGY SECTORS**

Analysis years 2001 & 2002

December 2004



The DTI drives our ambition of 'prosperity for all' by working to create the best environment for business success in the UK. We help people and companies become more productive by promoting enterprise, innovation and creativity.

We champion UK business at home and abroad. We invest heavily in world-class science and technology. We protect the rights of working people and consumers. And we stand up for fair and open markets in the UK, Europe and the world.

# Comparative Statistics for the UK, European and US Biotechnology Sectors – Analysis Years 2001 & 2002

This report was prepared by Critical I Limited  
for the Department of Trade and Industry

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# Executive Summary

The objective of this report is to provide the DTI with a robust and defensible analysis of the UK biotechnology sector's comparative standing against some of its key European competitors and the United States. The report analyses company performances in the calendar year 2002 and, on a country by country basis, compares that performance with metrics for 2001 that have been calculated using the same methodology

The European countries covered by this study are: United Kingdom, Denmark, Finland, France, Germany, Ireland, Israel, Norway, and Sweden. For brevity, we refer to this collective set of nine as "Europe", although it should be noted that there is a significant concentration of commercial biotechnology activity in Switzerland, The Netherlands, and Belgium. Sectors are also starting to emerge in Austria, Italy and Spain.

Our study identified 1743 European companies in 2002 and 1658 in 2001 in "Europe" whose primary commercial activity fell within the definition of biotechnology agreed with the DTI (the sector and sub-sectoral definitions used in this study are shown in Appendix C). This definition specifically excludes some companies that alternative definitions of biotechnology or life sciences often encompass (particularly clinical research

organisations, suppliers of biological reagents for research purposes, medical device companies, and those drug companies which use little biology). Consistent adherence to a transparent definition of the sector is key to any comparison of biotechnology data sets, either between nations or between different time periods for a single nation or region.

At the end of 2002 Europe's biotechnology industry:

- Employed approximately 87,000 people (2001: 80,000);
- Had 502 new drugs in clinical development or awaiting approval (542 in 2001);
- Generated nearly €20 billion of revenue (2001: €18.5 billion)
- Raised over €1.6 billion of investment in 2002 (2001: €3.5 billion)
- Had 95 publicly quoted companies with a total market capitalisation of €30.1 billion
- Formed 116 new companies (2001: 200)

As in 2001, the UK was the single biggest contributor to this picture. In 2002 the UK sector:

- Comprised 486 companies (2001: 450)
- Employed approximately 25,931 people (2001: 24,435)
- Had 225 new drugs in clinical

development or awaiting approval (2001: 200)

- Generated over €6.4 billion of revenue (2001: €5.0 billion)
- Raised over €676 million of investment (2001: over €1.9 billion)
- Had 47 publicly quoted companies with a total market capitalisation of €9.7 billion, compared to 45 companies in 2001 valued at €20.6 billion

The slowing down in the rate of new company formation across Europe that started to become apparent in 2001 became more pronounced in 2002. With 42 new companies, the UK came closest to maintaining its 2001 rate of new company formation, which saw 48 new companies formed. In Germany, 26 new companies were formed in 2002, as against 64 in 2001. The UK accounted for over a third of the new European companies in 2002 but less than a quarter in 2001.

In this report, we examine for the first time in detail, the performance of biotechnology companies in the United States. In 2002, the US biotechnology industry:

- Comprised 1817 companies;
- Employed approximately 160,000 people
- Had over 1150 new drugs in clinical development or awaiting approval
- Generated nearly €36 billion of revenue
- Raised €6.7 billion of equity, and a further €4.3 billion of debt
- Had 358 publicly quoted companies with a total market capitalisation of €165 billion
- Formed over 103 new companies

It is clear that in absolute terms Europe can barely mount a serious challenge to US supremacy, except perhaps at the level of company numbers and rate of

company formation. The section entitled **Europe and the USA compared** analyses some of the key performance differences between the two regions. Our analysis indicates that governmental encouragement for entrepreneurialism, seed funding, cluster formation and centres of technical excellence are unlikely to reap significant benefit unless more fundamental questions of financing and competitive business management are resolved. In particular, our analysis indicates that the performance of European companies significantly lags that of their US peers of comparable age when one compares mean average levels of investment raised, employment, R&D employment, R&D expenditure and revenues generated. It would be instructive to identify the extent of the performance differential between Europe's best performers and their US counterparts since aspirations to world-class levels of performance demand world-class benchmarks.

The **Key findings** section compares the UK's performance to that of its European and US peers against a range of key metrics. The **Country profiles** section includes a profile for each of the ten countries covered in the study and tracks changes in the performance and local environment for each national sector over the 2001 and 2002 period.

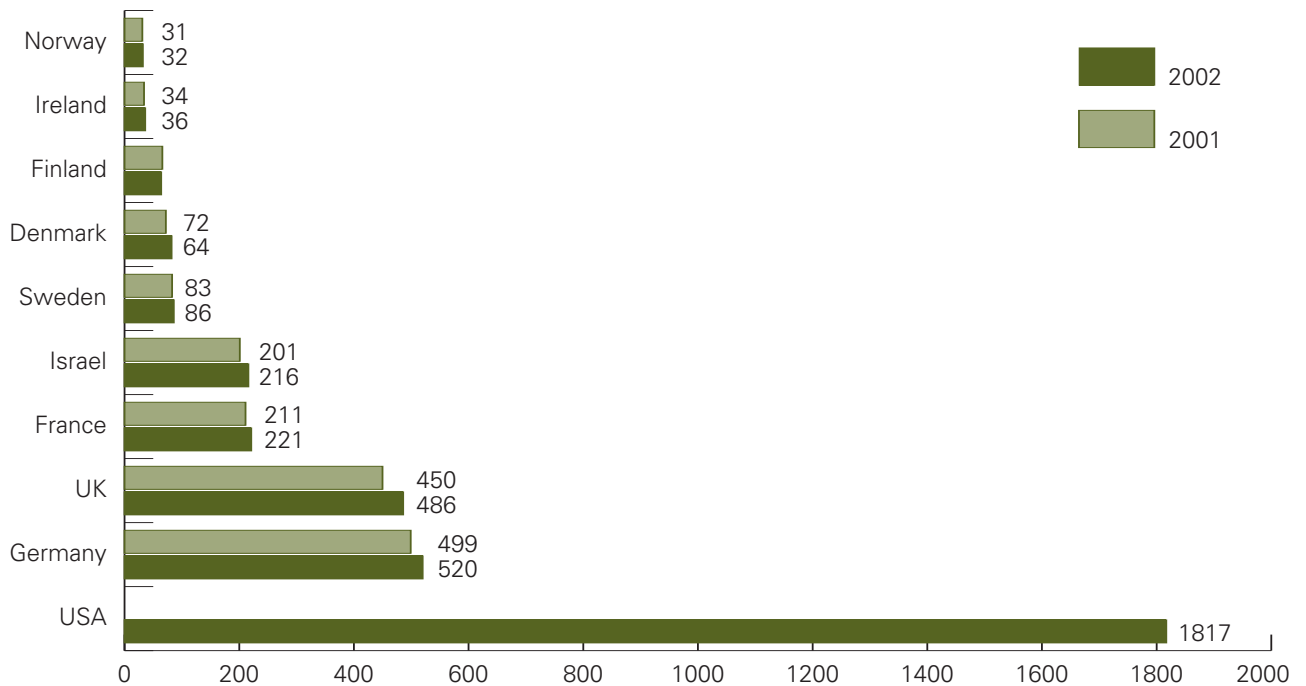
Finally, we believe that the extrapolated totals given in this report can be used with confidence, as in each case they are based on a solid foundation of real, verifiable data. For example, 85% of the Total employment figure for the ten countries studied is made up of known, verifiable employee numbers, with only 15% being extrapolated. The corresponding ratios for Total revenues and Total R&D expenditure are 74% and 51% respectively.

# Key Findings

## Number and distribution of companies

At the end of 2002 there were 1743 biotechnology companies in the nine European countries surveyed – an increase of 116 over the 2001 total. By contrast, we have identified 1817 companies in the United States at the end of 2002, which are discussed in more detail later.

### Total number of companies by country in 2001 vs 2002



The number of companies is the least meaningful of the metrics we have surveyed, since it bears little or no relation to the economic contribution made by a biotechnology sector to its national economy. As a result, we believe that little reliance should be placed upon it and that one should look to more insightful comparisons of national biotechnology performance.

As far as critical mass of companies is concerned, the European biotechnology sector falls into four tiers. Tier 1 is occupied by Germany and the UK, both of whom have over 450 companies. However, as discussed below, the UK sector is significantly larger and more robust than Germany on virtually all other metrics considered. France and Israel occupy the second tier, each with more than 200 companies, followed some way behind in Tier 3 by Sweden, Denmark and Finland, each of whom has between 50 and 100 companies (although Denmark has two of Europe's most significant players). Ireland and Norway make up the final tier of countries with less than 50 companies each.

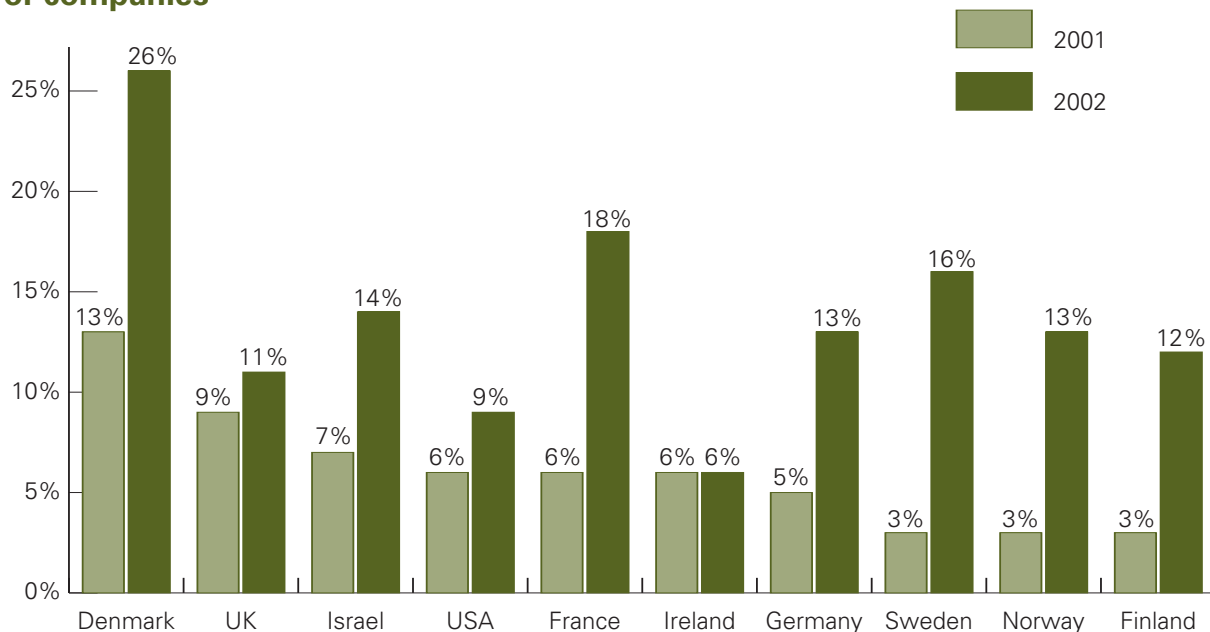
<b>Total no. of companies</b>	<b>2002</b>	<b>2001</b>	<b>% change</b>
USA	1817		
Europe:			
Germany	520	499	4
UK	486	450	7
France	221	211	5
Israel	216	201	7
Sweden	86	83	3
Denmark	82	72	12
Finland	64	66	-3
Ireland	36	34	6
Norway	32	31	3
Europe Total	1743	1647	6

## Rate of new company formation in the US, the UK and Europe

From 1996 through 2001 the UK created new companies at a fairly constant rate of about 50 new entities per year. In 2002 this fell to 42 companies – a modest fall in relative terms, compared to many of its international peers.

Indeed, the fairly steady rate of new company creation in the UK is in marked contrast to the frenetic bursts of activity that have been such a feature of the French, Danish, German and Swedish biotechnology sectors in recent years. The UK's share of European biotechnology companies appeared to be dropping from around 31% in 1999 to 28% in 2002. However, 2002 marked a turning point. New company formations fell across Europe from 224 in 2001 to 116 in 2002. (Over the same period the rate of new company formation in the USA halved to 103 companies). Of particular note were the dramatic slowdowns in Germany (from 64 to 25), France (37 down to 14) and Sweden (from 12 down to 3). One of the main causes was the paring back of start-up funding as venture capitalists instead focused their attention on providing intensive care and survival funding for their existing portfolio companies. It is worth noting that we are aware of a number of companies that have been formed, but awaiting activation until the funding environment, and hence their chances of commercial success, have improved.

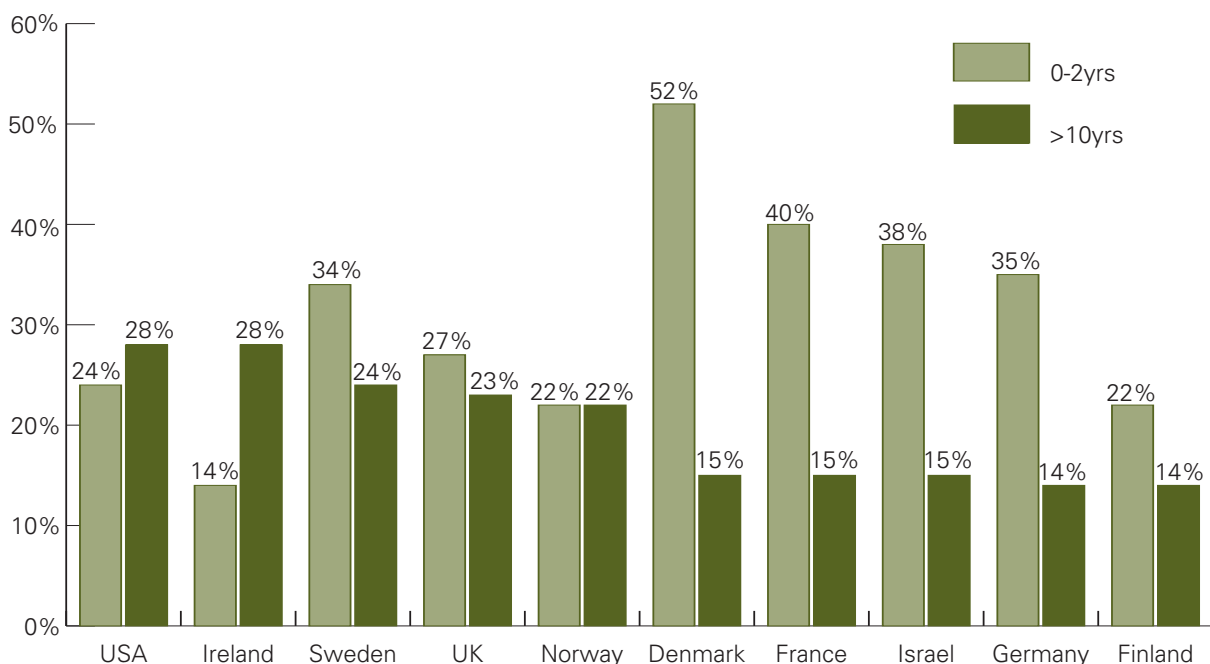
### New company formation in 2001 and 2002 by country as a % of total number of companies



The chart above brings the comparative maturity of the European and US biotechnology sectors into sharp relief. As can be seen, the recent dash for growth made by Denmark, France, Germany and Israel is built upon only a modest foundation of mature companies. This is in contrast to the UK, which displays a maturity-youth profile more akin to that of the USA. Clearly,

this analysis does not take into account the financial and technological resources underpinning either company age-band. The analysis of employee numbers by maturity of company shown below does, however, provide evidence that the UK sector is, arguably, built upon a more robust and ultimately sustainable foundation than that of some of its European peers.

### National sector maturity: 2002 (number of companies as % of total number of companies)



## Activity profile of European and US companies

In 2002 Human Healthcare companies were the dominant force in the European biotechnology landscape, accounting for 39% of companies. Service and Technology Service Providers made up 32% of the industry, Biodiagnostics companies represented a further 17%, and Agbio and Environmental companies have a 12% share. As discussed later, the activity profile of the US sector was broadly in line with that of its European peers.

The European industry has undergone a dramatic shift in its complexion since the mid-1990s. In 1995, for instance, Human Healthcare companies represented 28% of the industry. There were an almost identical number of Service and Technology Service Providers, taking almost a 28% share, followed by Biodiagnostics companies (22%) and Agbio and Environmental companies (22%).

Our analysis shows that the most dynamic national markets are those in which an increasing emphasis has been placed on the Human Healthcare and Technology Service Provider sectors. Those countries where the Agbio and Environmental segments have significant shares are likely to be among the laggards in making the transition into global biotechnology powers.

National activity profiles differed from the European average in a few notable instances. Human Healthcare companies accounted for 42% of UK companies. Germany (39%) and Denmark (36%) both had a disproportionately high number of Service Provider and Technology Service Provider companies. Norway is the one country in which

Agbio companies (19%) feature to any great extent, although this is due in large part to its strength in aquaculture. Biodiagnostics companies (28%) feature most prominently in the Irish sector's activity profile.

## Employee numbers in the UK and Europe

Employment in biotechnology is a key metric because it is a more substantial measure of wealth creation potential than company numbers and an earlier indicator than revenue generation. In order to assess the UK's performance, we analysed two metrics:

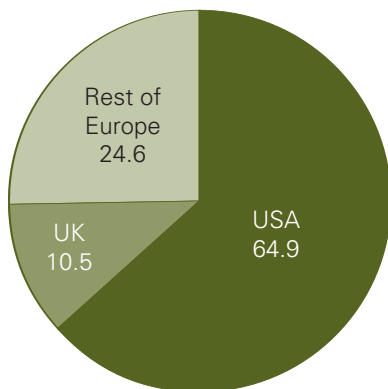
- overall employment figures - since these will reflect the size of a country as well as other factors; and
- size and employment performance relative to national populations.

## Overall employee numbers

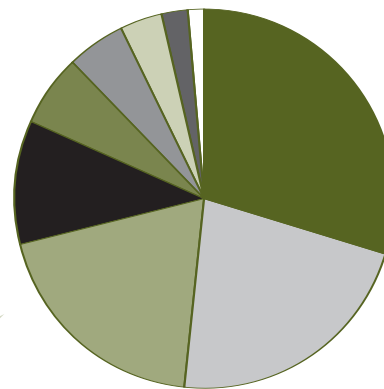
In 2002 the UK biotechnology sector, which accounted for 26% of Europe's biotechnology companies, employed:

- 26,000 people – 30% of the European total;
- 1,900 people in Agbio (35%);
- 2,450 people in Biodiagnostics (23%);
- 770 people in the Environmental sector (31%);
- 13,600 people in Human Healthcare (28% - or 37% if one discounts Denmark's Novo Nordisk);
- 6,400 people in the Service Provider sector (39%); and
- 730 people in the Technology Service Provider sector (17%).

### Home employees: (Europe & USA) in 2002 as % of regional total



### Home employees: (Europe) in 2002 as % of regional total



UK	10.5
GERMANY	7.7
DENMARK	6.8
FRANCE	3.7
ISRAEL	2.2
IRELAND	1.7
SWEDEN	1.3
FINLAND	0.8
NORWAY	0.4

Total home employees	2002	2001	% change
USA	159600	na	na
Europe:			
UK	25900	24400	6
Germany	18800	16700	13
Denmark	16700	15300	9
France	9100	7900	15
Israel	5300	4800	10
Ireland	4200	5800	-28
Sweden	3200	2800	14
Finland	2000	1700	18
Norway	1000	1000	0
Europe Total	86200	80400	7

At the sub-sectoral level, the UK accounted for a disproportionately high share of total European employment in the Biopesticides (57%), Crop agriculture (45%), Biocleaning (60%), Biomaterials (40%), Contract manufacturing (43%) and Contract research (54%) sub-sectors. The UK may owe its strength in the latter two sub-sectors to its strong history of pharmaceutical research.

On the other hand, the UK employs comparatively few of Europe's employees in the Environmental diagnostics (6%), Gene therapy (12%), Bioprocessing (4%) and Functional genomics (2%) areas.

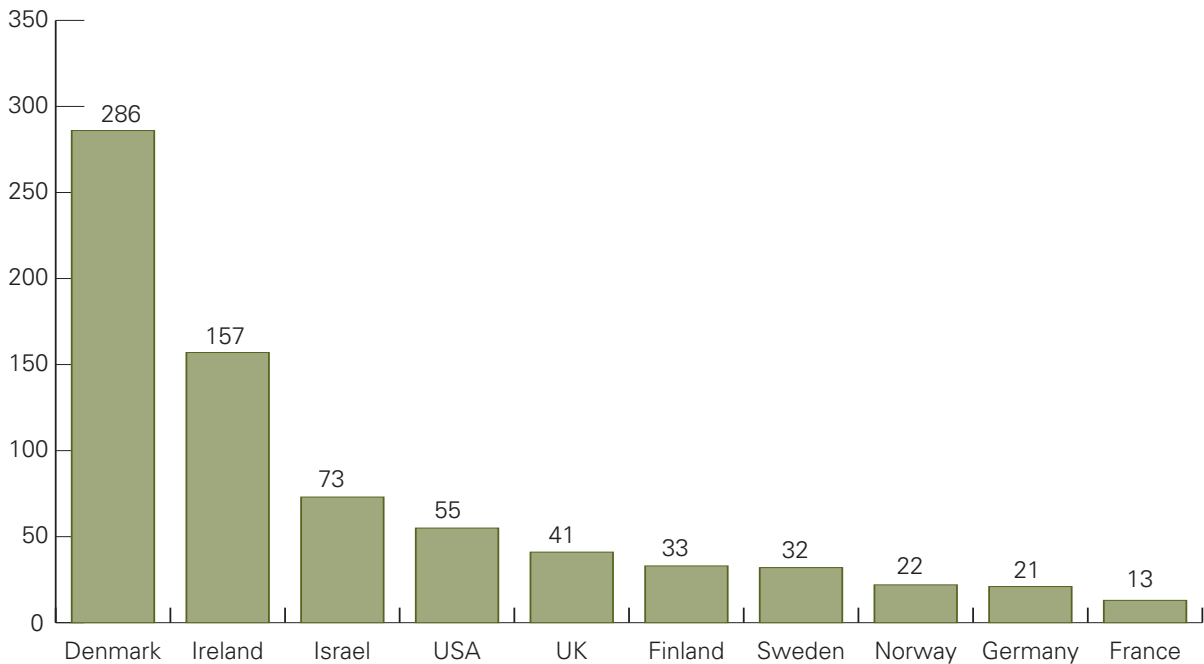
### Biotechnology employment relative to national populations

The national resource base must, we believe, provide part of the benchmark by which comparative employment levels in biotechnology are assessed. When the total employees in a country are divided by that country's population, national achievements are put in perspective.

The chart below shows that Denmark and Ireland outstrip the rest of Europe and the US in the number of biotechnology employees per head of population. Both countries have small populations, but are home to one or two very large companies

– Novo Nordisk and Novozymes in the case of Denmark, and Elan in Ireland. Among the larger biotechnology players, the UK comes closest to the US, with Germany and France achieving only half or a third, respectively, of the penetration levels in the UK.

