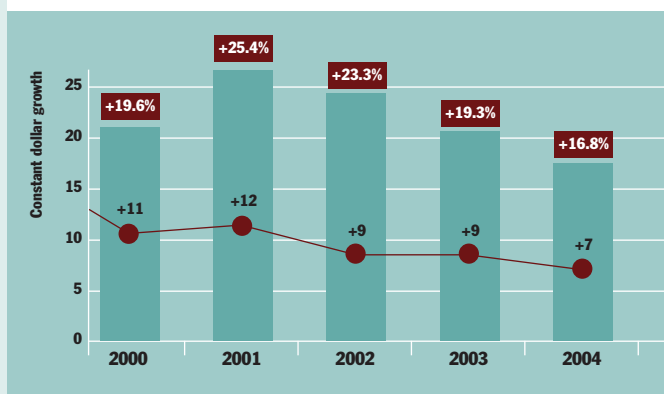


INDUSTRY IN FIGURES

BIOTECH KEY DRIVER OF PHARMACEUTICAL GROWTH

Over the last five years, the biotech industry has endured a number of significant challenges, notably in technology, market dynamics and regulations. Despite this, the sector strengthened in 2004, a trend that is expected to continue until 2010. Guy Bate and Eva Edery of IMS Management Consulting take a look at biotech's promising future.

Figure 1. Biotech vs pharma growth over last five years

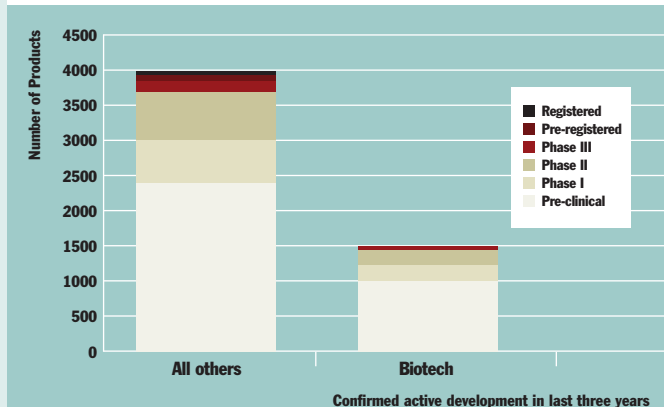


Source: IMS Health; MIDAS, MAT Dec 2004

In spite of recording its slowest growth rate in five years (see Figure 1), the biotech industry continued to gain ground in 2004, again outpacing pharma (17 per cent vs 7 per cent growth) and driving 23 per cent of total industry growth. Sales reached \$44bn, representing 8 per cent of total industry revenues (excludes direct sales from manufacturers that are currently not supplied to IMS). Almost 16 per cent of products achieving blockbuster status (defined as global sales exceeding \$1bn) in 2004 were biotech drugs and at its current rate of evolution the sector is expected to represent an increasing proportion of the blockbuster market. Biotech projects already account for 27 per cent of the current pipeline (see Figure 2), and notwithstanding the patent expiry of seven major biotech molecules over the next five years, the future looks good.

Notable technology advances permit the delivery of protein- and peptide-based agents without the need for injections

Figure 2. Biotechnology projects within active pharma pipeline



Source: IMS R&D Focus, Dec 2004

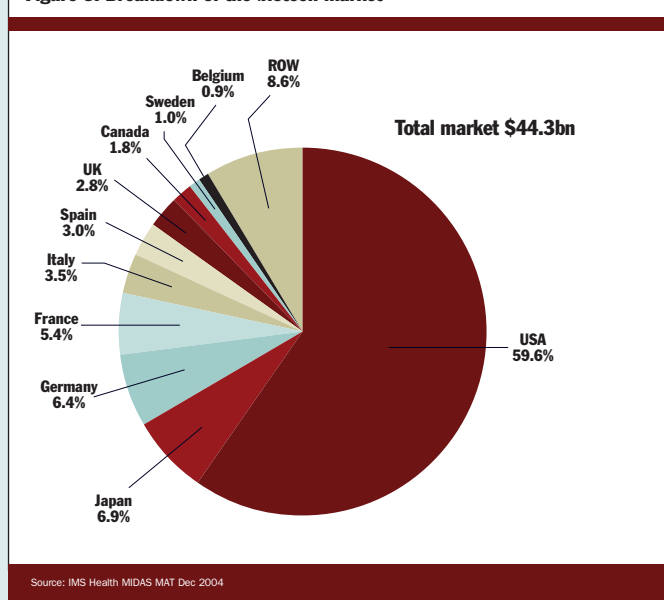
The sector is also facing significant environmental challenges – changes in technology, market dynamics and regulatory systems – which are reshaping biotech and call for a new definition of the optimal business model for commercialisation of new products globally.

