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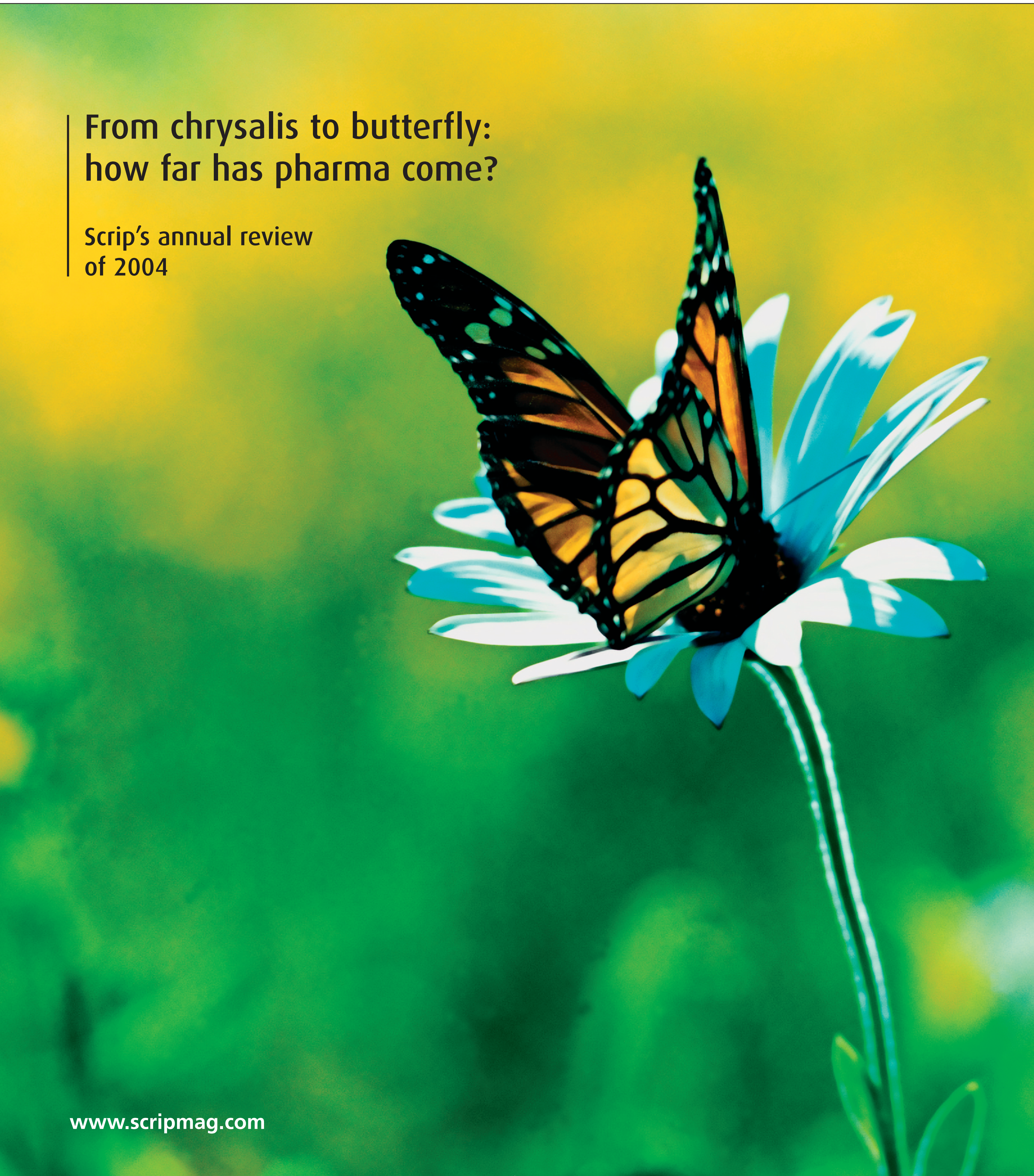
Pharmaceutical issues in perspective



From chrysalis to butterfly: how far has pharma come?

Scrip's annual review of 2004

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Growth, in moderation

Data for 2004 show a slowdown in global pharma sales, with the US largely responsible for this trend. But the rapidly expanding biotech industry offers hope for the future, as did a strong year of growth across Latin American, Asian and small European markets, write Graham Lewis, Selena Class and Eva Edery

When Moving Annual Total figures to September 2004 are finally gathered and totalled, they are expected to show global pharma revenues at ex-manufacturer prices well in excess of US$500 billion – a new milestone – and a figure 8-9% up on 2003. However, this is less than the compound average growth rate of 10% observed between 1999-2003. The key region responsible for the sales slowdown in 2004 was North America (essentially the US), where the growth rate fell from 14.5% between 1999-2003 to a forecasted figure of just under 10% for 2004.

The ex-manufacturer price is only one basis for measuring industry performance. Clawbacks and other forms of taxation, especially in Europe; market dynamics such as parallel trade; and intensifying competition mean that actual growth was probably at least 1% lower than that derived from ex-manufacturer prices.