### Home employees: 2002 per 100,000 head of population



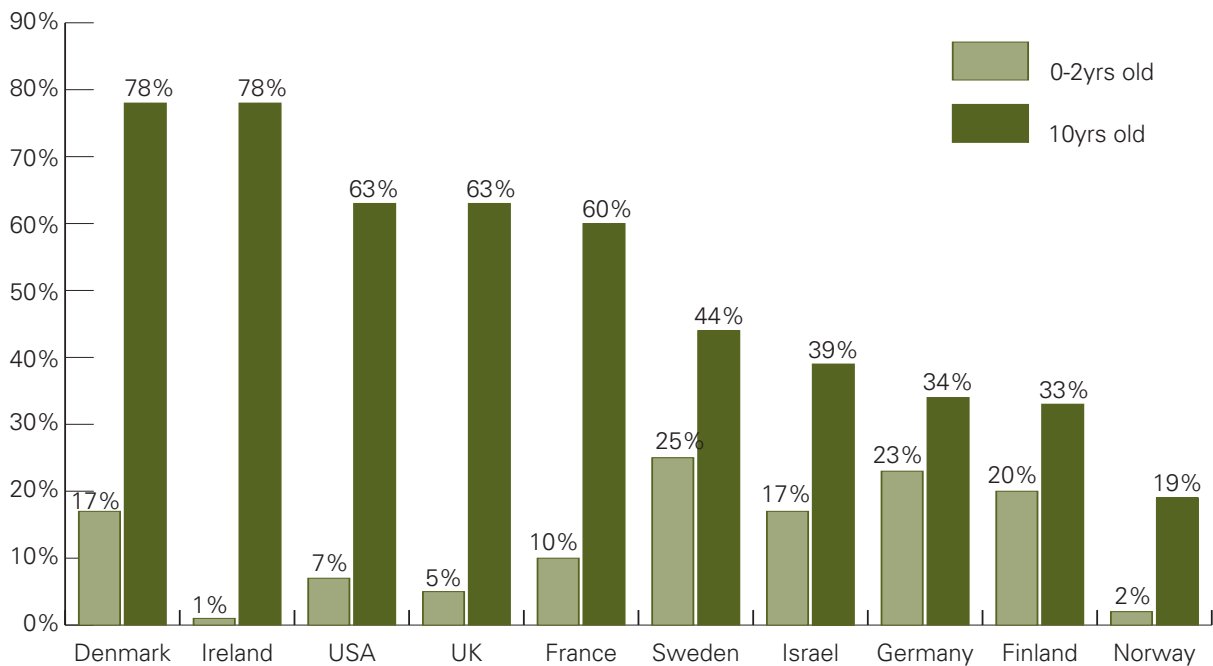
### Comparative sector maturity and employment levels

We believe that the ratio of employees in the youngest and oldest age-bands is a useful starting-point for evaluating the maturity and sustainability of national biotechnology sectors because, to a large extent, a company's ability to withstand market volatility and to provide significant and stable levels of employment increases with age.

As the chart below illustrates, nearly two-thirds of UK and US biotechnology employees work for companies that are at least ten years old. In Germany and Scandinavia (if one discounts Denmark's Novo Nordisk) the ratio is closer to one-

third. France appears closer to the UK and US than the other European nations, but this is largely due to the presence of the global diagnostics company, Biomerieux. It also shows that Sweden, Germany and Finland's employment bases are significantly more dependent on companies under two years old and therefore, it might be argued, are more vulnerable than those of the other countries studied.

## Home employees: relative dependency on older vs younger companies



## Comparative revenues

Revenue generation is a direct measure of the contribution of biotechnology companies to national wealth. In 2002 UK companies generated €6.4 billion (32%) of the €20.47 billion revenues generated by the European sector.

This represents a 22% increase in the UK sector's 2001 turnover and maintains the UK's position as Europe's highest revenue generator. (2002 revenues for the US were, incidentally, €36 billion, almost six times the UK figure).

Germany and France increased their earning by a similar percentage to the UK, while earnings in Sweden and Finland grew substantially between 2002 and 2001, albeit from a small base. The individual companies driving revenue growth in each country are discussed in the **Country Profiles** section.

UK companies made particularly significant revenue contributions in a number of sub-sectors, namely:

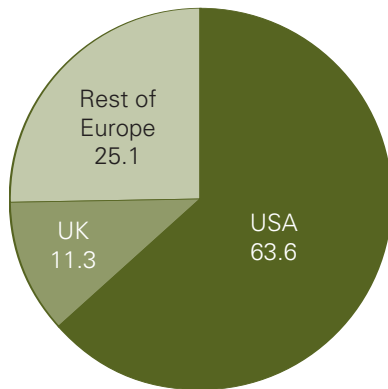
- Biocleaning (69% of the European total);
- Biopesticides (67%);
- Vaccines (64%);
- Contract Research (50%);
- Contract Manufacturing (55%); and
- Crop Agriculture & Horticulture (49%).

The UK's comparative revenue contribution was significantly below average in:

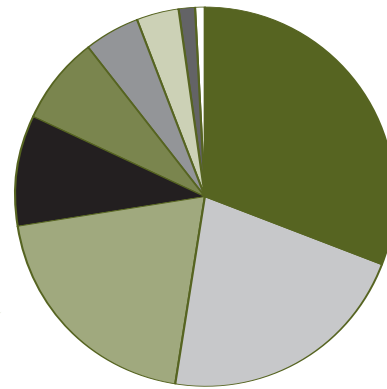
- Environmental Diagnostics (1%);
- Functional Genomics (3%); and
- Gene Therapy (8%).

Across the Human Healthcare sector as a whole, the average UK company generated 18% higher revenues than its European counterparts. However, within Drug Discovery – the largest sub-sector – the average UK company generated revenues 13% lower than its European peers.

### Regional revenue as % of 2002 total revenues



### National revenue as % of 2002 European total



UK	11.3
GERMANY	7.9
DENMARK	7.3
FRANCE	3.5
IRELAND	2.7
ISRAEL	1.7
SWEDEN	1.3
FINLAND	0.5
NORWAY	0.3

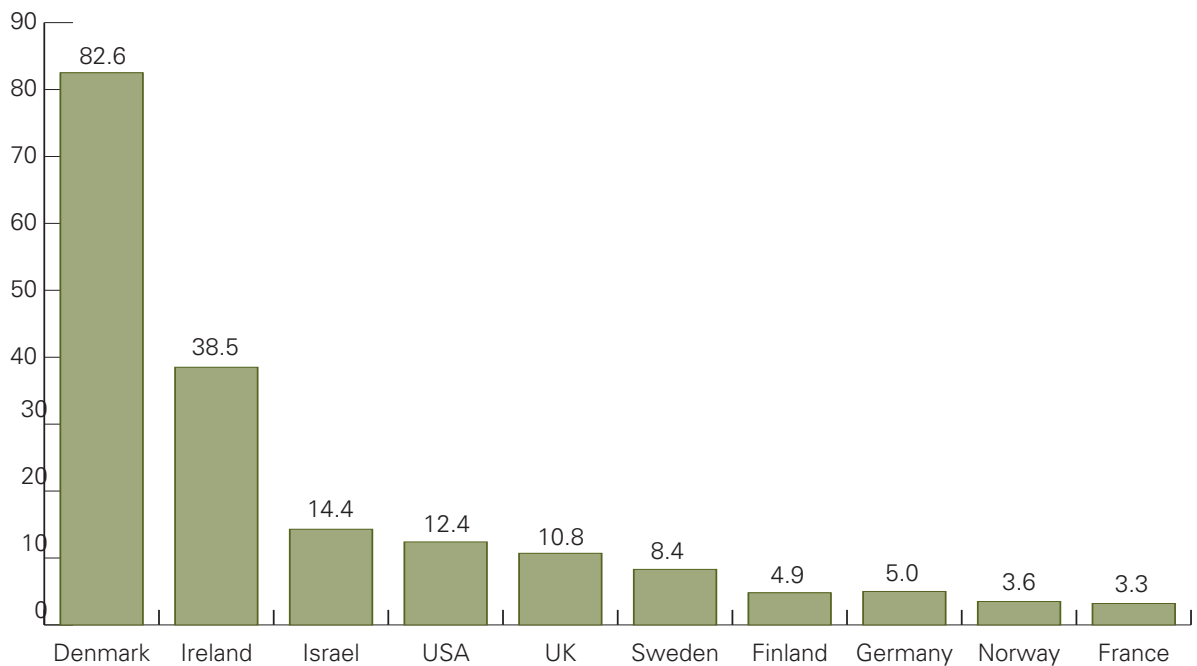
### Comparative revenue growth 2001-2

Revenue (€m)	2002	2001	% change
USA	35830		na
Europe:			
UK	6360	5220	22
Denmark	4440	4370	2
Germany	4110	3480	18
France	1950	1550	26
Ireland	1500	2170	-31
Israel	950	830	14
Sweden	750	350	114
Finland	250	100	150
Norway	160	140	14
Europe Total	20470	18210	12

A comparison of biotechnology revenues generated per head of population provides a useful, albeit high-level, indicator of the comparative economic contribution being made by national biotechnology sectors. The chart below shows that in 2002 the UK and Israel's revenue generation performance, on a per capita basis, was on a par with that of the USA, while that of France and Germany, in particular, lagged some way behind. Once again, Denmark and Ireland's strong performance on this measure are distorted by Novo Nordisk and Elan, respectively. National rankings, on revenues per head of population, are thus broadly the same as those for biotechnology employment per capita shown above. (It should be noted that this analysis is based on the total, as

opposed to domestic, revenues generated by each company and, in the case of holding companies, their subsidiaries. For example, the revenues generated by Shire Pharmaceuticals' overseas operations are included in our calculations).

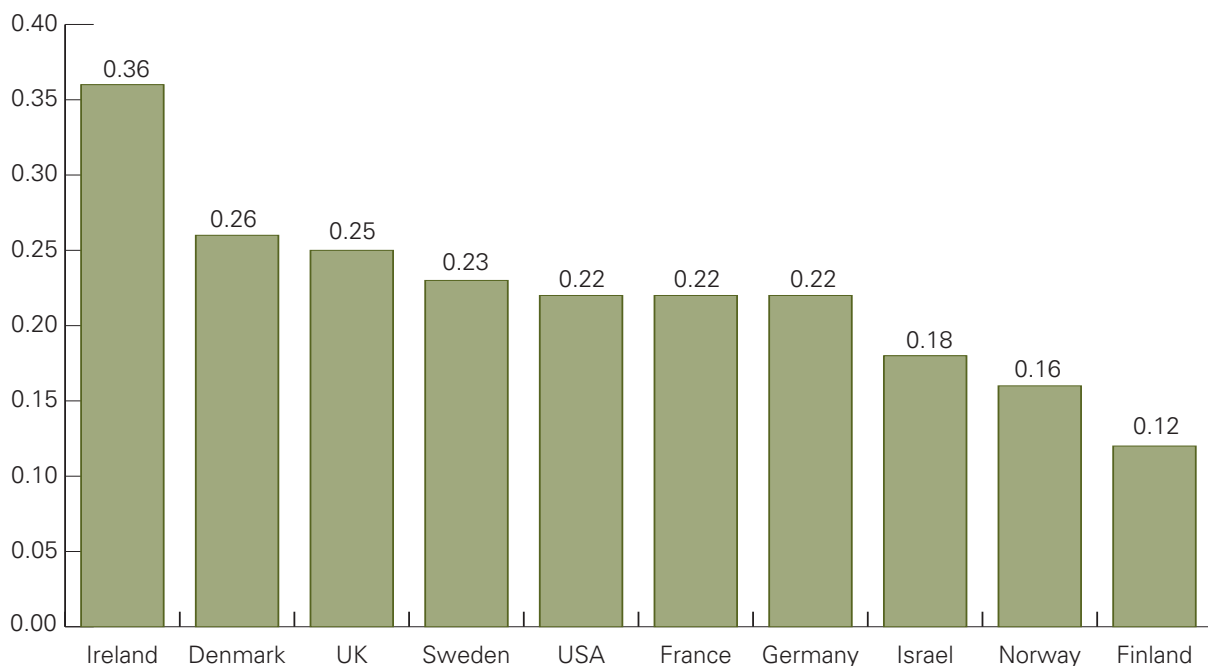
### Revenue: 2002 per 100,000 head of population (€m)



The rankings do, however, change somewhat if one analyses revenues generated per home employee. Such an analysis is, of course, subject to the same distorting effect of using group-wide revenues as that above. However, in many cases it is not possible to isolate revenues attributable to a company's domestic operations from those generated abroad as some

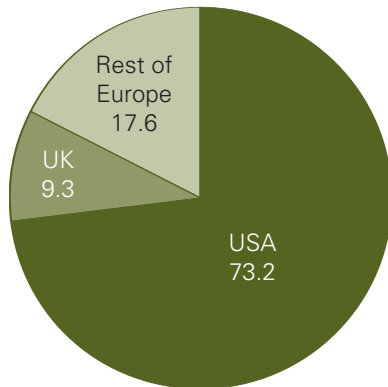
companies report their revenues only on an aggregated basis. As the following chart shows, the UK outperforms the USA on this measure, while the German and French sectors are on a par with the USA. That said, in most countries annual revenues attributable per home employee fell within the relatively narrow 220,000-260,000 band.

### Revenue: 2002 per home employee (€m)

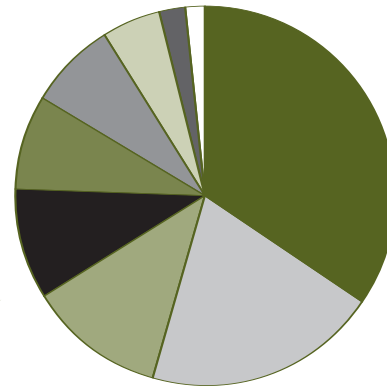


## Comparative R&D spending

**Regional R&D spend as % of 2002 total R&D spend**



**National R&D spend as % of 2002 European total R&D spend**



Country	R&D Spend (€m)
UK	9.3
GERMANY	5.4
DENMARK	3.2
ISRAEL	2.5
FRANCE	2.2
IRELAND	2.0
SWEDEN	1.4
FINLAND	0.6
NORWAY	0.3

R&D Spend (€m)	2002	2001	% change
USA	22100	na	na
Europe:			
UK	2800	2270	19
Germany	1620	1140	30
Denmark	970	850	11
Israel	740	540	27
France	670	560	16
Ireland	600	540	10
Sweden	410	330	20
Finland	190	150	21
Norway	90	70	22
Europe Total	8090	6460	20

R&D spending is regarded by many as a defining feature of the biotechnology universe. As the pie-charts above indicate, R&D spending in the United States dwarfs that of any European nation or, indeed, of Europe as a whole. While US companies spent approximately €22 billion on R&D in 2002, European companies spent just over €8 billion. The causes and corollaries of this are explored later in greater depth in the section entitled **Europe and the USA compared**.

In 2002 the UK accounted for 35% of Europe's total R&D spend, a figure that is slightly ahead of both its share of employees (30%) and its revenues (29%), and disproportionately high compared with its share of companies (26%).

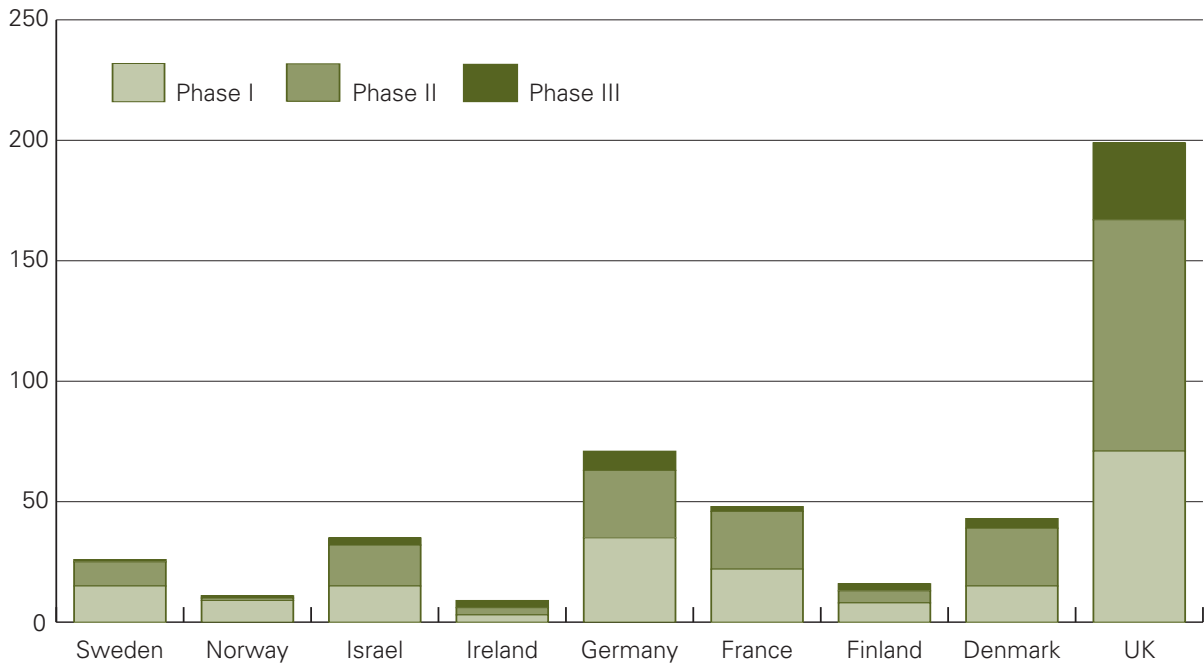
In the highly competitive Human Healthcare arena, the average UK company invested €11 million in R&D – over 30% more than its European peers. Interestingly, the number of R&D employees per company is not significantly different, with the exception of Genomics and Vaccines companies, which on average had twice as many R&D employees as their European counterparts.

In 2002 the average R&D spend per R&D employee in the UK was €230,000, mid-way between that of its European (€210,000) and US (€255,000) peers.

## Product development pipelines

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Phase I	15	9	15	3	35	22	8	15	71
Phase II	10	1	17	3	28	24	5	24	96
Phase III	3	1	3	3	8	2	3	4	32

### Human healthcare products in Phase I to III clinical trials (2002) by country



Based on our analysis, at the end of 2002 Europe’s 677 Human Healthcare companies had 582 products on the market, a further 43 awaiting approval, and 463 in clinical trials. (The comparable figures for the USA were 666 products on the market, 60 awaiting approval and 1114 in clinical trials). We have identified just under a thousand further products at either the preclinical or feasibility stage. It should be borne in mind that the above numbers include products developed by Biomaterials and Drug Delivery companies, many of which enjoy either an unregulated or less regulated route to market than therapeutic products.

At the end of 2002 the UK had the most extensive pipeline with 225 products in the clinic or awaiting approval. It was

also the most mature, accounting for 32 of the 61 compounds that were in Phase III trials and 26 of the 43 awaiting approval. Germany had the second highest number of compounds in the clinic at 71 (plus 3 awaiting approval), followed by France with 48.

The combined biotechnology sectors of the countries covered in this survey compared favourably with pharmaceutical industry benchmarks. In 2002, AstraZeneca, the British pharmaceutical giant, posted revenues of €17.02 billion, invested €2.93 billion in R&D, and a pre-tax profit of €3.85 billion. At the end of 2002, the company had 8 compounds in Phase III trials, 6 compounds in Phase II trials, and 11 compounds in Phase I trials.

## Equity markets

Biotechnology companies found 2002 a difficult year in which to raise equity capital. European companies raised €1.98 billion – about half the 2001 total. By comparison, their US peers raised almost 3.4 times as much as their European peers. At the same time valuations of biotechnology companies listed on public markets also declined across the globe.

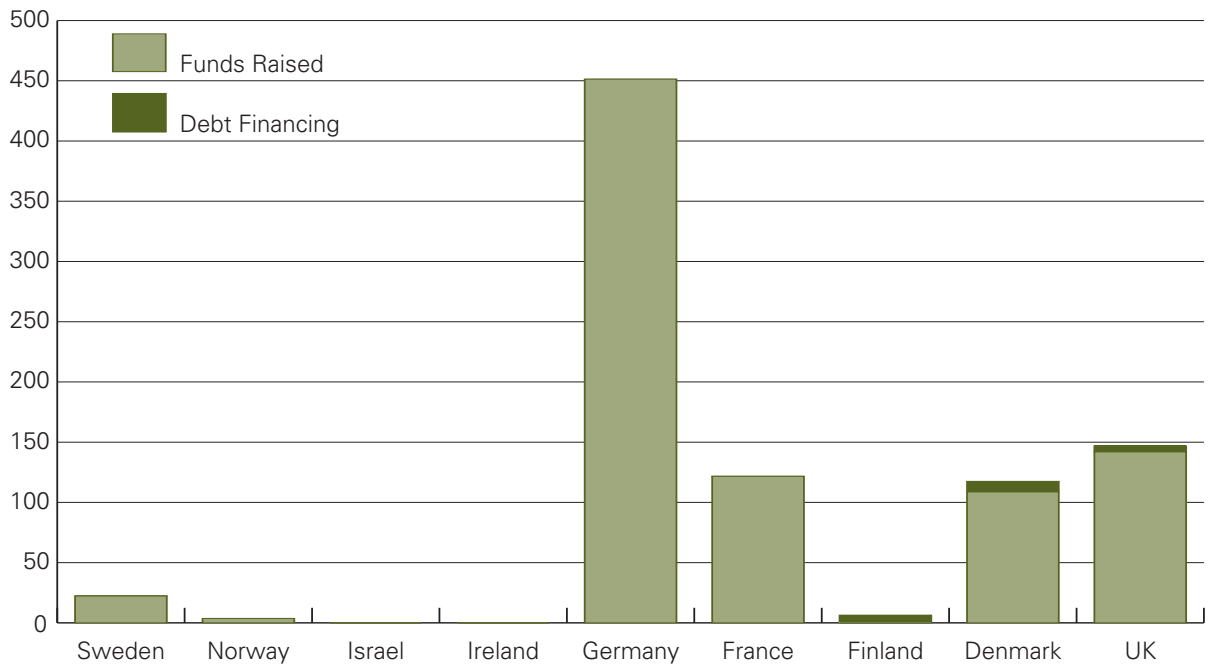
While the sums going into the UK sector were much lower than in 2001, British biotechnology companies still raised more money through equity sales than any other European nation. The only European companies to achieve initial public offerings in 2002 were also British, namely Cobra Biomanufacturing, Cyprotex and NeuTec Pharma. German fundraising during 2002 held up remarkably well given the dire share price performances of its public companies. This in part reflects the decisions among German venture capitalists to make adequate provision for those companies deemed most likely to survive the current bear market and achieve longer term sustainability, instead of pursuing new investment opportunities. French and Danish biotechnology equity investments also held up strongly as both countries continued their push to promote the creation of new biotechnology companies.

Equity funds raised (€m)	2002	2001	% change
USA	6671		
Europe:			
UK	670	1907	-65
Germany	644	695	-7
France	354	369	-4
Sweden	93	285	-67
Denmark	193	115	68
Israel	11	191	-94
Norway	4	13	-69
Finland	37	55	-33
Ireland	12	19	-37
Europe Total	2018	3649	-45

Debt financing instruments provided US biotechnology companies with another substantial source of finance. US biotechnology companies were able to raise an additional €4.3 billion through debt in 2002 – which included a €2.7 billion convertible offering completed by Amgen alone. In contrast, European companies raised just over €200 million using debt, with UK companies attracting the lion's share. Raising finance through debt only works if companies have an ability to pay it off – i.e. a revenue stream or at least the promise of one. The more mature a sector, the more likely it will be able to obtain debt finance.