Notable technology advances that may impact the market include new formulations and new devices to permit the delivery of protein- and peptide-based agents without the need for injections. Other technological trends worth watching are in the areas of wound healing and stem cell research. Both are receiving enormous investment, with the potential to bear very rich fruit. Despite the ethical debate around stem cell applications, new start-ups are rapidly clustering within this new space.

From the regulatory perspective, arguably the most significant, and most uncertain, challenge is the introduction of biologics and biosimilars. A number of biotechnology products are facing this threat over the next five years and the regulatory framework for generics approvals in the biotech sector is not yet fully clear.

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Figure 3. Breakdown of the biotech market



Europe accounts for more than 25 per cent of the total biotech market

Table 1. Top ten fastest-growing biotech companies

	% Market share		% Growth constant \$	
	\$m MAT Dec 2004*	2004	2004	CAGR 99-03
Global biotech market	44,353	100.0	17.0	21.6
1 Amgen	10,610	23.9	25.1	25.4
2 Roche/Genentech	6644	15.0	26.7	27.4
3 Johnson & Johnson	6424	14.5	3.4	31.4
4 Lilly	3325	7.5	3.1	11.8
5 Novo Nordisk	3036	6.8	15.4	15.9
6 Serono	1486	3.4	14.8	23.0
7 Schering-Plough	1412	3.2	-17.0	12.2
8 Biogen Idec	1333	3.0	16.9	17.5
9 Sanofi-aventis	1273	2.9	51.4	37.3
10 Wyeth	1029	2.3	60.2	33.7
Top 10	36,573	82.5	16.4	23.0

Legend: Growth below major biotech markets (indicated by red text in original)

* Excludes direct sales from manufacturers that are currently not supplied to IMS

Source: IMS Health MIDAS MAT Dec 2004

Table 2. Top 20 pharma companies with a commitment to biotech industry

	Biotech sales rank	Biotech sales \$m	Biotech % total sales
1 Pfizer	13	688	1.3%
2 GlaxoSmithKline	14	564	1.7%
3 Sanofi-aventis	9	1273	4.6%
4 J&J	3	6424	26.1%
5 Merck & Co	23	165	0.7%
6 Novartis	32	52	0.2%
7 AstraZeneca	-	-	-
8 Roche/Genentech	2	6644	37.4%
9 BMS	384	0	0%
10 Wyeth	10	1029	7.2%
11 Abbott	12	927	6.5%
12 Lilly	4	3325	26.2%
13 Amgen	1	10,610	99.6%
14 Takeda	91	4	0%
15 Boehringer Ingelheim	21	235	2.8%
16 Schering-Plough	7	1412	20.4%
17 Bayer	20	263	4.1%
18 Schering AG	11	1021	20.7%
19 Eisai	34	45	0.9%
20 Teva	117	2	0.1%
Total biotech market		44,353	8.5%

Source: IMS Health MIDAS MAT Dec 2004

Geographical split

Geographically, the USA dominates the biotech sector with 60 per cent of the market, a share that has nearly doubled over the last nine years (see Figure 3). This growth has largely been achieved at the expense of Japan, where a number of newer biotech products have not yet been launched, reducing its stake in the market from 27 per cent to 7 per cent since 1995. Europe accounts for more than 25 per cent of the total biotech market and is currently growing faster than the USA (20 per cent vs 17 per cent growth in 2004).

Company performance

The biotech market is more concentrated than pharma overall, with sales almost entirely centred around ten corporations, some of which are among the fastest growing in the sector (see Table 1). Together, the top ten global biotech corporations account for more than 80 per cent of sales. Amgen, the market leader, alone is responsible for nearly 24 per cent of total sales. Its closest rivals are Roche/Genentech with a 15 per cent market share and Johnson & Johnson with 14 per cent. In Europe, four out of the top ten biotech corporations are growing above the market rate (Wyeth, Amgen, sanofi-aventis, Roche/Genentech).

With the exception of Roche/Genentech, Johnson & Johnson, and Lilly, which derive 37 per cent, 26 per cent and 26 per cent of sales, respectively, from biotech projects, surprisingly few large pharma, including Pfizer and AstraZeneca, count biotech drugs among their leading products (see Table 2). Nor do many include them as an integral part of their own in-house research efforts. Amgen remains the only pure player within the top 20 corporations.