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Funds Raised	22.24	3.67	0	0	451.33	121.62	0.02	108.65	141.88
Debt Financing	0.04	0	0	0	0	0.07	6.38	8.84	5.04

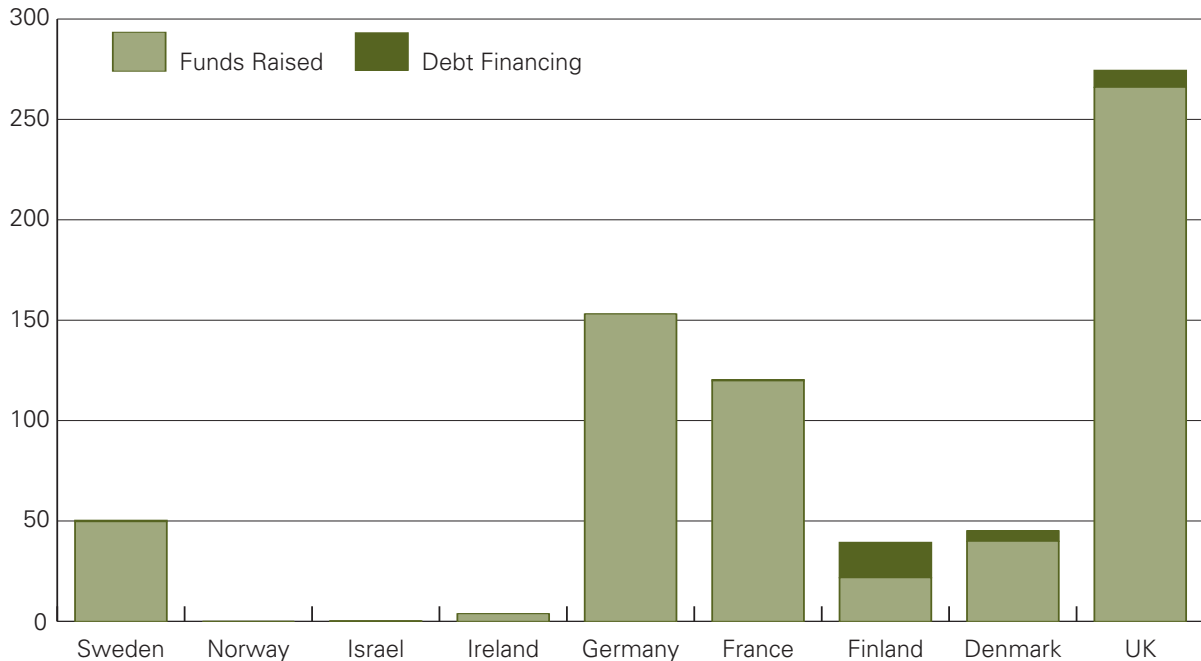
**Funds raised (2002) by 0-2yr old companies by country (€m)**



In 2002 more companies under 5 years old secured equity investment than those over 5 years of age. Most of the funds raised by companies in the 0-2 year old age band were from angel networks, seed funds or venture capitalists. There were some notable high velocity start-ups attracting large bonuses of cash including the €375 million leveraged buyout in Germany of Viatris from Degussa Group and France’s ProSkelia, a spin-out from Aventis, which raised €60 million in a first round. Not surprisingly, very little debt was raised by this age group. While European companies under three years old raised €474 million in equity, their US peers raised €1.88 billion.

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Funds Raised	49.63	0	0.2	3.8	153.1	119.78	21.7	39.88	265.98
Debt Financing	0.76	0	0	0	0	0.64	17.69	5.26	8.5

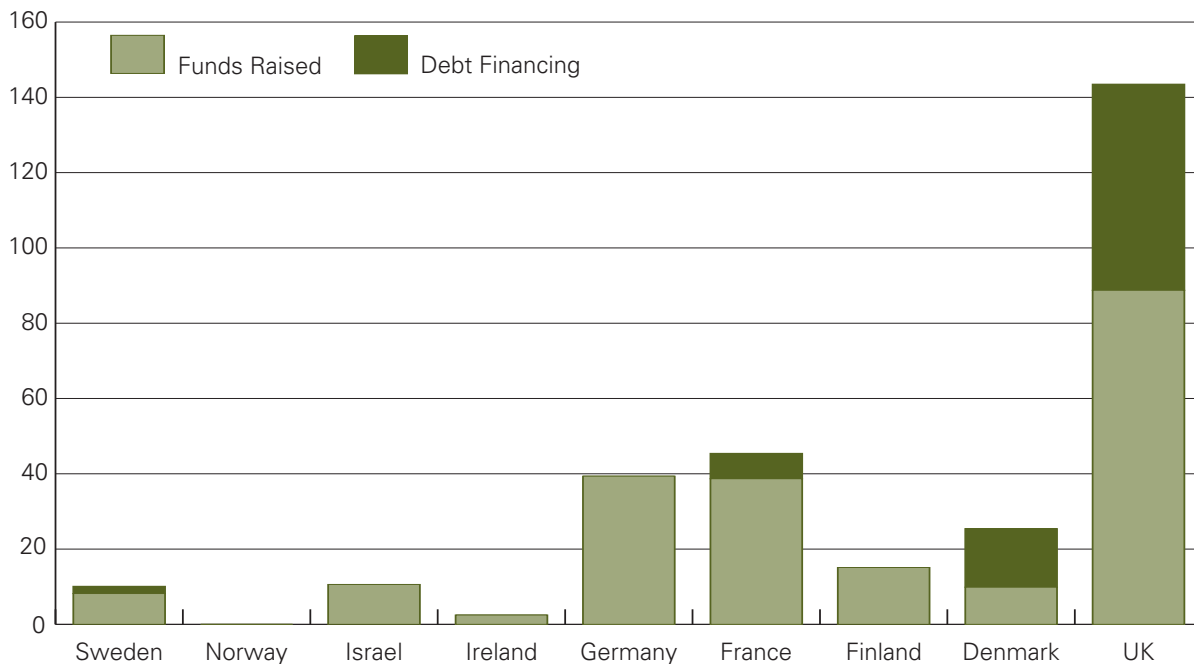
### Funds raised (2002) by 3-5yr old companies by country (€m)



Venture capital was also the primary source of equity finance for 3-5 year old companies, although some were able to sell equity to strategic partners as part of biopartnering activities. In Europe, the UK biotechnology sector was again the prominent fundraiser, with a number of pre-IPO companies raising venture capital to drive their development programmes, as well as three companies raising finance through initial public offerings. Similarly, a number of pre-IPO US biotechnology companies were able to attract large tranches of VC money. Also some publicly quoted companies – mainly in the US – were able to attract funds through rights issues and secondary offerings. Again, given the relative immaturity of the age group, debt was not a prominent source of finance.

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Funds Raised	8.18	0	10.59	2.48	39.37	38.68	15.1	9.87	88.73
Debt Financing	1.94	0	0	0	0	6.76	0	15.57	54.76

### Funds raised (2002) by 6-10yr old companies by country (€m)



By the time companies reach the 6-10 year old age band, their reliance on venture capital has all but disappeared. Our analysis shows, however, that for US companies this is the time when they are most likely to raise large sums of finance as they drive their companies towards building sustainable businesses (see **Europe and the USA compared** later). Private companies were raising money from alternative sources such as strategic partners or institutional investors with an interest in non-public equity. Publicly quoted companies also tend to raise additional funds through a series of instruments including follow-on offerings, rights issues and even via PIPEs.

It is clear that European companies have a problem at this stage of the growth cycle. It is apparent that their ability to raise large sums of money, either by selling shares or through debt is way down on that of their US counterparts. It is not uncommon to see US biotechnology companies of this age raising €100 million plus in either follow on transactions or convertibles. In 2002, European companies in this age group raised almost €200 million by selling equity and €79 million through debt. In contrast, US companies raised €1.36 billion in equity and €276 million in debt.

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Funds Raised	7.07	0	0	0	0	0.01	0	0	91.85
Debt Financing	1.58	0	0	0	0	6.76	0	0.36	53.53

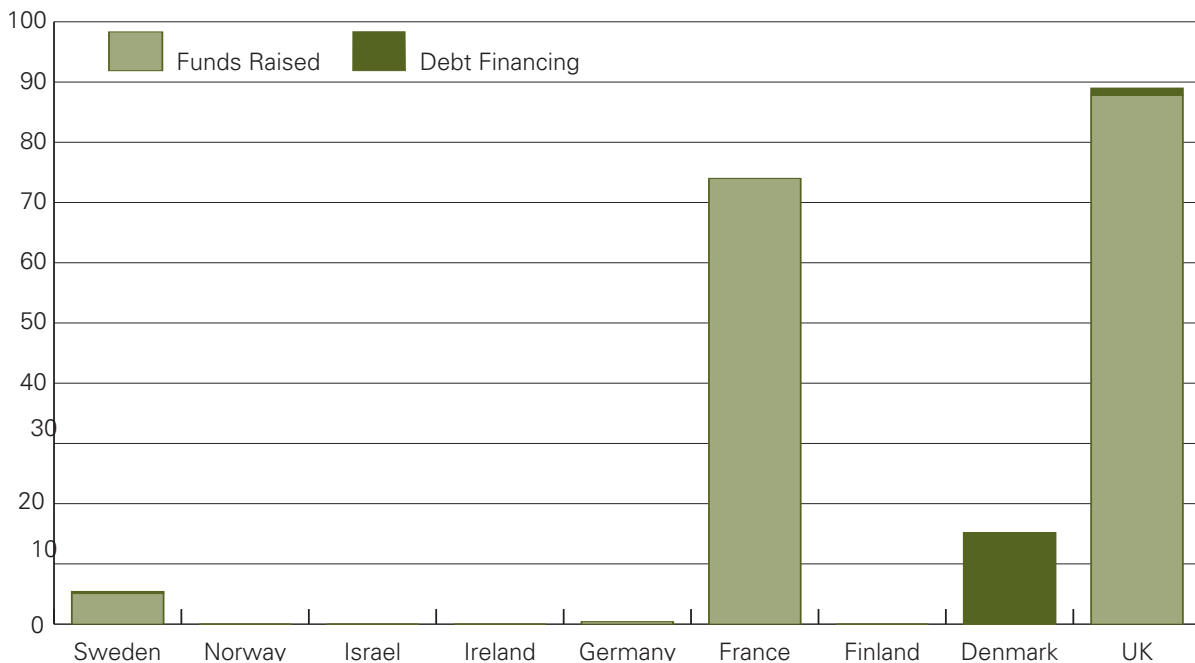
**Funds raised (2002) by over 10yr old companies by country (€m)**



Companies over 10 years old tend to have reached the stage where they are generating both sustainable revenues and profits. Their need to raise finance from external sources becomes less important. Consequently, the financing needs of companies in the 10-15 year old are reduced. Companies are just as likely to raise additional funds through debt as they are by selling equity. In many cases the equity stakes are sold as part of biopartnering activities. In 2002, European companies between 10 and 15 years old raised €92 million in equity and €62 million in debt. Their US peers raised €982 million of equity and a further €905 million of debt, respectively.

	Sweden	Norway	Israel	Ireland	Germany	France	Finland	Denmark	UK
Funds Raised	5.7	0	0	0	0.41	74	0	0	87.77
Debt Financing	0.36	0	0	0	0	0	0	15.21	1.23

**Funds raised (2002) by over companies 15yr old 0r more by country (€m)**



Companies over 15 years old are likely to have access to both sustainable revenue and profit streams, and thus tend to raise equity or debt only when they wish to finance specific projects or acquisitions. During 2002, European companies such as France’s Ethypharm, which had hoped to complete an IPO, and the UK’s SkyePharma, were among those raising money through equity deals. US companies in this age-band raised almost €1.14 billion in various equity transactions and, led by Amgen’s €2.64 billion offering, more than €3 billion in debt.

Biotechnology companies across the globe suffered at the hands of the public equity markets. Most national biotechnology sectors suffered brutal valuation mark downs in 2002; worst hit were some of Europe’s new markets. The Neuer Markt’s demise clearly has

had a dramatic impact not only on the fate of its listed companies but on investor confidence across the board. And it is not as if the industry was awash with bad news during 2002. Indeed, the volatility of the markets between 2000 and 2003 illustrate how much they are driven, if not more so, by emotion and sentiment as they are by fundamentals.

It is clear from the analysis of financing sources that European biotechnology companies are disadvantaged just at the point when they need large boluses of money to accelerate their development. Companies that are six or more years old cannot expect to rely on private equity sources to finance their attempts to build genuinely sustainable businesses. US companies have historically been able to tap into the public capital markets repeatedly from IPO and subsequent follow-on offerings.

It is not clear when European biotechnology companies will enjoy similar levels of access. Indeed, a major financing issue facing most European biotechnology companies is that of liquidity, or rather the lack of it. Trading volumes of European-listed biotechnology stocks are much lower than major biotechnology companies trading on the US exchanges. During 2002, the aggregate average daily volume of Europe's 100 public companies – including companies in countries not covered by this survey – was about 30 million compared with 115 million for the 100 largest US biotechnology companies. Moreover, a disproportionate share of the volume is concentrated in a few companies. Europe's five largest biotechnology companies account for about half the sector's total volume.

So even if European companies held an equivalent standing to their US peers it is likely that there would still not be enough liquidity for the major institutions to provide sufficient support. The practical inability of funds to exit stocks rapidly acts as a very strong deterrent to taking positions in local microcap companies even if the investor believes strongly that the stock will yield some near term upside. In addition, the relatively arcane regulatory rules on the main European exchanges make follow-on offerings difficult. Even in bear markets, US companies have been able to complete secondary offerings.

# Europe and the USA compared

No single European nation – not even the UK – compares with the USA in the sheer scale of its biotechnology effort. However, a comparison of the nine European nations, taken as a whole, to the US biotechnology sector is informative.

By the most basic metric – company counts – Europe compares well against the US. There were 1817 US companies that fitted the definitions of biotechnology used in this study and 1743 in Europe. The number may even be converging since the USA formed fewer companies (103) in 2002 than did Europe (116). It is certainly the case that a European grouping also containing Switzerland, Belgium, The Netherlands, Spain and Italy would register more companies than the USA: we estimate that this enlarged Europe would have had over 2000 biotechnology firms in 2002 and probably over 2100 by the end of 2003.

The distribution of the companies among the various sectors is broadly similar, too, with Human Healthcare companies representing the biggest sector in each geographical area (904 companies in the US, 677 in Europe), followed by Service Providers and either Technology Service Providers (the third biggest group in the US, and fourth

biggest in Europe) or Biodiagnostics (fourth biggest in the USA, and third in Europe). Agbio companies constitute the fifth biggest class, with Environmental companies the smallest in each case. Perhaps surprisingly, the number of European Agbio and Environmental companies employing exclusively biological techniques – 144 and 74, respectively – exceeds that in the US – 91 and 19 respectively.

That, more or less, is where the similarities end, and also where any vestiges of European superiority end, too. Across a whole raft of other metrics, the European group taken as a whole tends to be smaller, slower, less intensive and generally more prone to failure (or, at least, less prone to success) than their US counterparts. They attract less money, spend less, and generate less income. They hire fewer people, increase head-count more gradually, and employ proportionally fewer in research and development. In 2002 the European Human Healthcare group entered half as many product candidates into pre-clinical trials and had around 60% fewer compounds in clinical studies.

Analysing the employment figures provides a good starting point for getting to the differences underlying the

comparative performance of US and European companies. Although the number of companies in each region is roughly the same, US companies employed approximately 83% more people (160,000) in 2002 than their European peers (87,000). In Human Healthcare, the US figure of 97,000 is over twice the European equivalent. Among Technology Service Providers, nearly three times as many people are employed by US companies than by Europeans. Even in Agbio and Biodiagnostics, where the numbers of US companies are substantially lower, employment levels are higher.

The number (and proportion) of employees involved in R&D, too, is substantially higher in the US than in Europe. Our analysis indicates that there are around 87,000 US R&D employees (54% of total employees) compared with 38,000 in Europe (43% of total employees).

One key factor in the differing employment levels, of course, is the relative maturity of companies in the two regions. Around 43% of US Biodiagnostics companies, but only 24% in Europe, are over ten years old. In Human Healthcare, 24% of US companies, but only 12% of European companies, are as old. However, this is only part of the explanation in these sectors, and cannot explain the huge differential in Technology Service Provider employment, where mature companies represent less than 10% of all companies in both Europe and the US. Neither can it account for the R&D employee figures in the US since with maturity usually comes an influx of manufacturing, sales, and marketing personnel that reduces the relative proportion of R&D employees.

A more complete explanation may come from the observation that US companies grow much faster. Our preliminary investigations support this proposition. The table below looks at the average employee numbers across all the sectors by age-band. Companies in our most mature age-band have been excluded from the analysis because the category – older than 15 years – is open-ended. The startling conclusion from this data is that in every sector except for Service Providers (where there is approximate parity) the average employee levels in US companies are equivalent to the levels one age-band later (or more) in European companies.

Thus in Agbio, an average employment of 30 people – attained in Europe by companies more than ten years old – is reached in the US by 3-5 years. The mean US Biodiagnostics company in the 6-10 year old group is larger than the mean European company in the 11-15 year band. Staffing levels in Human Healthcare companies start at parity but diverge thereafter.

Average number of employees per company						
Region	Sector	Age - years				
		0-2	3-5	6-10	11-15	
USA	Agbio	20	60	33	107	
Europe	Agbio	14	15	18	31	
USA	Biodiagnostics	22	22	73	83	
Europe	Biodiagnostics	9	27	28	57	
USA	Environmental	63	25	50	17	
Europe	Environmental	0	6	25	17	
USA	Human healthcare	26	44	79	173	
Europe	Human healthcare	23	33	47	122	
USA	Service providers	24	28	34	81	
Europe	Service providers	32	19	32	58	
USA	Technology service providers	24	42	176	94	
Europe	Technology service providers	12	33	34	62	

This “one age-band ahead” advantage persists in other metrics at which we have looked. As might be expected from the higher proportion of R&D employees across the board in the US, the differentials between Europe and the US in R&D employees are more pronounced than those for employees. As a consequence, the few Environmental companies that do exist in the US have R&D staffing levels by

the age of two years that their European counterparts never achieve. This is, to some extent, explained by the fact that European companies, thanks to a multiplicity of different national and regional regulatory regimes, have to compete in a European market that is significantly more fragmented than the domestic market in which their US peers compete.

Average number of R&D employees per company						
Region	Sector	Age - years				
		0-2	3-5	6-10	11-15	
USA	Agbio	12	20	17	26	
Europe	Agbio	7	7	8	13	
USA	Biodiagnostics	9	9	32	26	
Europe	Biodiagnostics	5	11	9	24	
USA	Environmental	33	12	25	5	
Europe	Environmental	0	2	5	6	
USA	Human healthcare	16	28	50	104	
Europe	Human healthcare	16	22	26	70	
USA	Service providers	13	15	18	47	
Europe	Service providers	12	10	13	32	
USA	Technology service providers	15	25	112	63	
Europe	Technology service providers	8	22	26	30	

With more R&D staff, average R&D expenditures in the US exceed those in equivalent companies in Europe. The differential is particularly pronounced for Technology Service Providers: the US companies outspend the Europeans by a factor of two in the 0-2 year company band, by a factor of three in the 3-5 year band, and by a factor of five in the 6-10 year band. This observation may go some way to explaining the virtual disappearance of European Technology Service Providers after ten years. In providing technical services, the greatest risk to a business is that the method used will be superseded by new techniques. By not investing as intensively in R&D, European companies in this sector may be increasing their exposure to this risk.

The differentials in R&D spending among Human Healthcare companies are also very marked. Levels of R&D

spending achieved by US Human Healthcare companies of 3-5 years of age are barely exceeded by their European counterparts in the 11-15 age group. Put another way, US Human Healthcare companies on average spend two to three times more than their European peers of an equivalent age. If there is a breakthrough to be made or a clinical milestone to be passed, US companies are able to back their research effort to a substantially greater level than European companies are. The product development data gathered in this survey supports the conclusion that this particular bet does pay off: US Human Healthcare companies had almost exactly twice as many compounds in preclinical studies as European companies (682 versus 344) and had more than twice as many clinical developments, too (1114 versus 463).

Average R&D expenditure per company (€m)					
Region	Sector	Age - years			
		0-2	3-5	6-10	11-15
USA	Agbio	4.19	0.36	3.61	4.89
Europe	Agbio	1.98	1.23	0.57	3.31
USA	Biodiagnostics	2.31	2.85	8.51	3.80
Europe	Biodiagnostics	0.73	3.28	1.91	2.05
USA	Human healthcare	7.81	14.95	21.02	32.12
Europe	Human healthcare	1.58	5.84	10.55	17.60
USA	Service providers	0.34	0.48	1.90	0.94
Europe	Service providers	1.21	0.44	1.14	2.83
USA	Technology service providers	1.57	9.84	24.31	11.50
Europe	Technology service providers	0.85	3.40	5.58	3.09

\*The Environment sector has been omitted because of the paucity of R&D spend data

Part of the reason why US companies are able to spend so much more on R&D is because they raise more revenue from their operations. The data indicates that the “one age-band ahead” rule still pertains with respect to revenues for Agbio and Technology Service Provider companies, very markedly so for the latter. However that

is clearly not the whole explanation for either the Biodiagnostics sector or for the numerically dominant Human Healthcare sector. Indeed, the revenues of European Human Healthcare companies closely match those of US companies across the four age-bands analysed here.

Average Revenues per company (€m)					
Region	Sector	Age - years			
		0-2	3-5	6-10	11-15
USA	Agbio	4.6	3.0	8.2	19.5
Europe	Agbio	2.3	3.8	1.6	7.1
USA	Biodiagnostics	1.4	0.7	9.0	17.8
Europe	Biodiagnostics	0.4	3.4	3.5	10.9
USA	Environmental	0.0	0.3	1.8	1.0
Europe	Environmental	0.0	0.3	4.2	0.9
USA	Human healthcare	2.8	5.8	9.7	43.8
Europe	Human healthcare	2.3	2.3	8.1	38.4
USA	Service providers	2.2	3.0	9.7	16.2
Europe	Service providers	5.1	1.8	6.7	9.8
USA	Technology service providers	0.3	6.5	38.5	2.8
Europe	Technology service providers	0.4	2.0	3.8	9.8

By the time they reach ten years of age, both the European and the US Human Healthcare companies, on average, earn more than they spend on R&D. Yet US Human Healthcare companies spend twice as much a year on R&D. To emphasise the point, over a 15 year period represented by the four age-bands, a composite European company would spend around €150 million in R&D; its American counterpart would spend €300 million. The composite revenues over this same 15 year period would amount to approximately €196 million for the European company and €234 million for the US equivalent.

The shortfall between revenue and R&D and other expenditure must come from investment. This is where the USA really wins hands down over Europe. At every stage in a company’s development, substantially more capital is available in the US than in Europe. In investment, US companies are not just “one age-band ahead”. The data for 2002 shows that the 233 US Human Healthcare companies aged two years or less raised nearly €1.6 billion in early finance, a mean of €6.85 million each. The 252 European equivalents raised only €362 million, yielding an average investment of €1.44 million. The total of European

investment in Human Healthcare companies was only €1.24 billion, barely 80% of the US figure just for its early stage companies. US investors committed another €6.1 billion to companies older than two years, including €3.1 billion for the 6-10 year-old groups. With this as background, it becomes relatively easy to understand why US pre-eminence in biotechnology is likely to remain unchallenged by Europe for some years to come.

In summary, then, the backers of US companies appear to be much more disciplined than their European counterparts in distributing capital. They start fewer companies but fund them more generously, not only at the outset but all the way through their development life cycle. Public finance is available earlier (when the market is open), not because the market is willing to back riskier companies, but because the companies have grown faster to that point when it is appropriate for them to become quoted companies.

As a consequence, US Agbio, Biodiagnostics and Service provider companies move more rapidly into significant revenue generation. For Human Healthcare companies the higher levels of investment capital allow more intensive pursuit of R&D goals not only in the initial proof-of-concept phase but throughout product development. The hybrid business model (R&D expenditure defrayed by separate revenue generation activities) so beloved of many European investors is hardly necessary in the US, thus saving the agony of corporate bifurcation and allowing US companies to focus on well-defined technical and market-oriented goals.

Comparing US and European metrics in biotechnology teaches many things, but the fundamental lesson is that critical mass in investment is key.

The above analysis demonstrates that the European sector significantly lags behind the US even when comparing mean European performance to that of the US biotechnology sector. Benchmarks for the upper quartile of the US sector would be both instructive and valuable if the UK and its European peers are to aspire to, and ultimately achieve, world-class levels of performance and competitiveness since they would provide valuable insights as to the approaches and parameters by which such levels of success might be achieved.

## Europe vs USA Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	Europe	US	Europe	US	Europe	US	Europe	US	Europe	US	Europe	US	Europe	US
# of companies	144	91	293	189	74	19	676	904	373	410	183	204	1743	1817
Age of company (% of sector total):														
0-2 yrs	22%	16%	29%	17%	8%	5%	37%	26%	29%	18%	54%	42%	33%	24%
3-5 yrs	21%	22%	28%	16%	26%	21%	34%	26%	27%	19%	34%	35%	30%	25%
6-10 yrs	24%	20%	20%	24%	36%	37%	17%	24%	21%	25%	9%	16%	19%	23%
11-15 yrs	16%	7%	9%	15%	14%	11%	7%	13%	12%	17%	2%	2%	9%	13%
Over 15 yrs	17%	35%	15%	28%	16%	26%	5%	11%	10%	21%	1%	5%	9%	16%
Total # of FTE employees (home)	5467	7670	11374	18404	2203	722	47409	97019	15673	23399	4283	12410	86409	159623
# of new companies formed during calendar year 2002	7	1	19	10	1	1	48	62	21	22	20	7	116	103
Sector outputs:														
Overall R&D spend (M€)	294.82	306.02	710.64	1094.64	57.62	7.30	5867.56	18109.02	740.70	818.62	407.82	1763.62	8079.16	22099.22
Overall revenues (M€)	1398.46	1674.45	2511.46	2880.91	351.00	55.50	12788.38	23779.88	3091.75	5508.13	328.36	1933.08	20469.41	35831.96
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)														
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility							646	1003						
- Preclinical							332	682						
- Phase I trial							193	467						
- Phase II trial							208	465						
- Phase III trial							59	182						
- Awaiting approval							42	60						
- Approved							505	649						
Funds raised - Total (M€)	13.3	159.6	97.8	365.4	9.4	4.8	1583.4	5720.2	167.8	173.2	111.6	247.6	1983.29	6670.77
0-2 yrs	9.8	7.7	26.6	45.2	0.0	4.8	702.9	1597.3	54.1	99.7	56.0	129.6	849.4	1884.2
3-5 yrs	3.0	46.4	28.2	30.3	0.0	0.0	474.5	1133.3	92.8	39.1	55.6	57.0	654.1	1306.1
6-10 yrs	0.6	0.0	11.4	58.8	1.6	0.0	184.2	1239.2	15.2	5.6	0.1	56.4	213.0	1360.0
11-15 yrs	0.0	0.0	1.8	111.8	0.0	0.0	97.1	866.4	0.0	4.0	0.0	0.3	98.9	982.4
Over 15 yrs	0.0	105.6	29.7	119.4	7.8	0.0	124.7	884.0	5.7	24.9	0.0	4.3	167.9	1138.1

# Country Profiles

## USA

Biotechnology, in essence, speaks with an American accent. Despite the increased competition between countries across the globe to build the most supportive environments for biotechnology research and development - from economic incentives through to relaxed legislation - the US still dominates the world scene in the most meaningful metrics. It has almost four times more companies than any other country, has historically been more successful in launching new medicines, and consequently generates the highest revenues.

### Profile

At the end of 2002, there were 1817 US companies that fulfilled the biotechnology definitions as set out by the UK Department of Trade & Industry. These companies employed almost 160,000 people - including nearly 87,000 in R&D functions - generated revenues of €35.8 billion and invested €22.1 billion in R&D. In 2002, the US biotechnology sector raised €6.67 billion in equity capital and further €4.3 billion using debt instruments, including a €2.64 billion convertible debt offering by Amgen alone. Four US biotechnology companies were able to debut on public

stock exchanges in 2002, raising €435 million, and at the end of the year the US was able to boast 358 public biotechnology companies with a combined market capitalisation of €165 billion.

The US is home to the world's largest biotechnology companies: Amgen alone has a market valuation much larger than the whole of the European biotechnology industry put together. By that measure it is also larger than some of Europe's leading pharma multinationals such as Aventis and Sanofi Synthelabo.

Company	Focus	Market Cap € billion
Amgen	Human Healthcare	59.9
Genentech	Human Healthcare	16.4
Chiron	Human Healthcare	6.8
MedImmune	Human Healthcare	6.5
Gilead Sciences	Human Healthcare	6.4
Genzyme General	Human Healthcare	6.1
Biogen	Human Healthcare	5.7
Idec Pharmaceuticals	Human Healthcare	4.9
Cephalon	Human Healthcare	2.6
Millennium Pharmaceuticals	Human Healthcare	2.2

Human Healthcare companies account for the majority of US biotechnology activity. While the sector accounts for just under half the total number of companies in the US industry, it accounts for 60% of employees, two thirds of the revenues, and 82% of the R&D budgets.

While the US biopharmaceutical industry has been developing for a quarter of a century, it is still a very vibrant and young industry. Nearly half the companies in the industry are less than five years old and the rate of new company start-ups does not seem to have slowed in recent years. According to the US Biotechnology Industry Organization, which has a more restricted definition of biotechnology than that used for this survey, the total number of US biotechnology companies looks to be growing modestly.

This implies clearly that there is a high turnover of companies. During 2002, there were some high profile examples of industry rationalisation - mergers, acquisitions, bankruptcies, and hibernations. Many companies have shifted their primary activities, notably Technology Service Providers that migrated from platform technologies to product development or full-blown contract research. The primary force behind these changing business models is the necessity to create maximum revenues from any given technology platform. Service Providers generate steady revenue streams, but not at the levels that can be expected from therapeutics sales. Thus, if a technology does have application to drug development, there is a corporate and shareholder drive towards applying the technology in that way and creating higher revenues.

The US industry's activity profile is roughly in line with that of European biotechnology markets. The US has historically had a more welcoming attitude to plant biotechnology innovations and so it is not surprising that it has a fairly robust Agbio sector. However, while the Environmental sector looks small, this top level analysis does not tell the whole story. Much environmental biotechnology in the USA is found in companies that are using it as one element in a diversified mix of technologies.

## Products

However, for most industry watchers, biotechnology means innovative medicines and it is in this sector - and those that support it - that the US is dominant. Over the past decade, increasing numbers of US companies have launched new products and moved into profit. Many of the top tier US companies have successfully launched several new medicines each, and those such as Amgen and Genentech are now considered to be must-haves in fund portfolios. Both of these companies have successfully managed to replenish maturing pipelines with new innovative medicines that should drive top and bottom-line growth.

**Top US Biotechnology Products 2002 \$M**

Product	Description	Company	Sales \$M
Epogen/Aranesp	EPO-based therapies	Amgen	2,676
Neupogen/Neulasta	Anti-cancer GCSF franchise	Amgen	1,843
Rituxan	Anti-cancer monoclonal	Genentech/Idec	1,163
Avonex	Beta interferon MS therapy	Biogen	1,034
Synagis	Anti-RSV monoclonal	MedImmune	667
Cerezyme	Enzyme for Gaucher's disease	Genzyme	619
Herceptin	Breast cancer monoclonal	Genentech	385
Enbrel	TNF inhibitor	Amgen	362
Integrilin	Cardiovascular drug	Millennium	304

The ability of the US biotechnology industry to progress products to the market was somewhat thwarted in 2002 by political events at the US Food and Drug Administration. For most of the year, the FDA was without a leader and this affected the FDA's review efficiency.

All of the major biotechnology medicines in the marketplace today are the products of the US biotechnology industry. We estimate that at the end of 2002 the US biotechnology sector had developed and was marketing medicines for more than 649 clinical indications (many of these indications are served by the same molecules). And the US pipeline of new innovations looks very vibrant. The US biopharmaceutical community had compounds in trials for 1114 different clinical indications. Biotechnology products were also awaiting approval for use in a further 60 indications.

**Finance**

2002 was the biotechnology industry's toughest year ever. The industry was beset with some high profile scandals, clinical disappointments, product setbacks, a harsh bear market and some

unwelcome political interference. The market capitalisation of the public US biotechnology companies fell by 37% over the course of the year, wiping some 80 billion off the sector's valuation. Nineteen public companies disappeared during the year through acquisition or merger, delisting, or business failure.

With stocks in meltdown, there was little appetite for initial public offerings. Only four companies - BioDelivery Sciences International, Dov Pharmaceutical, Ribapharm, and Zymogenetics - completed IPOs during 2002: others tried and had to withdraw. The share prices of this "class of 2002" fell markedly in the period following their debuts. However, this is not uncommon. Genentech was the first biotechnology company to go public, now more than 20 years ago. Since then over 500 US companies have followed suit. However, only one of them has never seen its share price fall below that offered at IPO, and that was Genentech.

For US biotechnology companies debt is an important financing option, and one that is less available in Europe. In 2002, the US biotechnology sector raised €8

billion using debt instruments, European companies only €200 million. This is not surprising as the ability to raise debt is inextricably linked with a company's maturity - that is, the ability to repay. Only those companies that have or anticipate sustainable revenue streams are likely to be able to call on debt.

Amgen, the industry's bellwether, concluded the largest ever debt transaction by a biotechnology company when it raised \$2.5 billion through a zero coupon senior convertible note. Despite the industry's lacklustre support for biotechnology generally, this offering underlined Amgen's overall strength in the marketplace. Other significant debt transactions included Idec Pharmaceuticals' \$675 million convertible debt offering, Gilead Sciences' raising \$300 million in convertible notes, and \$200 million convertible debt offerings from both OSI Pharmaceuticals and Abgenix.

Depressed stock prices in 2002 created opportunities for private equity investors to invest heavily in fairly mature but undervalued companies. US investment rules facilitate private investments in public equity (PIPEs). Investors like PIPEs because they provide an opportunity to acquire large stakes at attractive (discounted) prices, especially in smaller cap companies. US companies raised almost €1 billion in PIPE transactions during 2002, a large sum but only roughly half the amount raised through PIPEs in 2001.

In Europe, regulatory safeguards such as pre-emptive rights, make it more difficult for companies to sell discrete but large amounts of stock at discounts to the prevailing share price.

## Venture capital

By the end of 2002, the biotechnology industry was still deep in the midst of a bear market. Investors, particularly venture capitalists, were reserving any capital for the most promising of their existing portfolio companies. New financings had to demonstrate a compelling investment thesis.

Overall, the US biotechnology sector was able to raise €2.5 billion in venture capital, three quarters of that raised by the biotechnology industry worldwide. Among the new companies were a number that started as relatively mature entities. Infinity Pharmaceuticals, for example, founded in 2001 by Millennium Pharmaceuticals' former chief business officer, started life with 70 employees and was able to raise €81 million within its first 12 months.

Investors also warmed to the search-and-development companies - those that intend to in-license compounds that are in Phase II clinical trials or later - and to spin-outs from big pharma companies. This is not exclusively a US phenomenon, but some of the largest in the class operate in the USA. In-licensing player Ovation Pharmaceuticals, established in 2000, for instance, received a €143 million equity financing commitment to acquire under-marketed drugs for niche markets. Pharmion, also founded in 2000, raised €111 million in the twelve months to November 2002. Such companies secured a major share of the sums earmarked for venture activity.

Amid tough financing conditions, many US biotechnology CEOs made cutbacks in order to preserve cash reserves. In 1999 and 2000, during the genomics frenzy, biotechnology companies

worldwide raised more than €40 billion from equity sources in 2000 alone. Many companies were given enough money to broaden their pipelines and step up their research activities and, consequently, their burn rates.

Ironically, while the investor mantra in the years between 1999 and 2002 was to focus more on the high margin and substantial potential of products instead of low margin platform offerings, some US companies decided the best way to avoid a cash crunch was to switch back to services in the belief that it would be easier to monetise such assets in a shorter timeframe. Large Scale Biology Corp did just that by putting its drug development activities on the backburner as it looked to its bioprocessing platform to generate revenues.

In some cases, companies had kept their heads in the sand hoping that investors would return to the sector. Nearly half the companies who announced savage staff cuts had less than a year's worth of cash in the bank. For some, however, restructuring followed key product failures. Corvas, for example, cut staff and dropped two out of five programmes after its lead product showed no effect in treating ischaemic stroke.

### **Mergers and acquisitions**

Not surprisingly, the cutbacks increased the calls for industry consolidation. There are too many companies in both the US and Europe chasing fewer and fewer potential partners and investors. There is the worry that if they don't prepare for consolidation many will run out of cash and simply disappear. And yet, in 2002, M&A activity remained surprisingly low key, notwithstanding several multi-billion dollar acquisitions.

At the end of 2001, Amgen unveiled its intention to "merge" with Immunex in a transaction that at the time was valued at \$16 billion. By the time the deal was consummated in mid-2002, this valuation had drifted down to \$10 billion. Amgen, which at the end of 2001 already had revenues above \$4 billion, wanted to add Immunex's blockbuster rheumatoid arthritis drug, Enbrel, to its portfolio.

Millennium Pharmaceuticals announced its intention to acquire Cor Therapeutics, which had a marketed cardiovascular product, for \$2 billion - a transaction that would have a significant role in Millennium's transition from a genomics platform company into a vertically integrated drug discovery company. MedImmune sought to reduce its heavy dependence on Synagis, a drug for infants that prevents a respiratory infection, by acquiring Aviron, a vaccines company which at the time had a nasal spray influenza vaccine awaiting FDA approval, in a \$1.3 billion stock transaction. Cephalon announced its plan to acquire the private French pharma company, Groupe Lafon, to eliminate a royalty obligation it was paying for the Provigil narcolepsy treatment and so raise its earnings per share at a stroke.

These deals, however, did not break the consolidation logjam. During 2002, there were but a few truly noteworthy M&As involving US biotechnology companies. At the end of the year, Laboratory Corp of America (a routine diagnostics service business, not included in this study) announced its intention to add to its already massive diagnostics business by acquiring Dianon Systems for \$600 million. Gilead Sciences announced it would acquire fellow anti-viral company Triangle Pharmaceuticals for \$464 million

in cash via a tender offer. Versicor, an anti-infectives company, acquired BioSearch Italia, a similar Italian company, in a deal valued at \$236 million.

## Collaborations

One of the major reasons why US biotechnology companies have not embraced consolidation is that they have been able to secure highly valued partnering deals with pharmaceutical companies. Indeed, if all the deals signed in 2002 achieved all their milestones and targets, the pharmaceutical industry would be committed to providing the biotechnology sector with an additional €10 billion.

During 2002, US biotechnology companies were able to secure a number of major collaborations. Potentially, the most lucrative transaction was between Pfizer and Eyetech Pharmaceuticals under which the companies agreed to develop and market Eyetech's Macugen pegaptanib VEGF-binding aptamer to treat age-related macular degeneration and diabetic macular oedema. The deal could be worth as much as €711 million to Eyetech. Pfizer, which had been busy on its acquisition of Pharmacia, also found time to agree a €500 million deal with Neurocrine Biosciences to develop and commercialise the biotechnology company's indiplon for the treatment of insomnia. And in a transatlantic deal, Aventis, the Franco-German pharmaceutical combine, agreed to pay Genta up to €458 million in cash, equity, milestones, and convertible debt for the right to develop jointly Genta's Genasense antisense apoptosis-inducing cancer drug candidate.

Biopartnering deals were once considered a strong validation of a biotechnology company's strengths. Now there is more scepticism following the fall-out associated with the 2001 €2 billion deal between Bristol-Myers Squibb and ImClone covering the anti-cancer prospect Erbitux. Under the original terms of the deal, ImClone received a large upfront fee, sold a 20% equity stake to BMS, and was promised milestones and royalties. When the regulators declined to expedite the drug's review, questions were asked of the integrity of BMS's due diligence process. The fall-out also cast a shadow over the biotechnology industry for some time and certainly through 2002.

## Selected announced restructuring activities at US biotechnology companies in 2002

Company	Date	Announcement
Aclara	Jul	Staff cut by 29% to 125
Advanced Viral Research	Nov	Cut staff by 70% to leave 10
Advanced Tissue Sciences	Nov	Filed Chapter 11 and laid off all 12 employees
Alkermes	Aug	FDA setback prompted 23% staff cut to 419
Argonaut	Aug	Reduced jobs by 35 to 140 to cut annual expense
ArQule	Dec	Cut 128 staff from company roll
Avigen	Oct	Cuts staff by 28% to 110 to stretch cash for 5 years
BioCryst	Jul	Staff cut 40% to 45 to extend cash pile beyond 2005
BioTransplant Inc	Jul	Reduced workforce by 23%
Calypte Biomedical	Apr	Bankruptcy threat forces headcount cut of 50% plus
Cell Pathways	Oct	Headcount shaved by 25% to 61
Cellegy	Aug	Cutting staff by 24% to 28 to curb burn rate by 40%
Corvas	Jul	Chopped staff back 40% to 67 for \$8m/year saving
Curagen	Nov	Shed 25% of staff to 384 people
Cytogen	Sep	Laid off 75% of staff to save \$1.4m a year in costs
Deltagen	Oct	Sought \$30m budget cut by pruning staff 30% to 303
Dor Pharma	Jun	Reduced its headcount to 12 from 22
Durect	Nov	Trimmed workforce by 16% to 135
Dyax	Sep	Hoped to save \$5m with 16% cut to 112
Eden Bioscience	May	To cut operating costs headcount down 20 to 66
EntreMed	Sep	Slashed burn rate by 60% with 40% staff cut to 50
Exelixis	Nov	Reduced early stage R&D effort losing 38 jobs
Genaera	Nov	Cuts in preclinical work cuts headcount by 19% to 46
Genaissance	Aug	Conserving cash with 20% staff reduction to 110
Genome Therapeutics	Sep	Cut early stage R&D by laying off 28 from 193 staff
Guilford Pharmaceuticals	Jul	Sought \$12m saving cutting staff by 25% to 225
Hyseq Pharmaceuticals	May	79 jobs from 204 axed in genomics to drugs shift
Incyte Genomics	Nov	Focus switch cuts staff by 37% to 440
Insmed	Sep	A 55% cut in staff to 27 to stretch cash for two years
Isis Pharmaceuticals	Nov	Cuts 25 in functional genomics activities
Large Scale Biology	Jun	Reduced staff to 127 from 185 to save \$10m a year
Lynx Therapeutics	Apr	Resource reallocation forces 30% staffing reduction
MaxyGen	Nov	Increased discovery focus prompts 10% cut to 285
Nektar Therapeutics	Dec	Unveiled plan to cut 20-30% from 145 staff
NeoRx	Jul	Staff reduced 30% to 79 to conserve cash reserve
NeoTherapeutics	Aug	Two purges result in 72% headcount cut to 21
Nexell Therapeutics	May	Financial crunch forces downsizing from 23 to 3
Neurogen	Oct	Cash stretch plan into 2005 with 10% cut to 216
Orchid BioSciences	Apr	Focus on genotyping causes 90 job losses from 600
Organogenesis	Sep	Over 9 months, sheds 215 jobs to 15, filed Chap 11
Paradigm Genetics	Apr	Headcount cut from 279 to 223 in agbio doldrums
Pharmacopeia	Aug	Axed 10% to 720 to reduce annual costs by \$8m
Pharsight	Nov	Cut headcount from 100 to 80 people
Prolinx	Nov	Reduced its headcount to 16 from 32 staff
Restoragen	Mar	Headcount reduced from 121 to 60
Sanguine	Sep	Cash stretch bid forces 40% reduction to 18 staff
Targeted Genetics	Dec	Cut headcount from 173 to 50 people during the year
The Immune Response Corp	Sep	Reduced its staff from 42 to 14 to save \$7.2m a year
Third Wave Technologies	Apr	Headcount cut by 25% to improve cash position
Valentis	Oct	Staff chopped from 110 to 13 to bring burn rate down
Variagenics	May	Activity shift cuts 40 HT screening jobs to leave 93

## USA Summary Data Set

Key Performance Indicator	Agbio	Biodiagnostics	Environmental	Healthcare	Service providers	Technology Service Providers	Sector overall
# of companies	91	189	19	904	410	204	1817
Age of company (% of sector total):							
0-2 yrs	16%	17%	5%	26%	18%	42%	24%
3-5 yrs	22%	16%	21%	26%	19%	35%	25%
6-10 yrs	20%	24%	37%	24%	25%	16%	23%
11-15 yrs	7%	15%	11%	13%	17%	2%	13%
Over 15 yrs	35%	28%	26%	11%	21%	5%	16%
Total # of FTE employees (home)	7670	18404	722	97019	23399	12410	159623
# of new companies formed during calendar year 2002	1	10	1	62	22	7	103
Sector outputs:							
Overall R&D spend (M€)	306.0	1094.6	7.3	18109.0	818.6	1763.6	22099.2
Overall revenues (M€)	1674	2881	56	23780	5508	1933	35832
Sector productivity:							
Average market capitalisation per quoted company employee as at 31/12/02 (000€)	620	339	14	2289	551	640	1773
Healthcare product development pipeline (# of prods by stage of development):							
- Concept/feasibility				1003			
- Preclinical				682			
- Phase I trial				467			
- Phase II trial				465			
- Phase III trial				182			
- Awaiting approval				60			
- Approved				649			
Funds raised - Total (M€)	159.6	365.4	4.8	5720.2	173.2	247.6	6670.8
0-2 yrs	7.7	45.2	4.8	1597.3	99.7	129.6	1884.2
3-5 yrs	46.4	30.3	0.0	1133.3	39.1	57.0	1306.1
6-10 yrs	0.0	58.8	0.0	1239.2	5.6	56.4	1360.0
11-15 yrs	0.0	111.8	0.0	866.4	4.0	0.3	982.41
Over 15 yrs	105.6	119.4	0.0	884.0	24.9	4.3	1138.1

## UK

For Britain's biotechnology industry, 2002 was a year of restructuring and realignment, as the sector sought to consolidate its position as Europe's most mature in difficult conditions. There was a modest increase in the number of companies and employees over 2001, and a substantial increase in industry revenues and R&D budgets. The UK provided three of the year's nine IPOs worldwide, but Britain's publicly quoted companies lost about half their value during the year. There was also some modest progress on the Human Healthcare product front with a number of medicines receiving the green light from the regulatory authorities.

### Profile

UK biotechnology executives will remember 2002 as an acutely painful year that was overshadowed by a lack of financial support. Globally, the industry was suffering from a post-genomics and Enron hangover which saw investors desert biotechnology companies as an asset class. At the end of 2002, 47 UK biotechnology companies were quoted on either the London Stock Exchange (LSE) or its Alternative Investment Market (AIM). During the year, share prices in the sector dropped by 50% in local currency terms, wiping €10.9 billion off company valuations. This was broadly in line with falls in US biotechnology valuations - but not as dramatic as those seen among some continental European Technology Service Providers. The UK biotechnology sector closed 2002 with a combined market capitalisation of €9.70 billion.

Not surprisingly, the decline in investor confidence among investors had a knock-on effect on the ability of

companies to raise additional money. While the University Challenge Fund continued to catalyse the creation of companies, the sums UK companies were able to attract from the investment community declined dramatically between 2001 and 2002. Companies raised a total of €674 million in equity, down from €1.9 billion in 2001. This was the lowest amount raised by the UK biotechnology sector since 1995. A further €98 million was raised using debt instruments.

During 2002, three British companies completed IPOs - Cobra BioManufacturing, Cyprotex, and NeuTec Pharma - raising just over €37 million. Ark Therapeutics, an Anglo-Finnish company, pulled its plan to raise €61.4 million in an IPO on the LSE, citing a lack of investor appetite. No other European companies were able to complete IPOs in 2002. Indeed, only nine IPOs were completed worldwide in 2002, four in the US on NASDAQ, while an Australian and a Canadian company both chose to list shares on the LSE. Antisoma, Provalis and Xenova were able to return to the capital markets to raise an additional €69.8 million in follow-on offerings. British companies were able to raise €438 million from venture capital and private equity sources.

Company	Year founded	Amount raised €m
KuDOS Pharmaceuticals	1997	45.28
Microscience	1997	39.14
Renovo	2000	32.23
Arakis	2000	24.56
Strakan Group	1995	23.62
Paradigm Therapeutics	1998	18.42
Avidex	1999	17.65
Procognia	2002	14.63
Sterix Ltd	1998	12.28
Vectura	1997	11.21

This drop in available finance during 2002 can be expected to have had immediate, near-term and some potential long-term effects on the industry. The most immediate apparent impact was the brake on recruitment levels. Employee levels in the UK biotechnology industry had been growing at double digit levels for a number of years. During 2002, however, the total number employed domestically in the UK biotechnology industry rose by just 2.4%, although the year-on-year increase in R&D employees remained fairly robust at 7%.