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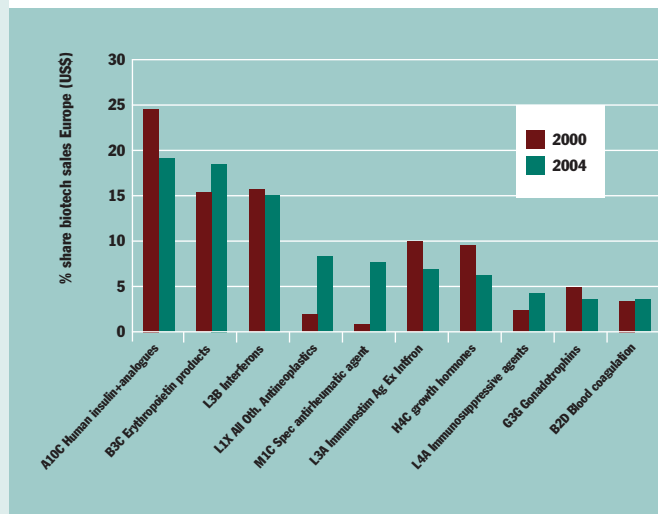
Table 3. Biotech pipeline leaders

	Biotech R&D pipeline*	Biotech late phase pipeline (pIII-reg)	% Total late phase pipeline (pIII-reg)	
1	Roche/Genentech	35	5	50%
2	GlaxoSmithKline	25	5	25%
3	Sanofi-aventis	23	3	12%
4	Amgen	21	3	75%
5	J&J	16	3	25%
6	Novartis	16	2	15%
7	Wyeth	14	1	7%
8	Lilly	13	3	33%
9	Merck & Co	13	2	22%
10	Schering AG	11	1	13%
11	BMS	9	4	27%
12	Bayer	8	1	20%
13	Boehringer Ingelheim	6	1	50%
14	Abbott	5	2	18%
15	Pfizer	5	1	7%
16	Schering-Plough	2	1	17%
17	Eisai	2	0	0%
18	Takeda	2	0	0%
19	AstraZeneca	0	0	0%
20	Teva	0	0	0%

*No of products/projects Confirmed active development in last three years

Source: IMS Health MIDAS MAT Dec 2004

Figure 4. Biotech therapy class spread



Source: IMS Health MIDAS MAT Dec 2004

The question is just how long biotech can and will be considered a separate sector

Pipeline leaders

Roche/Genentech, GlaxoSmithKline and sanofi-aventis have the most biotech products in their total R&D pipeline with 35, 25 and 23, respectively. From an R&D perspective, Roche/Genentech, Amgen, Lilly and Boehringer Ingelheim dedicate proportionately more of their R&D pipeline to biotech (see Table 3).

Top therapeutic classes

Biotech sales in Europe have extended their spread across therapy classes over the last four years (see Figure 4), branching out into markets traditionally served by major drug-makers, such as asthma/allergy, cardiovascular and atherosclerosis. Many of the leading biotech therapy classes are directed towards cancer, a market that is forecast to become the largest therapeutic area by 2009, reaching \$55bn in sales. A third of all oncology products launched since 2000 have a biotech origin.

In 2004, seven classes were responsible for almost all biotech revenues: L3B interferons; L4A immunosuppressive agents; L3A immunostimulant agents excluding interferon; A10C human insulin and analogues; B3C erythropoietins; L1X all other antineoplastics; and M1C-specific antirheumatic agents.

Alongside this broader spread, biotech drugs are beginning to emulate the class dynamics of traditional medicines, with several alternative molecules now available for a number of diseases, including anaemia, multiple sclerosis and rheumatoid arthritis.

Although the development of second-generation products helps to off-set the risk of imminent patent expiries, it does raise the question of just how long biotech can and will be considered a separate sector.

Product performance

The top ten biotech products worldwide in 2004 accounted for 43 per cent of sales, with six showing above-market growth: Aranesp (darbepoetin; Amgen); Enbrel (etanercept; Amgen/Wyeth); Remicade (infliximab; J&J/Schering-Plough); MabThera/Rituxan (rituximab; Biogen Idec/Roche/Genentech); Rebif (interferon beta 1A; Serono); Avonex (interferon beta 1A; Biogen Idec). All had sales in excess of \$1bn, with the number one product J&J's Erypo/Procrit (licensed from Amgen) reaching sales of \$3.9bn.

In total, Amgen was responsible for five of the top ten biotech products in 2004 (see Table 4), the remainder being accounted for by J&J (Erypo/Procrit; Remicade), Biogen Idec/Roche/Genentech (MabThera/Rituxan), Biogen Idec (Avonex), and sanofi-aventis (Lantus).