By the end of 2002, Britain's biotechnology sector consisted of 486 dedicated life science businesses, a net increase of 35 companies over 2001. While this is still fewer than the number identified in Germany, the UK has still by far Europe's largest biotechnology sector employing nearly 26,000 people, including 11,500 with R&D functions. The UK industry posted total revenues of some €6.36 billion, up 18.5% on 2001, while R&D budgets increased by 17.4% to €2.78 billion.

The Human Healthcare sector remains the dominant influence in the UK biotechnology industry. At the end of

2002, the Human Healthcare sector accounted for 42% of all companies, 52% of all employees, 65% of all R&D employees, 66% of the UK's industry's revenues and 80% of all R&D spending. That the number of people employed by the Human Healthcare sector remained virtually static at 13,500 or so reflects some of the restructuring that companies were beginning to institute during 2002 to conserve cash reserves. There was also some migration of companies from the Human Healthcare sector into the Service Provider sector as some firms put their drug discovery ambitions on the backburner and stepped up contract research activities in order to develop earlier sustainable revenue streams.

With investors falling out of love with Technology Service Providers such as Bioinformatics and Functional Genomics companies it was not surprising to see declines in the number of companies in the sector. These companies did not go out of business, however, but migrated into other sectors. Inpharmatica, for instance, firmly a bioinformatics company in 2001, had switched its primary focus to drug discovery by the end of 2002.

The UK biotechnology sector remains more mature than the rest of Europe, although it is substantially younger than the more established US industry. At the end of 2002, 54% of companies were less than five years old, compared with 57% at the end of 2001. In Europe, this age group represents 67% of all companies, and in the US, 49% of companies.

In 2002, a few UK companies disappeared. The most notable company failures were Scotia Holdings, a Stirling-based company, which was valued at

about £500 million in 1998, and Bioglan Pharma, a Hitchin-based company which was valued at £630 million as recently as 2000.

Both Scotia and Bioglan were victims of their own ambition. Scotia had raised £50 million using a convertible debt financing instrument in 1998. The funds were to be used to accelerate the development of its photodynamic compound Foscan, for which it had expected to receive early approval as a treatment for head and neck cancer. Such an approval would have enabled Scotia to either pay off its debt or encourage creditors to convert the debt into equity. Loss of its pharma partners put additional pressure on Scotia and it failed to get the compound approved by the time the debt was repayable. Ironically, the compound, which was sold by the administrator, was approved in a number of key European markets.

Bioglan's problems started when it tried to acquire a dermatology pipeline from Bristol-Myers Squibb. Unfortunately talks collapsed between the parties at the end of 2001. The attempt exposed weaknesses in the company's business which undermined support from the financial community. While debt was clearly an important source of financial support for US companies in 2002, the relative lack of maturity and sustainable revenue streams means that this is not yet an appropriate financial instrument for most British companies.

Despite these company failures, UK Human Healthcare companies did demonstrate fundamental progress during 2002. Indeed, a clear sign of why Britain's sector may be better positioned to grow sustainably lies in its clinical pipeline. During 2002, companies continued to advance compounds

through the pipeline and into the marketplace. The number of treatments in clinical trials or awaiting approval rose from 202 in 2001 to 225 in 2002.

A number of products emerged from that pipeline during 2002, most notably the European approvals achieved by Vernalis, with its migraine treatment frovatriptan, and Oxford GlycoSciences, with its Gaucher's disease treatment, Zavesca. Among those compounds under review at the year end were Cambridge Antibody Technology's rheumatoid arthritis treatment Humira, OGS's Zavesca, which was being assessed by the US Food & Drug Administration, and Shire Pharmaceuticals' Fosrenol, which was being reviewed by regulators in both Europe and the US as a treatment for high blood phosphate levels in patients with end-stage renal disease.

British companies closed 2002 with Phase III candidates for 30 different indications. Included in this group were CAT's Humira, which was being tested against juvenile rheumatoid arthritis and Crohn's disease, and GW Pharmaceuticals' sublingual cannabis extract spray which was in five Phase III trials as a possible treatment for conditions such as cancer pain, multiple sclerosis, neuropathic pain and/or spinal cord injury.

On the partnering front, Antisoma and Xenova both concluded deals for products in their portfolios. In a deal worth a potential €30 million, Xenova granted Genentech global rights to develop and market products based on Xenova's OX40 receptor protein and its preclinical anti-OX40 ligand antibodies to treat immune system disorders. In a deal that provided a huge fillip for UK biotechnology companies at the year end,

Antisoma granted Roche exclusive worldwide rights to develop, manufacture and market its oncology pipeline. Roche bought a €6.44 million equity stake and paid an upfront fee of €35.3 million. UK companies were not so active in mergers

and acquisitions, with Proteome Sciences' €17 million acquisition of Xzillion Proteomics topping the list. Denmark's TopoTarget acquired Prolifix in a deal promoted by venture capitalists who had invested in both companies.

## UK Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	39	39	69	74	37	34	181	204	81	95	43	40	450	486
Age of company (% of sector total):														
0-2 yrs	21%	15%	33%	32%	11%	6%	31%	30%	23%	20%	51%	48%	29%	27%
3-5 yrs	10%	10%	20%	23%	24%	24%	38%	32%	23%	24%	30%	33%	28%	27%
6-10 yrs	18%	23%	20%	15%	43%	47%	14%	22%	17%	26%	12%	13%	18%	23%
11-15 yrs	31%	28%	7%	7%	11%	12%	9%	8%	20%	15%	7%	8%	12%	11%
Over 15 yrs	21%	23%	19%	23%	11%	12%	8%	8%	16%	15%	0%	0%	12%	12%
Total # of FTE employees (home)	1154	1936	2470	2450	352	767	13882	13600	5789	6441	788	736	24435	25931
# of new companies formed during calendar year	2	1	10	6	1	0	21	24	4	6	10	5	48	42
Sector outputs:														
Overall R&D spend (M€)	103.95	99.26	96.77	119.93	20.42	22.60	1700.37	2250.27	219.48	252.04	130.89	53.55	2271.88	2797.66
Overall revenues (M€)	373.61	590.02	423.48	400.27	109.30	114.73	3297.91	4223.07	942.87	968.71	70.33	60.81	5217.50	6357.61
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	924	227	0	0	2259	1308	1067	1428	822	373	2177	1186.0
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility								151						
- Preclinical								111						
- Phase I trial								71						
- Phase II trial								96						
- Phase III trial								32						
- Awaiting approval								26						
- Approved								129						
Funds raised - Total (M€)	2.5	0.5	55.6	65.7	0.2	8.3	1710.0	529.2	27.0	41.5	112.0	30.9	1907.3	676.2
0-2 yrs	2.1	0.1	10.8	18.3	0.0	0.0	157.0	93.2	2.4	7.0	38.1	23.3	210.4	141.9
3-5 yrs	0.0	0.0	0.1	5.4	0.1	0.0	467.6	233.6	11.5	19.4	70.7	7.6	550.0	266.0
6-10 yrs	0.4	0.5	5.1	11.3	0.2	0.9	148.2	60.9	13.2	15.2	3.2	0.0	170.3	88.7
11-15 yrs	0.0	0.0	3.7	1.0	0.0	0.0	587.0	90.9	0.0	0.0	0.0	0.0	590.7	91.9
Over 15 yrs	0.0	0.0	35.9	29.7	0.0	7.3	350.2	50.7	0.0	0.0	0.0	0.0	386.1	87.8

## Denmark

Denmark has long been associated with advancements in classical biotechnology. Danish companies were the first to use pure yeast strains in fermentation and the first to market pure bacterial cultures and enzymes for cheese production. Danish companies were the first to market insulin and were among the first to provide recombinant versions of the therapeutic protein. Denmark is the base for one of the world's largest biotechnology companies, Novo Nordisk.

In 2002, Denmark continued to show the highest rate of new company formation, with 13% of its companies being formed during the year. At year-end it comprised 82 companies and employed 16,750 people, including 4,200 in R&D functions. Over the 2001-2 period sector revenues were relatively static at €4.43 billion, while R&D investment increased by almost 13% to €966 million. Denmark was the only country to raise more equity in 2002 than in 2001.

### Profile

Denmark's biotechnology environment is dominated by the influence of a few mature companies. Novo Nordisk, one of the first companies to use recombinant technologies to develop commercial products, is the standard bearer of the Danish biotechnology industry. Indeed, through its own corporate venturing activities and the spinning out of non-core businesses, Novo Nordisk has been responsible for nurturing the new generation of biotechnology companies, most of which are based at the Symbion Science Park.

The Agbio sector is dominated by Pharma Nord, the Food Technology and nutritional supplements company, which accounted for virtually all of the sector's employment growth in 2002. In the Biodiagnostics sector DakoCytomation, a global player in its field, dominates. In the Human Healthcare sector Novo Nordisk has an over-riding presence and influence. The company employed 11,100 of the estimated 13,300 workers in the Danish Human Healthcare category, and accounted for 96% of its revenues and 70% of its R&D budget. The increase in Human Healthcare employment was largely due to Novo Nordisk, although NeuroSearch, 7TM Pharma and Genmab posted (for companies of their size) notable increases in headcount.

Amongst the Service Providers, Novozymes dominates. The company, along with Polypeptides, was largely responsible for the 4% fall in sector employment during the year. Only in the Technology Service Provider segment is the Danish industry not influenced by a dominant market player. But it is the presence of global players on their doorstep that has nurtured the burgeoning Technology Service Provider sector. It is high throughput screening companies, such as Exiqon and Sophion Bioscience, that are driving the sector's growth in the key employment, revenues and R&D spending metrics.

Publicly quoted Danish biotechnology companies - excluding Novo Nordisk - witnessed a dramatic 62% slump in their combined valuation from €744 million to €285 million. Genmab's value slumped 85% during 2002, while Pharmexa and Neurosearch saw their valuations fall by 62% and 60%,

respectively. The Danish numbers would have looked much worse had not Bavarian Nordic returned a 148% increase in its valuation during the year.

Genmab, which received a €20 million equity injection from a strategic partner, suffered from its association with the German biotechnology industry, owing to its dual listing on Germany's Neuer Markt. NeuroSearch, which was still busy spinning out new companies during 2002, saw its value undermined by disappointing clinical results with three of its leading compounds. Nevertheless, the company was still able to develop its biopartnering relationships with major players such as GlaxoSmithKline, Abbott Labs, and Boehringer Ingelheim. In spite of making clinical progress, Pharmexa also suffered at the hands of the capital market.

Like Britain's Acambis, Bavarian Nordic was the beneficiary of a post-9/11 dividend, winning contracts to provide smallpox vaccine as well as establishing a strategic alliance with PowderJect Pharmaceuticals. Bavarian Nordic was able to return to investors to raise an additional €9.0 million, in stark contrast to early 2001 when it had failed to raise funds. Nevertheless, conscious that investors can be fickle, the company still embarked on a restructuring to focus entirely on infectious disease vaccines development and reduce operating costs by about €5.4 million a year by closing certain labs in Munich and laying off 10 of its 75 staff.

As in the previous year, in 2002 it was the therapeutic focused companies that attracted the lion's share of the sector's €158m funding. Five of the six companies who attracted sums in excess of €10 million were Drug Discovery companies. The exception was CMC Biopharmaceuticals, the contract manufacturer, that raised €35m through a combination of venture funding and debt finance, the Danish Government's Vaekstfonden (Growth Fund) being one of the investors.

## Danish Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	4	4	8	9	3	3	31	37	15	18	11	11	72	82
Age of company (% of sector total):														
0-2 yrs	25%	25%	63%	67%	33%	0%	61%	57%	47%	39%	70%	73%	56%	52%
3-5 yrs	0%	0%	13%	11%	0%	33%	19%	27%	7%	17%	30%	18%	15%	21%
6-10 yrs	50%	50%	25%	22%	33%	33%	6%	5%	7%	11%	0%	9%	11%	12%
11-15 yrs	0%	0%	0%	0%	33%	0%	6%	5%	7%	6%	0%	0%	6%	4%
Over 15 yrs	25%	25%	0%	0%	0%	33%	6%	5%	33%	28%	0%	0%	11%	11%
Total # of FTE employees (home)	308	354	154	108	49	78	12176	13326	2519	2634	146	246	15352	16745
# of new companies formed during calendar year	1	0	4	2	0	0	5	4	2	3	6	2	18	11
Sector outputs:														
Overall R&D spend (M€)	2.70	6.19	4.49	10.02	0.13	4.150	700.83	773.89	141.06	145.44	7.55	25.98	856.75	965.67
Overall revenues (M€)	50.82	64.92	7.87	6.93	5.04	16.56	3478.09	3512.18	823.86	825.31	7.57	8.78	4373.26	4434.68
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	0	0	223	320	1377	739	0	0	0	0	1371	754.0
Healthcare product development pipeline (# of prods by stage of development):	0													
- Concept/feasibility								69						
- Preclinical								35						
- Phase I trial								15						
- Phase II trial								24						
- Phase III trial								4						
- Awaiting approval								2						
- Approved								26						
Funds raised - Total (M€)	10.8	4.7	0.2	3.9	0.0	0.7	92.6	107.5	0.1	35.2	11.0	6.4	114.7	158.4
0-2 yrs	0.0	4.7	0.2	3.9	0.0	0.0	36.7	58.6	0.1	35.2	11.0	6.4	48.0	108.7
3-5 yrs	0.0	0.0	0.0	0.0	0.0	0.0	7.7	39.9	0.0	0.0	0.0	0.0	7.7	39.9
6-10 yrs	10.8	0.0	0.0	0.1	0.0	0.7	30.9	9.0	0.0	0.0	0.0	0.1	41.7	9.9
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	17.4	0.0	0.0	0.0	0.0	0.0	17.4	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

## Finland

Strong government support for biotechnology has resulted in a Finnish sector that fights above its weight. At the end of 2002 Finland had 64 biotechnology companies employing just over 2000 people (just under 1150 of them in R&D), an 18% increase over the year. The sector's revenues topped €250 million for the first time, while R&D spending increased by 22% to €187 million. One-third of companies were in the Human Healthcare sector, with a further third pursuing a service-based business model.

### Profile

Finland punches the highest above its weight of all the countries in this survey in terms of the number of biotechnology companies. Finland is one of the smaller countries within the European Union and its economy was, until recently, dominated by state-owned monopolies in such sectors as chemicals and oil. The rising economic influence of the telecommunications and the prominence of Finnish companies in that global market prompted the Finnish government to look at other new-economy sectors to support. Biotechnology is one of the sectors to win backing.

This has had consequences for the age profile of the Finnish biotechnology industry. Around 60% of Finnish companies were less than five years old in 2002, with the Technology Service Provider Sector being the youngest sector. With its pole position in global telecoms it is unsurprising that Finland should be making in-roads at the IT - biotechnology interface.

Finland's Agbio presence reflects the influence of Kemira, the former state-owned chemicals company. Kemira was

active in the development of crop biotechnology in the late 1980s and 1990s. A number of former Kemira business units have been spun out and it is these that have underpinned the nation's Agbio sector. One of those companies, the biopesticides specialist Verdera, accounted for virtually all the job losses in the Agbio sector in 2002 as it restructured itself from being part of a major company into a leaner entrepreneurial business. Perhaps the most notable feature of the sector, however, is the dominance of Food Technology companies, who accounted for seven of its nine companies. They range from the fruit extracts specialist Aromtech to Hormos Nutraceuticals, with the latter accounting for much of the sector's increased R&D spend.

There were job losses in Finland's Bidiagnostics sector (largely accounted for by one company, Orion Diagnostics), but the sector saw both revenues and R&D spending increase by 50% and 21% respectively. Finland's Bidiagnostics companies are all primarily focused on Human Healthcare applications. Its Human Healthcare sector is notable for the fact that 30% of its companies are biomaterials specialists. All six Biomaterials companies emerged from 2002 relatively unscathed. Perhaps the most newsworthy event in the Finnish Human Healthcare sector was the tripartite merger of Control Pharma, Carbion and BioTie Therapies Corporation in October to form BioTie Therapies.

The merger of the three companies into one was accompanied by a €15.1m private placement. Along with the €16m raised by Bidiagnostics company, Inion, the two deals accounted for the lion's share of Finland's fund-raising in 2002. Yet, while funding for pharma projects is more available in Finland than it was a

decade ago, the sums involved are probably too low to allow promising projects to mature into international successes.

Finnish biotechnology is not as well capitalised as in other countries partly because Finland's private equity and VC sectors are not as developed as elsewhere. In addition to SITRA, the Finnish National Fund for Research & Development, the most prominent home grown specialist life sciences venture

capitalist is BioFund Management. Finnish companies have to rely on SITRA or BioFund taking the lead with less focused funds joining the syndicates.

BioTie Therapies was, and remains, Finland's only public biotechnology company. During 2002, its market capitalisation collapsed from €75.3 million at the start of the year to close 2002 with a valuation of just €11.3 million - less than the cash it had in the bank.

## Finnish Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	9	9	12	12	1	1	20	20	17	14	7	8	66	64
Age of company (% of sector total):														
0-2 yrs	11%	11%	17%	8%	0%	0%	25%	25%	24%	14%	86%	63%	27%	22%
3-5 yrs	33%	33%	17%	25%	0%	0%	35%	35%	47%	50%	14%	38%	32%	36%
6-10 yrs	22%	33%	42%	42%	100%	100%	25%	25%	24%	29%	0%	0%	26%	28%
11-15 yrs	11%	11%	8%	0%	0%	0%	5%	10%	6%	7%	0%	0%	6%	6%
Over 15 yrs	22%	11%	17%	25%	0%	0%	10%	5%	0%	0%	0%	0%	9%	8%
Total # of FTE employees (home)	132	110	655	586	15	15	702	983	133	201	75	123	1711	2017
# of new companies formed during calendar year	0	1	1	0	0	0	3	0	1	0	2	1	7	2
Sector outputs:														
Overall R&D spend (M€)	2.44	6.32	17.27	20.96	0.03	0.15	121.58	140.82	3.35	6.17	8.40	12.12	153.07	186.53
Overall revenues (M€)	12.44	7.40	29.48	44.40	0.16	1.07	34.69	177.69	12.71	11.72	6.43	9.65	141.00	251.92
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	0	0	0	0	1711	104	0	0	0	0	1711	104.0
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility								17						
- Preclinical								7						
- Phase I trial								8						
- Phase II trial								5						
- Phase III trial								3						
- Awaiting approval								1						
- Approved								141						
Funds raised - Total (M€)	0.8	0.0	0.5	16.0	0.0	0.0	53.0	18.3	0.5	2.5	0.2	0.0	55.0	36.8
0-2 yrs	0.1	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.2	0.0	1.0	0.0
3-5 yrs	0.1	0.0	0.0	16.0	0.0	0.0	43.9	3.2	0.0	2.5	0.0	0.0	44.0	21.7
6-10 yrs	0.1	0.0	0.1	0.0	0.0	0.0	3.1	15.1	0.0	0.0	0.0	0.0	3.3	15.1
11-15 yrs	0.5	0.0	0.0	0.0	0.0	0.0	6.0	0.0	0.0	0.0	0.0	0.0	6.5	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

## France

France remains ambitious in biotechnology and, based on its academic strength in biology, still has the potential to become a considerable player. However, it is still failing to provide investment support for its medium and late-stage companies. During 2002, with presidential elections approaching, France Biotechnology, the French industry lobby group, had obtained commitments from both main candidates to institute a series of fiscal measures that would relax constraints on investment and employment for young high-technology companies. However, faced now with Euro-zone pressure to run a tight budget, some of the promised support measures look as though they may at least take a long time to come to fruition.

### Profile

New biotechnology companies continued to form in France in 2002 although at a slower rate than in 2001. As elsewhere, venture investors in France have tended to support existing companies within their portfolios rather than create new companies. Thus, although French companies less than 2 years old attracted twice as much money in 2002 (€121 million) than in 2001 (€50.5 million), only 14 new companies were formed, compared with 37 in 2001.

Companies under 2 years old represented 40% of the sector total in France but provided only 10% of its employment. Companies over 10 years old accounted for 63% of the employment. At first sight, this profile would appear to be typical of a biotechnology sector that is relatively mature, much like the UK.

Notwithstanding the fact that UK biotechnology has over twice as many companies as France and employs three times as many people, the French figures are distorted by the presence of Biomerieux, a powerful international player in the Human Healthcare diagnostics arena, which employed nearly 2100 people within France. Taking it out of the calculation, the mature companies account for around 52% of the workforce while companies founded in or since 2000 employ 13% of the biotechnology workforce. This indicates that France's profile in 2002 was only slightly more mature than countries such as Sweden, which entered the biotechnology arena much later.

Part of the problem certainly is that French investors continue to find venture capital to fund the growth of companies up to five years old but do not provide sufficient capital beyond that. Only €112 million was raised by French companies over 5 years old in 2002. This figure was substantially down on the €170 million of the previous year, and significantly below the €261 million raised in the UK by older companies in 2002.

The French biotechnology sector fared much better in the public markets than its international counterparts. During 2002, the total market capitalisation of France's publicly quoted companies dropped only 33% to €670 million. Drug delivery technology company Flamel Technologies actually recorded a significant increase in value during the year following some positive news linked to strategic alliances. This increase cushioned the impact of the 60% decline in valuation at Technology Service Provider, Cerep.

The French Human Healthcare sector is the largest single sector, and accounts

for 36% of French biotechnology companies and 43% of its employees.

Established companies such as IDM (ImmunoDesigned Molecules), Exonhit, Cerep, and Imtix Sangstat all added significant numbers of employees during 2002, and newer ventures such as Carex, Aptanomics, Nautilus, BioAlliance Pharma, Urogene and Cytheris grew by thirty to fifty percent. The most spectacular growth in employment came from Proskelia, the spin-out from Aventis' bone disease division. Formed as a shell company in 2001, Proskelia got into full swing in 2002, adding around 100 new employees that year, a large part drawn from its parent company.

There were head-count reductions elsewhere though, even among young companies such as Clinigenetics (founded 2002) and Libragen (founded 2001). However, the most significant reductions came in what in 2001 was still France's flagship company, the genomics specialist, Genset.

Founded in 1989 as an oligonucleotide synthesis service company, Genset became Europe's premiere genomics company during the 1990s, having recruited human gene mapping pioneer, Daniel Cohen, as its Chief Scientific Officer. Then came a series of strategic miscalculations, the most important of which left the company drastically short of finance. While US companies such as Celera, Millennium, and Human Genome Sciences raised hundreds of millions of dollars in the genomics funding boom of 2001/2000, Genset raised just €50 million, issuing a convertible bond in 2000. This was insufficient to allow the company either to pursue its pharmacogenomic analysis business more vigorously or to acquire and develop later-stage products (the

strategies adopted by a number of other genomics firms). With its 2001 R&D spending at €35 million, no product revenue on the horizon, and the financing window closed for public companies, Genset's future was bleak. In June 2002, the company's board accepted an acquisition offer from the Swiss biopharmaceutical company, Serono, for Genset to become its genomics arm. The rationalisation that accompanied acquisition saw Genset cut its R&D by €19 million and reduce its French headcount from 315 to 146.

In essence, employment in French biotechnology differed very little between 2002 and 2001. Nearly all of the rise of 1100 in the overall number of employees between 2002 and 2001 is accounted for by one company, the large drug delivery company, Ethypharm, for whom employee data was only made available to us for 2002.

France's Service Provider sector remains solid, particularly in Contract Manufacturing where 75% of the companies for which comparative data was available increased their workforce during 2002. In the Technology Service Provider sector, things were more patchy as might be expected in a sector where all the players are under ten years old and most are less than five. For example, while functional genomics company, Genfit, took on more staff, another functional genomics company, GenOdyssee, shrank.