Lantus (insulin glargine; sanofi-aventis) was the fastest growing product in 2004, increasing sales by nearly 81 per cent, followed by Aranesp (darbepoetin; Amgen) with nearly 78 per cent and Enbrel (etanercept; Amgen/Wyeth) with 59 per cent.

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Table 4. Top 10 biotech products

Products	\$m 2004 Sales	% Change	CAGR 99–03	% Market share 2004
Global biotech market	44,313	17.0	21.6	100.0
Erypo/Procrit [J&J]	3988	-4.2	23.0	9.0
Epogen [Amgen]	2897	-3.8	14.1	6.5
Enbrel [Amgen/Wyeth]	2578	58.8	42.1	5.8
Aranesp [Amgen]	2569	77.9	***	5.8
Remicade [J&J/SP]	2506	19.8	130.8	5.7
MabThera/Rituxan [Roche/Genentech]	2191	24.5	62.7	4.9
Neulasta [Amgen]	1873	52.1	***	4.2
Avonex [Biogen Idec]	1383	16.4	18.1	3.1
Neupogen [Amgen/Roche/Genentech]	1343	-6.9	2.4	3.0
Lantus [sanofi-aventis]	1013	80.6	***	2.3
Total top 10	22,342	20.7	31.3	50.4

■ Growth below global biotech markets ■ Negative growth

Source: IMS Health MIDAS MAT Dec 2004

Paradise lost

Biotechs – the last bastion of exclusivity for brands – now face generics threat, as early as 2008 in major markets. Seven major biotech molecules could incur potential losses of almost \$9bn when patents expire – epoetin alfa; interferon beta 1A; somatropin; filgrastim; epoetin beta; insulin human isophane; and interferon beta 1B (see Table 5).

Many biogenerics are already marketed in China, Eastern Europe, India and South America, and Omnitrope (somatropin; Novartis) was approved in Australia in October 2004. Other applications are under review and in development, such as interferon alpha (BioPartners, EU), and recombinant human insulin (SciGen, India). With EU legislation amended, FDA willingness to study the issue, and insulins and growth hormones approved under the Food, Drug & Cosmetic Act, the trend has already begun. The key players in this sector are Novartis, BioPartners, SciGen, Cangene, GeneMedix, LG Chemicals, Pliva, Rein Biotech, Roemmers, Stada and Teva.

The high cost of brand biotechs makes biogenerics attractive. However, biologic brands may still fare better than small

molecules. Although the prospects for biogenerics look better, challenges remain. Most notable is the lack of clear legislation. Regulatory procedures are expected to affect whether follow-on biologics will be able to compete in the market in a similar way to traditional generics, as ‘me-too’ pharmaceuticals, or somewhere in between these two extremes. This will have implications for time to market, cost of development, pricing and promotional costs for biogenerics companies.

Biogenerics regulations are being debated at the disease-specific level and procedures for filing will differ according to the therapy area and nature/complexity of the molecule. Initially, however, applications will be assessed on a case-by-case basis and early cases will act as benchmarks and precedents that will influence the evolution of guidelines.

Other challenges to biogenerics entrants will include the complexity of the manufacturing process, immunogenicity, multiple patents and the introduction of second-generation brand products. The high cost of materials and production will limit discounting and hence brand share erosion. Nevertheless, it is no longer a case of if biogenerics are launched, but when.

Conclusions

As pharma struggles to justify the value received from discovery, biotech companies are showing themselves to be demonstrably more effective in generating new compounds. Licensing as the main model has attractions on both sides, enabling pharma to build franchises more effectively with lowered discovery risk, and reducing the risks of commercialisation for biotechs through partnerships with established pharma companies in a given therapeutic area. **END**

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Table 5. Major biotech molecules to expire 2005–09

Brands	Leading substances	Marketer	2004 \$m	% Sales expired/expiring 2005–09
Erypo/Procrit/Epogen	Epoetin Alfa	J&J/Amgen	7304	13%
Avonex/Rebif	Interferon Beta 1A	Biogen Idec/Serono	2245	90%
Genotropin/Humatropo/Norditropin	Somatropin	Pfizer/Lilly/Novo Nordisk	1785	76%
Neupogen	Filgrastim	Amgen	1565	35%
Recormon	Epoetin Beta	Roche	1410	96%
Ins. Protaphane HM/Novolin N/Actraphane HM/Humulin NPH	Insulin Human Isophane	Novo Nordisk/Lilly	1948	100%
Betaferon	Interferon Beta 1B	Schering AG	844	92%

Source: IMS Health: MIDAS, MAT Dec. 2004; IMS Patent Focus, Dec 2004; SMR Team Analysis, 2005