The underlying trend in revenue generation by French biotechnology companies was much the same in 2002 as in 2001, despite an upward shift in the headline numbers. Revenues in 2002 were approximately €1.9 billion, with over half of that (€1.06 billion) coming from the well-established Biodiagnostics sector dominated by

Biomerieux. In 2001, the overall revenue figure was €1.55 billion with €886 million from diagnostics. Much of the 22% year-on-year increase arose in the Agbio sector where Genoplante Valor, Biogemma and others all made good progress. Biomerieux chipped in €145

million of the €178 million gains seen in Biodiagnostics. In Human Healthcare, significant gains were contributed by the replacement tissue operations of Laboratoires Genevrier, by drug delivery specialist, Flamel, and gene and cell therapy company, Gencell.

## French Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	20	20	32	33	5	5	78	81	49	50	27	32	211	221
Age of company (% of sector total):														
0-2 yrs	32%	20%	38%	42%	20%	20%	51%	37%	45%	40%	81%	59%	49%	40%
3-5 yrs	21%	30%	22%	12%	20%	20%	22%	36%	18%	18%	15%	34%	20%	27%
6-10 yrs	26%	25%	16%	21%	40%	20%	15%	16%	16%	22%	4%	6%	16%	18%
11-15 yrs	16%	15%	9%	6%	0%	20%	8%	7%	14%	10%	0%	0%	9%	8%
Over 15 yrs	5%	10%	16%	18%	20%	20%	4%	4%	6%	10%	0%	0%	6%	8%
Total # of FTE employees (home)	418	586	2821	2882	52	45	3204	4050	982	1027	445	476	7924	9066
# of new companies formed during calendar year	4	0	5	2	0	0	10	5	9	3	9	4	37	14
Sector outputs:														
Overall R&D spend (M€)	31.61	75.45	123.66	127.77	0.75	1.69	330.58	372.59	28.04	48.09	48.10	41.69	562.73	667.27
Overall revenues (M€)	96.51	171.50	886.86	1064.00	3.69	3.83	417.67	552.62	119.09	126.33	23.46	31.32	1547.28	1949.59
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	0	0	0	0	797	747	121	341	0	0	352	602.0
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility							56							
- Preclinical							30							
- Phase I trial							22							
- Phase II trial							24							
- Phase III trial							2							
- Awaiting approval							0							
- Approved							19							
Funds raised - Total (M€)	0.1	0.1	0.5	1.7	0.0	0.0	332.3	320.4	13.7	30.3	22.3	1.7	368.9	354.1
0-2 yrs	0.0	0.0	0.1	1.7	0.0	0.0	42.4	118.2	5.1	0.1	2.9	1.6	50.5	121.6
3-5 yrs	0.1	0.0	0.1	0.0	0.0	0.0	132.6	89.5	8.1	30.2	7.0	0.1	147.9	119.8
6-10 yrs	0.0	0.1	0.2	0.0	0.0	0.0	81.9	38.6	0.4	0.0	12.4	0.0	94.9	38.7
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	12.3	0.0	0.0	0.0	0.0	0.0	12.3	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	63.1	74.0	0.1	0.0	0.0	0.0	63.2	74.0

## Germany

Once a shining example that political will, increasingly flexible capital markets and a strong academic base could be aligned, Germany's biotechnology sector began showing signs in 2002 that it may have run out of steam. Investors had clearly lost patience with the sector, company valuations which were already declining in 2001 continued to fall, while many of the country's leading companies had to embrace significant restructuring. And to make matters worse, the Deutsche Bourse's Neuer Markt was finally closed down in October 2002.

### Profile

Having expanded rapidly in the five years up to and including 2001, with almost three-quarters of its companies being formed during that time, Germany created fewer new companies than the UK and France for the first time since the BioRegio programme was first unveiled in 1996. It is certainly true that, by the end of 2002, Germany had more companies in its sector than any other European nation. But that is the only metric in which it can claim continental pre-eminence.

Indeed, the number of companies operating in Germany increased by 4% to 520. Domestic employment increased by 12% to just over 18,850; R&D spending rose by 42% to €1.62 billion; and revenues increased 18% to €4.1 billion. However, the financial constraints from restricted capital access were beginning to have an impact. The funding boom that had fuelled the German sector's growth over the previous six years was coming to an end, raising questions once again as to how sustainable the German biotechnology boom might be.

Demographically, as a consequence of its late enthusiasm for biotechnology, Germany's biotechnology sector is much younger than the UK, France, or the USA. Seven out of ten German biotechnology companies are still less than five years old. Germany's biotechnology industry is dominated by the Human Healthcare sector, which accounted for 32% of companies and 43% of the jobs in the industry. Given its comparative youth, Germany's Drug Discovery sector does have a disproportionate number of products in clinical trials. This is largely explained by companies spun-out from major pharmaceutical companies, with ready-developed product pipelines and sizable funding to progress their development.

The Human Healthcare sector was hardest hit by the funding squeeze, with new company formations dropping from 30 in 2001 to only six in 2002. Several of these were essentially cast-offs from existing businesses, no longer essential to the mother company's core mission. Sector R&D spending showed a healthy increase during the year to €917m, perhaps reflecting the fact that German companies were still feeling reasonably cash-rich and that the ramifications of the 2002 investment squeeze had not yet hit home. However, restructuring that was implemented by a number of major players to conserve precious cash reserves would suggest that such growth was unlikely to be sustained in 2003.

Service-oriented businesses accounted for half of the German sector's new companies in 2002, continuing apparent German enthusiasm for a service approach. (Between them the Service Provider and Technology Service Provider sectors account for 40% of all German biotechnology companies, compared with 28% in the UK, 31% in

Europe as a whole, and 34% in the USA). While the global investment community favoured companies pursuing a therapeutic focus, local German investors were still very keen to support business models that would provide early revenues streams.

Our analysis shows that many of the 44 Service Provider companies formed in Germany since 2000 were spawned from public sector research institutions and universities, with one of their main objectives being to service the institutions and markets from whence they came. International ambitions appear to be of limited interest to many of these companies, given the scale of their domestic market. Nevertheless, some of those Technology Service Providers, which have been backed by the blue chip venture capitalists, are more ambitious, both in terms of their determination to develop strong proprietary product/service platforms and in casting their net further afield in overseas markets.

Germany's Biodiagnostics sector is notable for its comparative youth; for the impetus that various Government genomics-based research programmes have given to the creation of new DNA-based molecular diagnostics companies; and for its comparatively high degree of focus on serving the food and beverage and agricultural sectors. Our study, however, revealed very few companies focused on environmental diagnostics.

Similarly, there were fewer dedicated Environmental companies than one might expect. We found no evidence of new environmental biotechnology companies being formed since 2000 although, as in the UK, there are many companies offering biotechnology-based environmental products/services in their

portfolio. Germany is host to one of the few public environmental biotechnology companies, Farmatic Biotechnology Energy AG, one of Germany's leading biofuels companies. The company tends to dominate the numbers.

Similarly, mature plant breeding and seed companies that have embraced the opportunities created by genetic modification and plant tissue culture techniques exert a strong influence on the Agbio numbers. Although many seed companies claim to use genetic breeding techniques, this survey includes only those companies who use molecular biology-based techniques as their primary technique for strain improvement.

Access to investors had been a major driver of German biotechnology fortunes and continued to be so. Unfortunately, it was the lack of investment that began to dominate the 2002 picture. Investors deserted Germany's public biotechnology companies. The total market capitalisation of the German biotechnology sector, which had already had a terrible year in 2001, continued to slump in 2002, falling a massive 74% to end the year at just under €1.4 billion. At the start of 2001, the German biotechnology sector had a combined market capitalisation of €12.73 billion.

The collapse of the Neuer Markt signalled the end of a new investment and shareholder culture in Germany. At its height in March 2000, the Nemax 50 - the Neuer Markt's index of its 50 leading high tech companies - reached €234 billion in value. By October 2002, when the Neuer Markt threw in the towel, the Nemax 50 had slumped by 95% to just €12 billion. The biggest victims of this collapse were small domestic institutions and retail investors. And while the blow-out was

more to do with over-valued TMT companies, biotechnology investors also lost significant sums.

While the German biotechnology sector needed a certain amount of revaluation, the correction may have overshot and completely ignored the genuine progress that some companies had made to their fundamental businesses. Qiagen, essentially a German business but headquartered in the Netherlands for tax purposes, finished 2002 trading at a P/E discount to its US peer group despite reporting an earnings growth rate of almost twice that of its counterparts. GPC Biotechnology closed the year trading at less than half its cash value, having secured €60 million in technology partnership commitments and boasting a potential cancer treatment in Phase III development.

Equity investment in German biotechnology companies dropped from €700 million in 2001 to €645 million in 2002. On the face of it, this looks like a modest decline given what was going on in the capital markets during 2002. However, one transaction, the €375m leveraged management buy-out of Viatrix from Degussa in May dominated the scene. Stripping this one financing event out illustrates the extent to which investors deserted the sector. Not surprisingly, no German biotechnology companies were able to raise finance through debt instruments. A continuing lack of finance will restrict the German biotechnology sector's ability to grow sustainably.

Following the example of their international counterparts, several of the more prominent German biotechnology companies restructured to survive. LION Bioscience, the German bioinformatics company which was valued as highly as

€1.5 billion in the genomics boom, abandoned its foray into drug discovery and returned to bioinformatics. The move resulted in staff cuts of some 30% and potential savings of €20 million a year. It also spawned the creation of new businesses such as the nuclear receptor technology company, PhenEx Pharmaceuticals.

Similarly, MediGene decided to spin out its cardiovascular and metabolic drug discovery programmes in order to concentrate on cancer. This move was prompted by the failure in Phase II trials of its Etomoxir carnitine palmitoyl transferase 1 inhibitor as a potential treatment of congestive heart failure. By spinning out the programme, MediGene hoped to cut its cash burn by €10 million a year and stretch the company's cash reserves through to 2005. The cardiovascular and metabolic programmes were spun out into a new company called Genovation which was started with 35 employees and about 10 validated clinical targets.

In other cases, the restructuring that began to take place was less subtle and tended to involve cutting headcount, not easy under German employment legislation. The most prominent cuts were at the antibody company MorphoSys and the Technology Service Provider Evotec OAI. MorphoSys cut its headcount from 120 to 91 to ensure at least three more years of operation, while Evotec OAI announced that it would reduce its headcount from 600 to 570 to contain costs.

A number of prominent private companies also began pruning back their ambitions. MorphoChem, which had merged with a US company, Small Molecule Therapeutics, in 1999 in a deal that was heralded as a potential new

model for transatlantic transactions, announced that it would be laying off up to 27 of the 32 employees it had in its US operations. The move reflected the company's shift from platform technologies to a more therapeutic-based focus. Also, citing the need to conserve cash, amaxa GmbH reduced its headcount from 100 to 80, Switch Biotechnology laid off 10 of its 75-strong workforce, and BioVisioN AG announced that it would reduce its workforce by 5 to 60 by the year end.

The greatest concern for Germany's biotechnology advocates was whether the announced restructuring wave was too little too late. A number of companies disappeared in 2002 through M&A or insolvency. Among the first to go to the wall were Technology Service Providers such as Elegene, GenProfile and Mermaid Pharmaceuticals, as well as the Service Provider, mice & more GmbH. They will not be the last.

In M&A, the most notable events were the merger of Curacyte with VitaResc Biotech, and the cross-border acquisitions of Rhein Biotechnology by the Swiss vaccines company Berna Biotech, and of Xzillion Proteomics by the UK's Proteome Sciences. Qiagen was Germany's only genuine consolidator as it acquired businesses to bolster its own activities.

The biggest challenge facing any meaningful M&A activity is the issue of who will foot the bill for such transactions. Interestingly, the call for more financial support from government agencies did not fall on deaf ears. The industry argued that government actions had created the situation and that government should take some responsibility for sorting it out. Between 1994 and 2001, the federal technology

investment institution, TBG, handed out €1.4 billion in loans to small high tech enterprises under the BTU program (Beteiligungskapital für kleine Technologieunternehmen). As part of BTU, 170 biotechnology companies received just over €370 million. The number of German venture capitalists with an interest in biotechnology increased from five to 150 over the same period. By 2002 though, many of the companies they had supported had the look of abandoned orphans.

The catalyst for the German biotechnology boom was the structure of financial support given to both companies and their venture backers. About 95% of TBG's funding was in the form of silent partnerships under which money was provided at favourable terms as subordinated loans that carried no voting rights. TBG matched venture capital investments in a German-headquartered start-up on a 1:1 basis up to €2.5 million. The capital entered the balance sheet as shareholder equity and was to be paid back after the end of the agreed period of the investment contract, and interest payments were made at a favourable fixed rate for the term. The run time of these types of "debt for equity" deals was typically six to 10 years.

What drew in the venture capitalists and other early stage backers, however, was the de facto insurance scheme offered by TBG. If a company failed within five years of formation, any private investor would receive from TBG up to 50 % of what TBG had put in as co-investor. Thus, if TBG had put €1 million into a company (matching €1 million from an investor) and then the company went into receivership, TBG would lose €1.5 million - the €1 million defaulted loan and €500,000 repaid to the investor.

This insurance cushion was even more comfortable in the former East Germany, where TBG guaranteed up to 80%. Unsurprisingly, however, the scheme has proved a substantial barrier to consolidation. Venture capitalists who have already lost all faith in biotechnology obviously prefer to allow companies to go bust and get 50% of their money back rather than allow merger or acquisition and receive next-to-nothing.

In accepting some of the responsibility for financing the creation of Germany's biotechnology sector in the first place, a joint working group of the Federal Ministry of Economics & Technology and the Federal Ministry of Education and Research opened up talks on a new fund to help VCs invest in M&A activities. However, it was not clear by the end of 2002 whether such an exercise would achieve anything more substantial than papering over the cracks.

## German Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	22	24	100	104	22	22	165	165	134	143	56	62	499	520
Age of company (% of sector total):														
0-2 yrs	45%	38%	33%	29%	14%	0%	51%	41%	46%	31%	61%	52%	45%	35%
3-5 yrs	23%	29%	27%	34%	18%	27%	31%	38%	25%	35%	30%	39%	27%	35%
6-10 yrs	14%	13%	19%	18%	23%	23%	10%	13%	17%	19%	9%	8%	14%	15%
11-15 yrs	5%	8%	11%	11%	27%	23%	4%	5%	7%	9%	0%	2%	7%	8%
Over 15 yrs	14%	13%	9%	9%	18%	27%	4%	4%	4%	6%	0%	0%	6%	6%
Total # of FTE employees (home)	467	820	3317	2913	1297	1246	6964	8060	3011	4113	1718	1703	16773	18855
# of new companies formed during calendar year	3	2	8	7	0	0	30	6	14	7	9	4	64	26
Sector outputs:														
Overall R&D spend (M€)	31.8	53.7	134.2	246.8	9.9	26.5	766.3	917.1	95.1	174.7	101.0	197.2	1138.2	1616.0
Overall revenues (M€)	201	266	565	625	231	208	1903	2184	481	718	96	110	3476	4111
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	554	81	641	87	1047	358	409	130	651	455	3302	247
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility							196							
- Preclinical							71							
- Phase I trial							35							
- Phase II trial							28							
- Phase III trial							8							
- Awaiting approval							3							
- Approved							136							
Funds raised - Total (M€)	6.4	8.0	43.0	8.8	35.5	0.4	518.4	558.4	17.7	20.4	73.6	48.2	694.6	644.2
0-2 yrs	6.4	5.0	8.0	2.0	0.0	0.0	211.0	432.0	15.9	11.9	31.2	0.5	272.5	451.3
3-5 yrs	0.0	3.0	35.0	6.8	0.0	0.0	218.8	87.1	1.8	8.5	41.9	47.7	297.5	153.1
6-10 yrs	0.0	0.0	0.0	0.0	0.0	0.0	87.6	39.3	0.0	0.1	0.5	0.0	88.1	39.4
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.9	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	35.5	0.4	0.0	0.0	0.0	0.0	0.0	0.0	35.5	0.4

## Ireland

The Irish biotechnology sector is small, light on research, and lacks significant investors. Despite an active pharmaceutical manufacturing sector, our data indicates that Ireland has only 36 biotechnology companies who employ an estimated 4,200 people (1,400 in R&D) in total. The Irish sector's dominance by Elan Corp was brought in to sharp relief by the accounting and management irregularities that came to light in 2001, and the rescue plan that Elan's new management team began to implement in 2002. The full impact of Elan's restructuring on the Irish sector will, however, only become apparent once the Group's 2003 results are released.

Bad news in the Irish Human Healthcare sector in 2002 was, however, offset by good news in Bidiagnostics, which saw healthy increases in sector employment, R&D and revenues. This was driven by a 50% increase in employee numbers at Biotrin and, more importantly, Trinity Biotech's acquisition of Xantra Inc's Biopool Hemostasis business and Sigma Diagnostics' haemostasis division.

### Profile

At the end of 2002, Ireland's Human Healthcare segment remained its largest, notwithstanding the savage slimming exercise forced upon Elan by its investors. Indeed, the company still accounted for 96% of the Human Healthcare sector's revenues and 89% of its R&D spend. As we commented in our earlier report, without Elan, Ireland appears underdeveloped.

Just under 30% of Ireland's companies are engaged in Bidiagnostics. They account for just under 20% of the

sector's employees - almost double that of 2001 - reflecting both Elan's woes and the acquisition trail embarked upon by Trinity Biotechnology in 2002 (and which the company has since continued).

Ireland's R&D-focused biotechnology sector has developed more slowly than elsewhere in Europe in recent years. Only one-seventh of Irish companies was under two years old - well below the European average of one-third and far behind the one-half of the Danish biotechnology sector that is under two years old. This apparent lack of dynamism in Ireland reflects the fact that national priorities and strengths in the life sciences lay elsewhere, notably in pharmaceutical manufacturing.

In addition, without local demand for specialised research functions, Ireland has no detectable Technology Services segment. It does, though, have a Service Provider segment of some seven companies, three of whom are suppliers of chemicals and biochemicals to pharmaceutical manufacturers.

The relative lack of growth in the Irish biotechnology sector can also be attributed to the absence of both a domestic research-based pharmaceutical sector and of a significant capital market. The pharmaceutical sector that exists in Ireland is focused on the manufacture of small molecule drugs and has been encouraged to grow by extensive regional development support and a sympathetic tax structure. That manufacturing growth is not yet likely to spawn small research based companies, and the development of small biotechnology enterprises requires a different environment. That the Irish model of support for chemical-drug manufacturing does not translate well

onto biotechnology may be indicated by the fact that we identified only one Biomanufacturing company in Ireland - Kinerton.

Ireland's capital markets are poorly developed. The country's biotechnology companies raised only €6.3 million through sales of equity in 2002 in four tranches. At the end of 2002, the market capitalisation of the three publicly quoted companies in the Irish sector stood at €757 million, compared to €17.59 billion a year earlier, an 96% fall, for which Elan was almost wholly responsible.

The main thrust of Elan's restructuring programme has been the divestment of non-core businesses and the disposal for cash of product marketing rights for a number of key products in major territories. Although the Irish Human Healthcare sector's product pipeline has not suffered numerically from Elan's difficulties as much as was anticipated, the company's restructuring and asset disposal programme has drastically reduced the medium-term likelihood of a revenue-based cash injection into the Irish sector. The "next generation" of Irish healthcare companies is small in number and has a lot of growing to do before it can make any impact on the clinical development process. In short, there is little indication from our data that Ireland is set to make a significant impact in biotechnology any time soon. While it may not be prone to the vagaries of biotechnology investors, it may lack the financial muscle to accelerate its biotechnology sector much beyond organic growth.

## Irish Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	4	4	10	10	4	4	9	10	6	7	1	1	34	36
Age of company (% of sector total):														
0-2 yrs	25%	0%	10%	10%	25%	0%	56%	30%	0%	14%	0%	0%	24%	14%
3-5 yrs	50%	75%	30%	10%	25%	25%	22%	40%	17%	14%	100%	100%	29%	31%
6-10 yrs	0%	0%	40%	50%	50%	75%	0%	10%	17%	14%	0%	0%	21%	28%
11-15 yrs	0%	0%	10%	20%	0%	0%	11%	10%	33%	29%	0%	0%	12%	14%
Over 15 yrs	25%	25%	10%	10%	0%	0%	11%	10%	33%	29%	0%	0%	15%	14%
Total # of FTE employees (home)	68	71	594	808	46	43	4918	2998	243	248	5	38	5874	4206
# of new companies formed during calendar year	0	0	1	0	0	0	1	1	0	1	0	0	2	2
Sector outputs:														
Overall R&D spend (M€)	0.32	1.11	12.64	14.48	0.47	1.72	500.42	551.20	22.51	31.50	0.16	3.76	536.51	603.77
Overall revenues (M€)	8.78	7.99	91.33	106.93	4.46	6.29	2010.15	1323.46	51.85	54.72	0.21	1.95	2166.78	1501.34
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	198	109	0	0	3779	264	0	0	0	0	3540	242
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility								10						
- Preclinical								5						
- Phase I trial								3						
- Phase II trial								3						
- Phase III trial								3						
- Awaiting approval								1						
- Approved								16						
Funds raised - Total (M€)	0.0	0.0	0.1	0.0	0.0	0.0	19.0	6.3	0.0	0.0	0.0	0.0	19.1	6.3
0-2 yrs	0.0	0.0	0.0	0.0	0.0	0.0	3.8	0.0	0.0	0.0	0.0	0.0	3.8	0.0
3-5 yrs	0.0	0.0	0.1	0.0	0.0	0.0	15.2	3.8	0.0	0.0	0.0	0.0	15.3	3.8
6-10 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	0.0	0.0	0.5	0.0	0.0	2.5
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

## Israel

Israeli biotechnology suffered a tough year in 2002. The total finance raised across all biotechnology sectors dropped to less than a tenth of the previous year, to €10.8 million. The number of new businesses formed was 15, half that in the previous year. However, R&D expenditure rose, albeit modestly, to €741 million, and overall revenues crept up to €952 million. It's always positive to have products approved, but the 18 approvals in 2002 fall short of the previous year's fifty-two. Nevertheless, these new products will help secure future revenues, potentially vital life blood, for a country short on investment. Israel has yet to escape its socio-political instability, undoubtedly making it less attractive to international finance and biopartnering opportunities. Without these, the growth of its life science sector will be difficult.

## Profile

Israel had a total of 216 companies in 2002, ranking it 5th in Europe by that metric. Israel's life science forte lies in Human Healthcare, with 98 companies in the field, including 6 new companies in the year. These build on a foundation of well-established companies, 23% of which were founded 6 or more years ago, and around 10% of them from over a decade ago. As in the previous year, these businesses generated more revenues than they spent on R&D, with €178,000 revenues per employee, compared to €139,000 R&D expenditure per employee. Both these figures are down on 2001, although the number of people employed rose by around 10% to 5,340. Israeli biotechnology has suffered from a lack of investment, attracting only €10.8 million in 2002, most of it by Human healthcare companies.

There remain concerns about the level of maturity of the companies in Israel, and whether they have the strategic forethought to align themselves with the demands of global investors and partners. Still, XTL Biopharmaceuticals showed signs of strong management in late 2002, through its full restructuring of the business to focus purely on developing treatments for hepatitis C. Despite this, investors in XTL put further pressure on the company, which nearly resulted in the removal of key members of the board. Settlement was reached whereby the board remained, but with significant cutbacks in salaries and overall expenditure.

On the drug development front, progress of products through the clinic has overall been slow. The thin late-stage pipeline looks unlikely to present many products for approval. In 2002, 18 products were approved, but this was from a backlog of products awaiting approval in 2001. The depleted stockpile of two products awaiting approval in 2002, backed up with only 3 products in Phase III, suggests that the recent flurry of approvals from Israel is now over. Further back along the chain, there is progress with basic research moving into preclinical research. The number of products in Phase I and Phase II trials has also risen slightly to 15 and 17 respectively.

Israel remains strong in the Agbio field. Approximately one in seven Israeli biotechnology companies operate in the sector (compared with 1 in 20 or less in most other countries), nearly one third of whom existed over a decade ago. Around another third were established in the last two years. This balanced position of companies in the field suggests that agbio could be an area of growth for Israel. Indeed, the number of

employees in Agbio increased by roughly a quarter in 2002 to 1,350. R&D expenditure across the 32 Agbio companies increased to €42 million. Reflecting this growth are the revenues, also up around one fifth to €228 million. Thus, Agbio provided just under a quarter of the total biotechnology revenues for Israel.

Israel also has notable activities in the Biodiagnostics, Service Provider, and Technology Service Provider arenas. Most substantial of these three is Biodiagnostics, which saw two new companies founded in 2002. The group as a whole consisted of 39 companies, employed 888 people and generated €160 million. Revenues in the Service Provider sector fell to €61 million, some €38 million ahead of the Technology Service Provider group.

Israeli companies found it very difficult to raise money during 2002. The geopolitical challenges deepened in 2002. Even domestic VCs were not putting their money into Israeli biotechnology companies and those companies that did raise funds were essentially repatriating it into offshore biotechnology entities, whether they were merger partners, as in the case of Procognia, or US affiliates. Israel has five publicly quoted biotechnology businesses listed on either in the US or on the London Stock Exchange. During 2002, the market capitalisation of these companies rose almost 15% from €8.04 billion to €9.24 billion.

Despite the heartening share price performance of its publicly quoted companies, overall, Israel's life science sector in 2002 had a rough time. One of the strongest advocates for the sector, Carmel Vernia, Chief Scientist of the Ministry of Industry and Trade,

unexpectedly resigned his post to join a semiconductor company. In his government position, Vernia championed the establishment of two new, privatised incubators dedicated to biotechnology companies. Vernia's departure came at the time when his department would normally issue grants to the biotechnology sector, throwing the process into chaos. Even the newly appointed co-chairman of the Israel Biotechnology Association (IBO), Michael Shickler, noted in an IBO newsletter (dated May 2002) that this was particularly painful given the lack of investor interest at the time, and that it could lead to companies going bust or young companies relocating outside of Israel.

## Israeli Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	32	32	36	39	4	5	94	98	24	26	11	16	201	216
Age of company (% of sector total):														
0-2 yrs	38%	34%	28%	18%	75%	60%	48%	44%	38%	38%	64%	44%	43%	38%
3-5 yrs	19%	16%	42%	46%	25%	40%	29%	27%	17%	15%	9%	38%	27%	28%
6-10 yrs	13%	19%	17%	21%	0%	0%	16%	18%	29%	27%	27%	19%	17%	19%
11-15 yrs	9%	9%	6%	5%	0%	0%	3%	6%	13%	15%	0%	0%	5%	7%
Over 15 yrs	22%	22%	8%	10%	0%	0%	4%	5%	4%	4%	0%	0%	7%	8%
Total # of FTE employees (home)	1084	1353	722	888	16	9	2357	2185	260	381	374	526	4813	5342
# of new companies formed during calendar year	3	3	3	2	0	1	19	6	2	1	1	2	28	15
Sector outputs:														
Overall R&D spend (M€)	32.06	41.83	39.96	131.38	0.16	0.77	416.67	497.37	29.11	28.39	23.39	41.37	541.36	741.12
Overall revenues (M€)	194.01	227.68	98.94	159.23	0.81	0.33	427.52	480.64	82.92	61.51	25.68	23.11	829.88	952.49
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	0	0	0	0	0	0	2039	9581	0	0	981	331	1792	949
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility								73						
- Preclinical								49						
- Phase I trial								15						
- Phase II trial								17						
- Phase III trial								3						
- Awaiting approval								2						
- Approved								18						
Funds raised - Total (M€)	0.2	0.0	25.9	0.0	0.0	0.0	138.8	10.6	3.1	0.0	22.5	0.2	190.5	10.8
0-2 yrs	0.2	0.0	4.0	0.0	0.0	0.0	38.2	0.0	0.7	0.0	22.5	0.0	65.6	0.0
3-5 yrs	0.0	0.0	11.6	0.0	0.0	0.0	43.8	0.0	2.4	0.0	0.0	0.2	57.8	0.2
6-10 yrs	0.0	0.0	10.3	0.0	0.0	0.0	41.2	10.6	0.0	0.0	0.0	0.0	51.5	10.6
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	15.5	0.0	0.0	0.0	0.0	0.0	15.5	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

## Norway

With no notable history of pharmaceutical development or technological entrepreneurialism, Norway is edging, rather than racing, its way towards having a biotechnology presence. The sector is small and not particularly young, which implies the sector is stable but not growing. Although there is no indication of an accelerated pace of development over recent years, 2002 was a good year for much of the Norwegian sector, with a healthy growth in revenues from a broadly static employee base.

### Profile

Norway has just 32 biotechnology companies employing just over 1000 people (about 400 of whom are in R&D) - one of the smallest sectors in this survey. About half of those people work in the Biodiagnostics sector (dominated by Axis-Shield) and a third in Human Healthcare. Norway's Agbio sector is notable for its strength in marine biotechnology. In common with other small and geographically peripheral nations, Norway has no Technology Service Provider sector to speak of. However, the formation of Interagon, a spin-off from knowledge management specialist Fast Search And Transfer (FAST), provided a welcome fillip to the category.

Norway is not spawning new companies particularly quickly. The 0-2 year old companies represent only 22% of the total number of companies, in striking contrast to its Scandinavian neighbours such as Denmark (52%) and Sweden (34%). Norway has the corporate demographic distribution of a maturing biotechnology nation such as the UK, in that a large proportion of its companies

have been established for over a decade. However, it only has a fraction of the number of companies relative to its population size.

Although overall employment remained steady in 2002, the Norwegian sector experienced encouraging revenue growth across all areas, except among Service Providers. The Human Healthcare sector was notable in that virtually all companies experienced a healthy rise in revenues. In Biodiagnostics, the story was more patchy, with Axis-Shield and Telelab accounting for most of the increase. In the Agbio sector it was the Food Technology companies NutriPharma and Natural ASA who accounted for the lion's share of the increased income.

Norwegian companies raised €3.7 million of equity investment in 2002 - a quarter of the 2001 amount, a fall much larger than the European average (50%) over the same period. The bulk of the Norwegian money was raised by Interagon, with its originating parent company retaining a 25% stake in the business.

Despite its small size, Norway does have two publicly quoted companies both listed on the Oslo Stock Exchange. These are the photodynamic cancer therapy company PhotoCure, and the nutraceuticals company NutriPharma. Over the 2001 and 2002 calendar years, these two companies had opposing experiences in share price movements. The total market capitalisation of the publicly quoted Norwegian biotechnology sector decreased by 70% over the year to close at €97.6 million.

Norway's path to biotechnology success is not going to be easy. It is a small nation with neither a strong financial sector to fund development nor a

pharmaceutical tradition from which to draw either experienced staff or exciting development projects. Within Scandinavia, Finland and Sweden have a recent history of high-tech entrepreneurialism, while Denmark and Sweden have relatively large pharmaceutical hubs around which

expertise, experience, and IP is generated. Norway has none of these advantages. However, the small amount of Norwegian biotechnology that does exist is relatively independent of the whims of financial markets, as it is funded largely from organically generated revenues.

## Norwegian Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	6	6	8	7	0	0	11	11	5	5	1	3	31	32
Age of company (% of sector total):														
0-2 yrs	0%	0%	13%	0%	0%	0%	64%	36%	20%	20%	100%	67%	32%	22%
3-5 yrs	17%	0%	63%	57%	0%	0%	27%	45%	20%	20%	0%	33%	32%	34%
6-10 yrs	50%	67%	0%	14%	0%	0%	9%	18%	0%	0%	0%	0%	13%	22%
11-15 yrs	17%	17%	0%	0%	0%	0%	0%	0%	60%	60%	0%	0%	13%	13%
Over 15 yrs	17%	17%	25%	29%	0%	0%	0%	0%	0%	0%	0%	0%	10%	9%
Total # of FTE employees (home)	125	129	532	526	0	0	169	214	167	118	13	48	1006	1035
# of new companies formed during calendar year	0	0	0	0	0	0	2	0	1	0	1	1	4	1
Sector outputs:														
Overall R&D spend (M€)	5.72	6.14	18.84	27.55	0.00	0.00	29.57	48.77	10.87	6.09	0.74	1.99	65.75	90.53
Overall revenues (M€)	37.17	52.85	80.87	84.63	0.00	0.00	2.83	8.06	20.79	16.35	0.56	0.91	142.21	162.80
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	2037	731	0	0	0	0	852	2476	0	0	0	0	5801	1952
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility								6						
- Preclinical								7						
- Phase I trial								9						
- Phase II trial								1						
- Phase III trial								1						
- Awaiting approval								7						
- Approved								6						
Funds raised - Total (M€)	0.0	0.0	3.6	0.0	0.0	0.0	8.9	0.9	0.0	0.0	0.0	2.8	12.5	3.7
0-2 yrs	0.0	0.0	0.0	0.0	0.0	0.0	3.9	0.9	0.0	0.0	0.0	2.8	3.9	3.7
3-5 yrs	0.0	0.0	3.6	0.0	0.0	0.0	5.0	0.0	0.0	0.0	0.0	0.0	8.6	0.0
6-10 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
11-15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

## Sweden

Sweden has a long tradition in biopharmaceuticals. Some of the first recombinant therapeutics involved Swedish companies such as Kabi Pharmacia. This has had an impact on the age profile of the 86 companies that made up the 2002 Swedish biotechnology sector, a quarter of whom are over 10 years old. But much of the recent drive can be attributed to the pro-business attitudes of the world-acclaimed Karolinska Institutet and its president, Hans Wigzell.

While biotechnology employment in Sweden showed only modest increases in 2002, there was encouraging growth in both R&D spend (€411m) and revenues (€748m), both driven by strong performances from leading Human Healthcare players. 2002 could not, however, match the sector's 2001 fundraising success where the exceptional event of Biovitrum spinning out of Pharmacia skewed the data. Finance raised in Sweden in 2002 dropped by two-thirds to €93m. As elsewhere, there was a marked slowdown in the number of new companies created.

### Profile

In recent years the Swedish sector has benefited from a big government push to support the development of biotechnology companies. The separate mergers of Sweden's former pharma giants, Pharmacia and Astra, also contributed to the development of an entrepreneurial biotechnology community. There were changes, too, in patent law, enabling individual scientists and not just institutions to file for and own the patents which are used to establish new companies. Sweden's

biotechnology industry is congregating around Stockholm and in the southern part of the country, adjoining Denmark, in the so-called Medicon Valley. The Karolinska Institutet with its own fund and dedicated tech transfer teams alone catalysed the creation of 10 companies between 2001 and 2002.

Other studies have estimated the size of the Swedish biotechnology community to be as large as 400 companies, but the vast majority are providers of generic technologies to the pharmaceutical and life science research companies. The 86 dedicated biotechnology companies that we have identified employed just over 3,200 people (2,000 in R&D - a ratio that puts Sweden at the top of the European league).

Sweden's Agbio sector is, as one would expect given its geographic location, small. It has only one Crop Agriculture company and one Biopesticides company, the remaining four companies being focused in the Food Technology area. The strong gains in the Biodiagnostics sector over the year were posted by Diffchamb Sverige, the country's sole food diagnostics concern. 2002 was an eventful year for the company, which extended its technology base and market reach by acquiring Eurochem SpA. All but one of Sweden's remaining Biodiagnostics companies - all focused on Human Healthcare applications - saw a modest decline in revenues.

The spinning-out of Biovitrum in 2001 provided a major boost to Sweden's Human Healthcare sector, with the company adding significantly to its headcount, more than doubling both its R&D spend (€80m) and revenues (€148m). Other companies posting similar rates of growth, albeit with smaller numbers, included Affibody and

Kara Bio. The Swedish Human Healthcare sector is, like Finland's, notable for having a significant proportion of Biomaterials companies. Unlike their Finnish peers, however, Sweden's ten Biomaterials companies had a torrid 2002 with virtually all of them shedding employees and reducing their R&D spend, although a couple did see modest increases in revenue.

At the end of 2002, Sweden had 28 compounds in clinical trials, with ten in Phase II and three in Phase III. There were a further 17 products in preclinical trials and 15 in Phase I, reflecting the relative youth of much of the Swedish Human Healthcare sector. 2002 was a steady-state year for the Technology Service Provider sector, which is dominated by Functional Genomics companies (they accounted for 350 of its 390 employees and all its revenues).

Swedish companies made some positive corporate and clinical progress during 2002. Biora has received European Union approval for a new indication for its biotechnology dental product, EmdogainGel. Active Biotechnology unveiled promising research associated with a multiple sclerosis treatment and was given the green light to start testing a potential anti-cancer compound by the UK authorities.

Biovitrum AB signed a worldwide agreement with GlaxoSmithKline to develop and commercialise its 5-HT<sub>2C</sub> receptor agonists for the treatment of obesity and other medical disorders. GSK promised to pay Biovitrum an upfront fee and periodic milestone payments related to development progress, regulatory submissions and approvals, which, if successful, would result in €140 million in revenue for the Sweden firm.

Swiss pharma major, Hoffmann-La Roche agreed to in-license from Medivir a non-nucleoside reverse transcriptase inhibitor, which was in pre-clinical development and had shown interesting resistance properties. Roche agreed up-front and milestone payments to Medivir totalling €40 million, should the product reach the market, including buying €1.9 million of Medivir equity and €2.9 million cash.

Pyrosequencing unveiled plans to accelerate the route to profitability, laying off 23 people at its headquarters in Uppsala. The restructuring was expected to decrease the cash expenses by approximately \$7 million on an annual basis beginning in 2003. And BioInvent International confirmed its plan to shift its business focus from biomanufacturing to drug discovery.

The Stockholm stock exchange is arguably one of Europe's strongest markets for biotechnology companies. Historical investment restrictions (now lifted) required Swedish pension funds to invest in indigenous companies, and had resulted in a relatively large group of listed companies in Sweden. However, despite the relatively positive newsflow emanating from the sector, Sweden's 10 listed companies closed the year with a combined market capitalisation of €495 million, 62% down from the start of the year, which was roughly in line with the results of the Danish sector.

The market downturn, however, clearly made Swedish investors wary, and funds especially tight for early stage companies. This is in spite of the presence of the well funded HealthCap biotech-focused venture capital funds. In addition, Sweden's tax system appears to disadvantage local venture capitalists. Investors were obliged to pay tax every time a portfolio company was sold at a

profit, reducing the ability of venture firms to recycle their funds. The Swedish parliament recommended, during 2002, to introduce certain capital gains tax exemptions for Swedish companies.

Three companies accounted for just over two-thirds of the €93m raised by Swedish companies in 2002. Personal Chemistry, the chemical synthesis subsidiary of Biotage, raised €32m of

venture capital, and Global Genomics and Melacure Therapeutics €33.5m in roughly equal tranches. The balance was split among a further sixteen companies. As we commented in our previous report, Swedish companies find it difficult to attract non-Nordic capital with much of the responsibility landing on the shoulders of local life science specialist investors, HealthCap, InnovationsKapital, and Innoventus.

## Swedish Summary Data Set

Key Performance Indicator	Agbio		Biodiagnostics		Environmental		Healthcare		Service providers		Technology Service Providers		Sector overall	
	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002	2001	2002
# of companies	6	6	5	5	0	5	48	50	16	15	8	10	83	86
Age of company (% of sector total):														
0-2 yrs	17%	0%	20%	20%	0%	0%	46%	34%	50%	27%	75%	70%	46%	34%
3-5 yrs	33%	33%	0%	0%	0%	0%	29%	36%	6%	27%	13%	20%	22%	30%
6-10 yrs	33%	33%	20%	0%	0%	0%	8%	12%	19%	13%	0%	0%	12%	12%
11-15 yrs	17%	33%	60%	60%	0%	0%	17%	16%	6%	13%	0%	0%	16%	17%
Over 15 yrs	0%	0%	0%	20%	0%	0%	0%	2%	19%	20%	13%	10%	5%	7%
Total # of FTE employees (home)	147	109	92	213	0	0	1879	1994	381	509	347	388	2846	3213
# of new companies formed during calendar year	0	0	1	0	0	0	10	2	1	0	0	1	12	3
Sector outputs:														
Overall R&D spend (M€)	5.15	4.85	4.00	11.76	0.00	0.00	262.91	315.58	24.10	48.28	28.86	30.14	325.02	410.60
Overall revenues (M€)	10.71	10.42	16.62	20.12	0.00	0.00	188.87	326.57	64.93	308.95	72.47	82.11	353.61	748.18
Sector productivity:														
Average market capitalisation per quoted company employee as at end of calendar year (000€)	1034	318	0	0	0	0	1190	439	1013	326	1615	758	1321	521
Healthcare product development pipeline (# of prods by stage of development):														
- Concept/feasibility							68							
- Preclinical							17							
- Phase I trial							15							
- Phase II trial							10							
- Phase III trial							3							
- Awaiting approval							0							
- Approved							14							
Funds raised - Total (M€)	0.0	0.0	0.0	1.7	0.0	0.0	242.1	31.8	37.8	37.9	4.8	21.4	284.7	92.8
0-2 yrs	0.0	0.0	0.0	0.8	0.0	0.0	163.2	0.0	2.3	0.0	4.8	21.4	170.3	22.2
3-5 yrs	0.0	0.0	0.0	0.0	0.0	0.0	35.4	17.4	6.4	32.2	0.0	0.0	41.8	49.6
6-10 yrs	0.0	0.0	0.0	0.0	0.0	0.0	11.7	8.2	0.0	0.0	0.0	0.0	11.7	8.2
11-15 yrs	0.0	0.0	0.0	0.9	0.0	0.0	31.9	6.2	0.0	0.0	0.0	0.0	31.9	7.1
Over 15 yrs	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	29.1	5.7	0.0	0.0	29.1	5.7

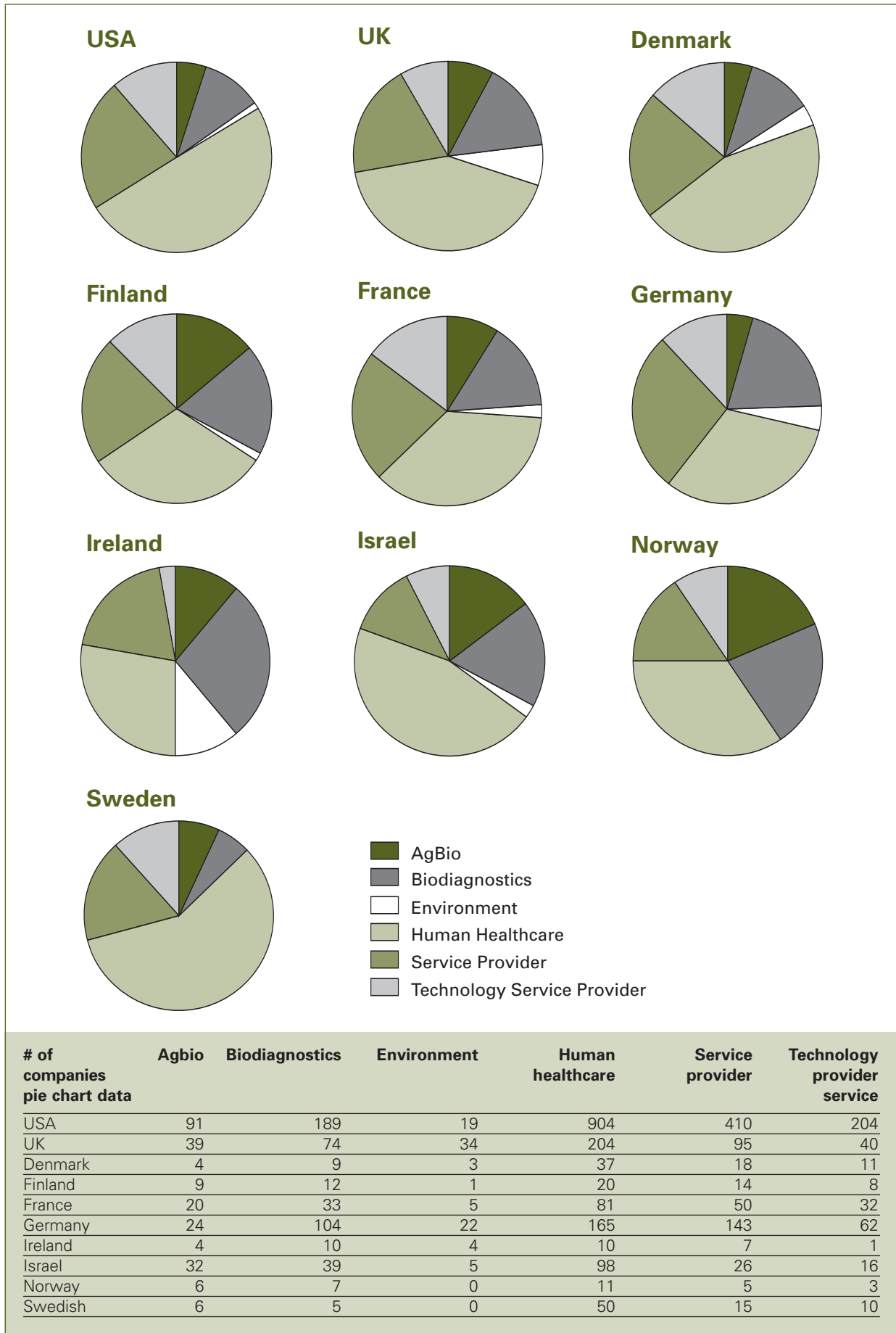
# Appendices

## Appendix A - Additional charts

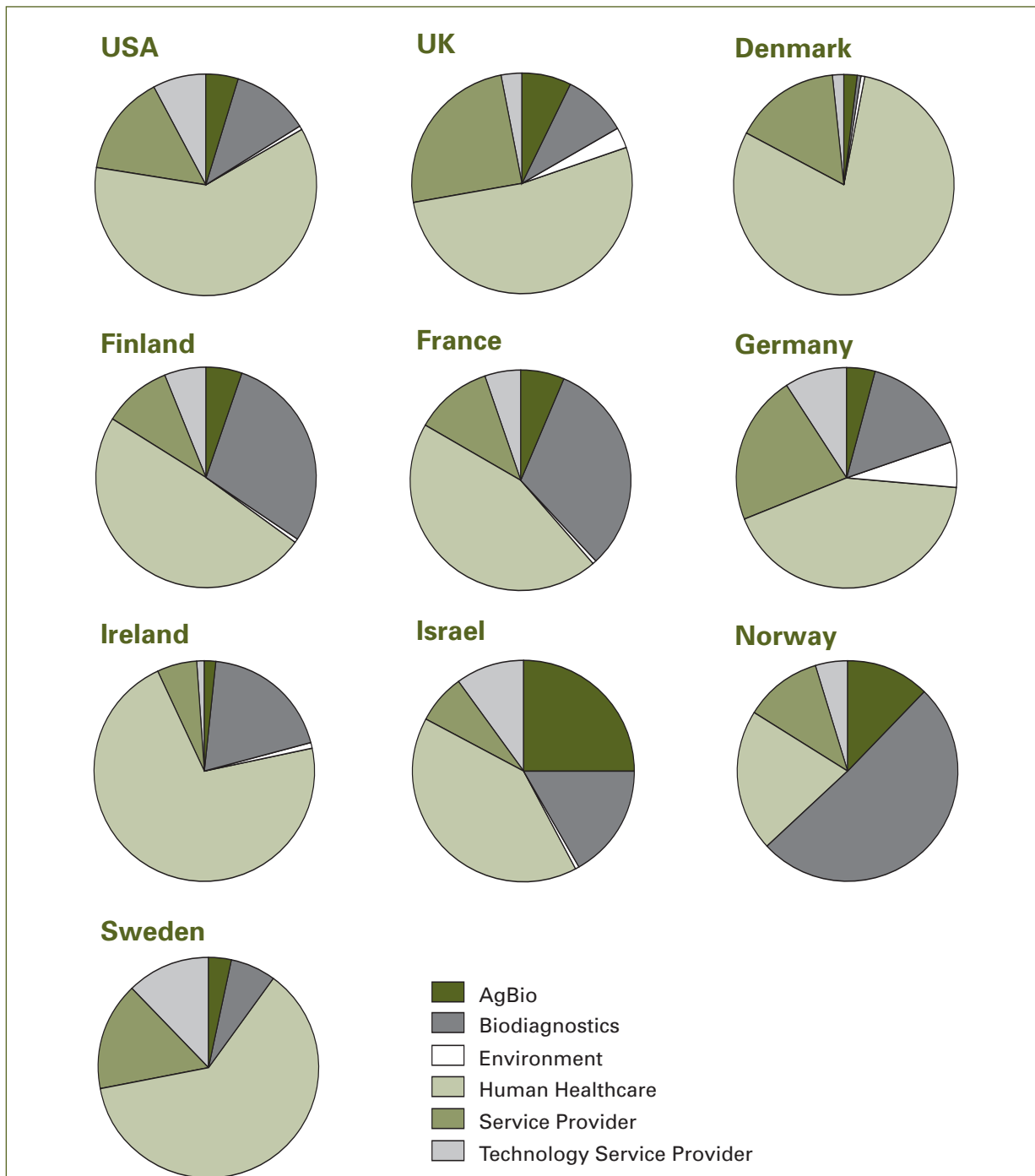
### Geographical profile

Profile	Page
<u>Number of companies</u>	65
<u>Employees</u>	66
<u>Revenues</u>	67
<u>R&amp;D spend</u>	68

## Number of companies

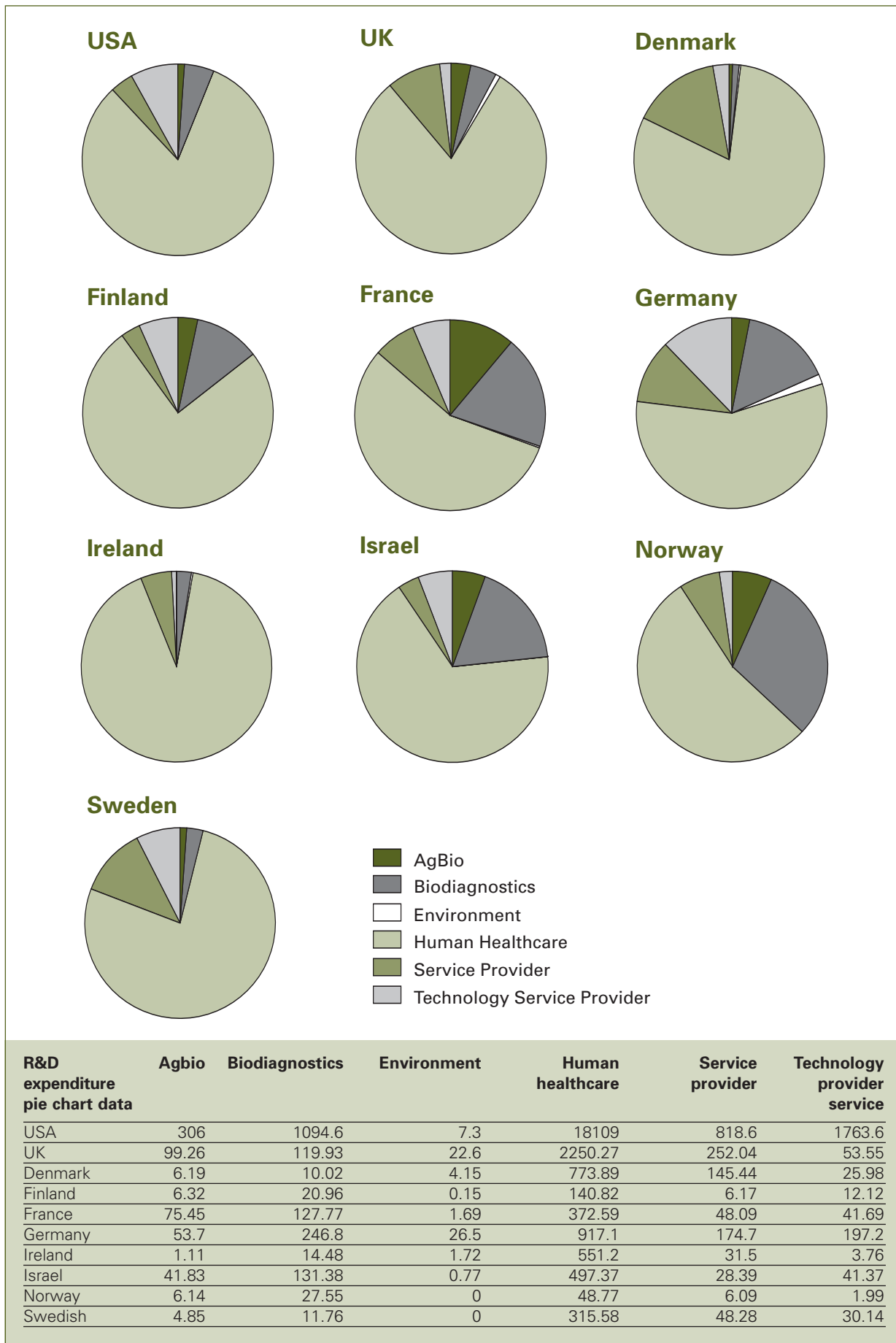


## Employees

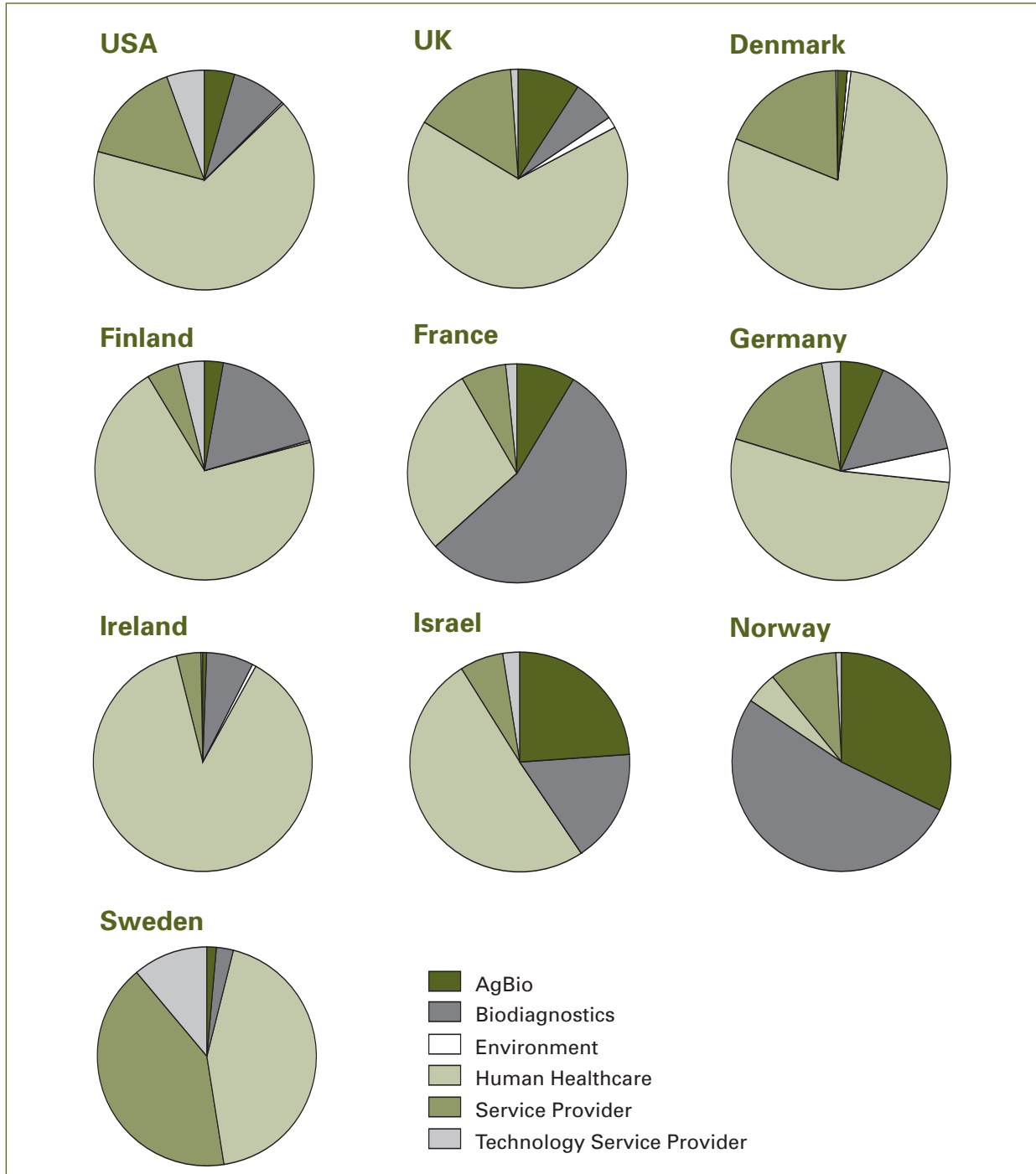


# of employees pie chart data	Agbio	Biodiagnostics	Environment	Human healthcare	Service provider	Technology provider service
USA	7670	18404	722	97019	23399	12410
UK	1936	2450	767	13600	6441	736
Denmark	354	108	78	13326	2634	246
Finland	110	586	15	982	201	123
France	586	2882	45	4050	1027	476
Germany	820	2913	1246	8060	4113	1703
Ireland	71	808	43	2998	248	38
Israel	1353	888	9	2185	381	526
Norway	129	526	0	214	118	48
Swedish	109	213	0	1994	509	388

## R&D Expenditure (€m)



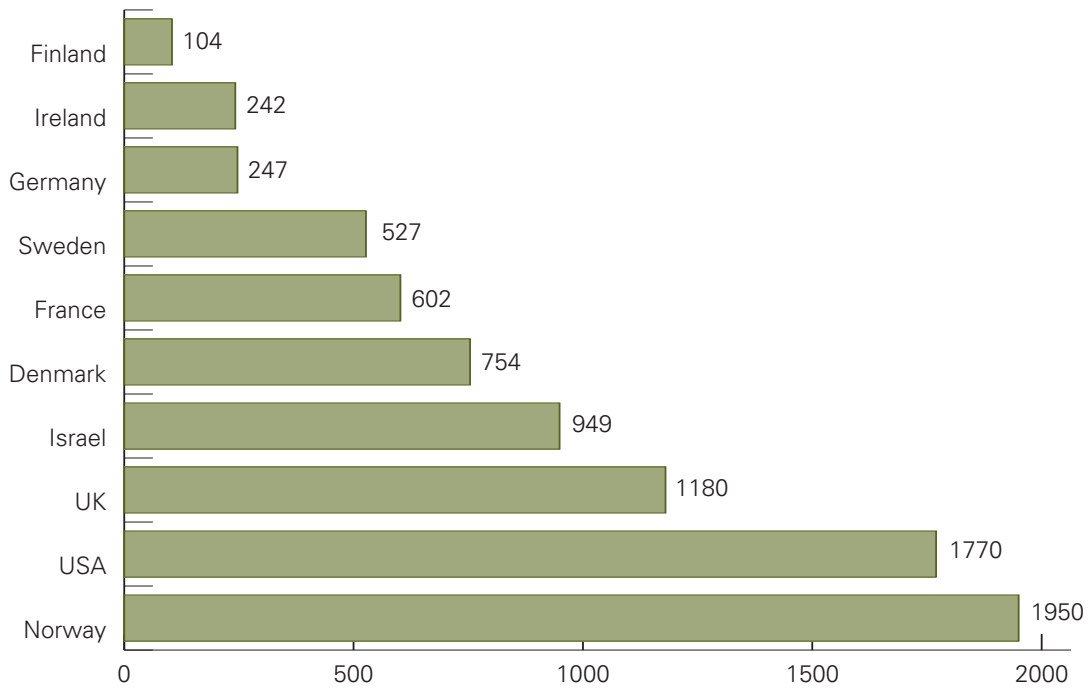
## Revenues (€m)



Revenues pie chart data	Agbio	Biodiagnostics	Environment	Human healthcare	Service provider	Technology provider service
USA	1674	2881	56	23780	5508	1933
UK	590.02	400.27	114.73	4223.07	968.71	60.81
Denmark	64.92	6.93	16.56	3512.18	825.31	8.78
Finland	7.4	44.4	1.07	177.69	11.72	9.65
France	171.5	1064	3.83	552.62	126.33	31.32
Germany	266	625	208	2184	718	110
Ireland	7.99	106.93	6.29	1323.46	54.72	1.95
Israel	227.68	159.23	0.33	480.64	61.51	23.11
Norway	52.85	84.63	0	8.06	16.35	0.91
Swedish	10.42	20.12	0	326.57	308.95	82.11

## Fund Raising

Market capitalisation per quoted employee by country, as at 31/12/2002 (€000s)



## Appendix B - Methodology

### Currencies

Prior to analysis all metrics were converted to Euros using the exchange rates below.

Currency to Euro	Exchange rate (31/12/2001)	Exchange rate (31/12/2002)
Dkr	0.135	0.135
US Dollar	1.14	0.95
GBP	1.634	1.535
S Kronur	0.107	0.110
Nkr	0.125	0.138
Shekkel	0.255	0.200

### Key challenges

There are many issues concerning collection of key performance indicators that are common to all emerging high technology sectors. They include:

- A lack of reliable data
  - ▶ Poor coverage of the sector by commercial databases, in particular:
    - Lack of revenue data
    - Poor or inconsistent categorisations of companies or data points
    - Difficulties in gaining access to information on new/emerging companies
  - ▶ Inadequacy of SIC Codes as a means of classifying fast-moving R&D-based enterprises, in particular:
    - The range of classifications may not encompass the spectrum of activities in which subject companies are engaged
    - The introduction of new SIC Classes may lag the pace of technology development in the subject industry

- ▶ Reluctance of companies to disclose information – public disclosure of information by US quoted companies is very thorough and, generally speaking, better than that of their European peers. However, it is equally, if not more, difficult to obtain financial information on private US companies as it is for their European peers as they are under no obligation to publicly file or disclose their annual results. Furthermore, survey fatigue is a potentially significant barrier to data access on both sides of the Atlantic
- Lack of consistently applied definitions
  - ▶ This issue, perhaps more than any other, has inhibited meaningful comparisons of the European and international biotechnology industry in the past. As a result, government agencies and other stakeholder groups have found it difficult, if not impossible, to base their decisions upon reliable and informed analyses.

### A consistently applied definition of biotechnology

The bedrock of our methodology lies in the consistent application of a definition of biotechnology that was agreed with the DTI at the outset of the study. Only companies whose primary commercial activity depends on the application of biological organisms, systems or processes, or on the provision of specialist services to facilitate the understanding thereof are included in the remit of this study.

Big pharma companies, other major corporates, and companies for whom biotechnology is an important but, nonetheless, minor part of their business are not included in this study. Dedicated biotechnology subsidiaries

of major corporates are included, however. As a result, the study does not, and was not designed to reflect, the full scope and extent of biotechnology activity in the countries surveyed. This is particularly relevant in the Agbio and Environmental sectors where the number of pure-play biotechnology companies is extremely limited, albeit that biotechnology-based techniques are both a widespread and increasingly vital part of their technology mix.

A rigorous application of this definition, likewise, means that many companies who might, and indeed, often do feature in reviews of the biotechnology industry have been excluded from this study. Examples include companies such R&D Systems, Genetix, Applied Biosystems and Quest Diagnostics, to name a few. By the same token, companies such as Novo Nordisk have been included, notwithstanding their scale, because they do satisfy the definition above.

### Sectoral analysis

Companies analysed in this study have been categorised according to their overall sector (eg healthcare, environmental) and according to their primary area of activity (eg vaccines, water and effluent treatment). The six overall sectors and 24 primary activities used for the purposes of our classification and analyses are as follows:

Activity category	Primary activity
Agbio	Animal healthcare, Biopesticides, Crop agriculture, Food technology
Biodiagnostics	Environmental diagnostics, Healthcare diagnostics, Industrial diagnostics
Environmental	Biocleaning, Bioremediation, Water & effluent treatment, Waste recycling
Human healthcare	Biomaterials, Drug delivery, Drug discovery, Gene therapy, Genomics, Vaccines
Service providers	Bioprocessing, Chemicals, Contract research, Contract manufacturing
Technology service providers	Bioinformatics, Functional genomics, High throughput screening

To further enhance the flexibility of the data and increase the accuracy and range of analyses, companies were split into five age bands, namely:

- 0-2 years
- 3-5 years
- 6-10 years
- 11-15 years
- Over 15 years

These age-bands were selected for two reasons. First, to ensure that companies for whom datapoints were not available were analysed on the basis of real metrics drawn from companies at a similar stage in their development cycle. Secondly, to build a composite picture of the sector based on an assessment of the dynamics and profile of clearly-defined market sub-segments. This approach resulted in analyses being generated from a universe of 120 sub-segments for each country covered in this report.

## Data-gathering

To ensure that we included only companies that fall within the above definitions and sectors/sub-sectors, and that their data profile was complete as possible, an extensive data gathering process was undertaken, using the following approach:

- **Identification of companies for potential inclusion**

Our starting point in each country was the universe of well known, readily identified biotechnology companies. Each initial country list was then supplemented by identifying potential additional companies via:

- ▶ The identification and searching of the directories and websites of university technology transfer offices, business incubators, regional development agencies, trade and industry bodies
- ▶ Contact with, and searches of the promotional materials issued by, investor groups
- ▶ Industry directory searches; and
- ▶ Contact with Critical I's own network of industry contacts

This resulted in an initial long-list of companies being compiled – in the case of the USA this extended to over 8,000 companies

- **Filtering of companies against the agreed definition of biotechnology**

- ▶ Information on the companies' operations and activities was then scrutinised, recorded in an Access database (to provide a record of activity transitions year-on-year) and used as the basis for deciding whether or not a company should be included and, if so, to which primary activity category (i.e. sub-sector) it should be assigned.

- ▶ Each selection and activity categorisation was approved by two members of our review panel. In the event of a split decision a third reviewer held a casting vote.

Continuing with the USA example, this stage of the process reduced the initial list down to 4,000 or so companies, and then the final tally of just over 1,800 companies.

- **Gathering raw data** – this phase involved the
  - ▶ Obtaining and analysis of **all** available company annual reports & accounts
  - ▶ The detailed review of company websites & other public information sources to gather the required metrics
  - ▶ Confirmation of each company's Primary Activity category
- **Validation of data** – this phase involved
  - ▶ Inviting CEOs/FDs to review and validate the metrics gathered on their company via a secure and password-protected website
  - ▶ Checking company submissions for accuracy/consistency/completeness
  - ▶ Clarifying those returns as required with each company, before accepting their data into the data base and incorporating it into the analysis data-set

## **Extrapolation of original data for each KPI Analysis Year**

The original data set was then used to generate a set of extrapolation multipliers from which to calculate proxy values for those companies in each sub-sector age group for whom original data was not available. Totals for each given metric covered in the study were then calculated by aggregating the original and proxy values for that metric for each sub-sector age group. Country sub-sector age group totals were then aggregated to build up composite metrics at sectoral and national sector level.

We shall be happy to provide further details of the methodology if required.

## Appendix C - Sector definitions and segmentation

The bedrock of the methodology and analysis in this study lies in the consistent application of a definition of biotechnology that was agreed with the DTI at the outset.

For the purposes of our research only companies whose **primary** commercial activity depends on the application of biological organisms, systems or processes, or on the provision of specialist services to facilitate the understanding thereof are included in analysis.

For analysis purposes the biotechnology industry was divided into six main sectors and twenty-four sub-sectors, as defined in the table overleaf. Further commentary on these definitions is provided in Appendix B which describes the methodology used in this study.

<p><b>Agbio</b> - companies using biotechnology to modify and enhance the components and characteristics of the food chain</p>	<p><b>Animal health</b></p>	<p>Application of molecular and cellular biology to veterinary drugs and vaccines, feed additives, and animal improvement (but not pharming)</p>
	<p><b>Biopesticides</b></p>	<p>Biologically-based techniques to protect plants or promote their growth or for the control of insect populations</p>
	<p><b>Crop agriculture &amp; horticulture</b></p>	<p>Application of molecular and cellular biology to plants, non-food crops and biofuels</p>
	<p><b>Food technology</b></p>	<p>Development and supply of enzymes and other processing aids (but excluding upstream processing through, for example, genetic modification of plants)</p>
<p><b>Biodiagnostics</b> - Development of products for defining status or susceptibility in any applications sector, using technologies such as immunoassays, monoclonal/polyclonal antibodies, and DNA based diagnostics</p>	<p><b>Environmental diagnostics</b></p>	<p>Development of products for detecting and monitoring of pollutants and other environmental markers in air, water and soil, and of remedial processes for the treatment of pollution</p>
	<p><b>Healthcare diagnostics</b></p>	<p>Development of products for detecting and diagnosing medical conditions. Technologies include immunoassays, monoclonal/polyclonal antibodies, and DNA based diagnostics</p>
	<p><b>Industrial diagnostics</b></p>	<p>Development of biological products or processes for detecting and monitoring both desired and undesired states in industrial processes</p>
<p><b>Environmental</b> - Application of molecular and cellular biology directly to the restoration or preservation of a healthy environment, or to the avoidance of adverse environmental effects, including biosensors &amp; bioremediation</p>	<p><b>Biocleaning</b></p>	<p>Development of biological products or processes, for example, enzymatic fat digestants, to clean and restore contaminated commercial and industrial environments</p>
	<p><b>Bioremediation</b></p>	<p>Development of biological products (living organisms) to degrade hazardous organic contaminants or to transform hazardous inorganic contaminants to environmentally safe levels in soils, subsurface materials, water, sludges and residues</p>
	<p><b>Waste recycling</b></p>	<p>Development of products to assist waste management via decomposition into harmless by-products and to derive useful products via recycling</p>
	<p><b>Water &amp; effluent treatment</b></p>	<p>Development of biological products to remediate contaminated water and effluents to environmentally safe levels</p>

<p><b>Human healthcare -</b> Application of molecular and cellular biology to the development of medical devices and biopharmaceuticals and to methods of improving their efficiency and effectiveness. Excludes diagnostics and clinical research organisations.</p>	<p><b>Biomaterials</b></p>	Development of non-drug materials that can be used to treat, enhance, or replace a tissue, organ or function in the body. Technologies include tissue engineering, artificial organs, bioceramics, medical devices and implantable drug delivery systems
	<p><b>Drug delivery</b></p>	Application of biochemical engineering to most efficiently and safely deliver an active pharmaceutical agent to the target site where it can effectively exert the desired therapeutic action
	<p><b>Drug discovery</b></p>	Application of molecular and cellular biology to the development of biopharmaceuticals
	<p><b>Genomics</b></p>	Application of biological techniques to the study of genomes, including gene sequencing and gene function, with the aim of linking gene to disease and developing highly targeted and specific therapeutics
	<p><b>Gene therapy</b></p>	Research into treating, curing or ultimately preventing disease by changing the expression of individual genes
	<p><b>Vaccines</b></p>	Use of biological techniques to develop a preparation of dead or weakened pathogens or derived antigenic determinants that is used to induce formation of antibodies or immunity against the pathogen
<p><b>Service providers -</b> companies providing essential biologically-based services to companies both within and without the biotechnology sector.</p>	<p><b>Bioprocessing</b></p>	Supply of fermentation, culture, separation, purification expertise and methods for manufacturing (including pharming)
	<p><b>Chemicals</b></p>	Development of biological products or processes for the fine, specialty and bulk chemical industry (includes the pharmaceutical industry)
	<p><b>Contract manufacturing</b></p>	Fee-for-service manufacturing to cGMP standards
	<p><b>Contract research</b></p>	Fee-for-service R&D
<p><b>Technology service providers -</b> developers of toolsets to aid the R&amp;D efforts of other companies.</p>	<p><b>Bioinformatics</b></p>	Bioinformation generation, storage, and handling tools, molecular modelling
	<p><b>Functional genomics</b></p>	Study of, or discovery of, what traits/functions (generally via proteins expressed) are conferred to an organism by given (gene) sequences
	<p><b>High throughput screening</b></p>	Development of laboratory tools that allow study of hundreds or thousands of samples at once