US determines global sales

Geographically, a mixed picture emerged in 2004, with clear signs of the increasing influence of the developing world. Latin America and Asia showed strong, double-digit, growth (see Figure 1), while Europe sustained its historical growth rate before clawbacks, etc of 8-9%. These performances, however, were not enough to offset the significant slowdown in the US and the continuing low growth in Japan of 2-4%, as these markets traditionally account for nearly 60% of global sales.

Clearly, as the most significant single market, the US merits special attention, although it is important to separate one-off factors from other trends that are likely to have a more permanent structural impact. For example, US sales were affected by a weak influenza season in the first quarter of last year; it is too early to assess the impact of vaccine shortages on total sales at year-end as the severity of the latest flu season is not yet apparent. From a more structural perspective, though, there were two emerging issues that may have a longer term effect: drug safety (see 'Demise of Vioxx leaves trail of confusion' on p52 and 'Late stage failures cause headaches in 2004' on p26) and cost benefit.

Figure 1 – Leading country markets

World rank	Country	Sales (US$ billion)	Percentage global sales (US$)	Fixed-rate growth (%)
1	US	232.7	45.6	9.0
2	Japan	56.4	11.1	3.0
3	Germany	28.6	5.6	5.0
4	France	27.4	5.4	7.0
5	UK	19.3	3.8	9.0
6	Italy	18.4	3.6	6.0
7	Spain	13.4	2.6	10.0
8	Canada	10.9	2.1	9.0
9	China	7.2	1.4	26.0
10	Mexico	6.3	1.2	10.0
Total		**420.6**	**82.4**	**9.4 (average)**

Source: IMS Health, Moving Annual Total (MAT) to September 2004

Co-payments discourage patients

On the cost-benefit side, it was already evident in 2003 that the creation of escalating multi-tier, co-payments had led some patients to give up prescription treatments altogether, especially with 'silent' disorders such as hypertension and hyperlipidaemia. These markets continued to grow but might well have grown faster without this financial disincentive. And the increase in the number of uninsured Americans to 45 million has not aided growth.

One direct impact on US growth in 2004, however, was the earlier transfer of Schering-Plough's non-sedating antihistamine Claritin (loratadine) and AstraZeneca's proton pump inhibitor Losec/Prilosec (omeprazole) to over-the-counter (OTC) status: a number of managed care organisations refused to reimburse other drugs in the same classes unless they could demonstrate a significant therapeutic benefit for a particular patient.

Interestingly, while generic sales continued to grow faster than those of patent-protected brands in 2004, growth was lower than in the previous year at 10%, influenced partly by the small number of significant generic events, but also by the slow growth in total prescriptions (after taking mail order into account). Cross-border trade also levelled off.

Mixed performances in Europe

In Europe, growth at Moving Annual Total (MAT) September 2004 was a steady 8.3%, although smaller countries, such as Turkey and Greece, together outperformed the top five. There were fluctuations in the five highest-ranking European countries (at ex-manufacturer prices), with Germany, Italy and France underperforming, and the UK and Spain achieving higher than average growth (see Figure 1). Parallel trade was relatively flat in 2004, influenced partly by more efficient supply-side management.

As in the US, generics uniformly outperformed brands in terms of growth, with the effect being particularly noticeable in smaller generic markets such as France and Spain, where growth at MAT September 2004 was 37% and 18% respectively. Moreover, for the first time, a major generic event – the loss of exclusivity for Merck & Co's Zocor (simvastatin) – took business away not just from the original molecule but from other, patent-protected statins. This was first seen in Germany and then in the UK. A similar pattern has now become evident with two Pfizer blockbusters: antihypertensive Norvasc (amlodipine) and the anticonvulsant Neurontin (gabapentin). In the UK, generic simvastatin is now the first-line therapy for the great majority of patients taking a lipid-modulating agent for the first time. In a move likely to be monitored closely by other countries, it also became available OTC in the UK, as Zocor Heart-Pro, during 2004.

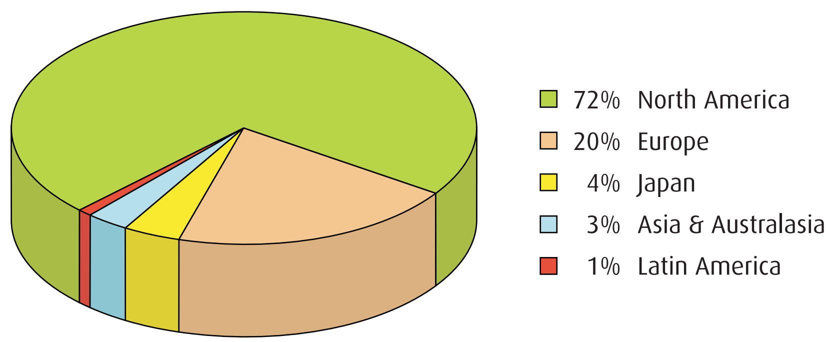
The regular price-cutting mechanism was employed once more in Japan in 2004, helping to restrain growth to the low single digits (see Figure 1). In the emerging markets China stands supreme, with a growth rate of 26% (hospital market only) for the 12 months to September 2004. This is a sector offering significant growth opportunities for both generic companies and patent-protected brands (see 'China breathes fire into Asian growth' on p20).

Biotech and blockbusters

Turning to the much-criticised subject of innovation, a significant development occurred in 2004: the surging growth of biotechnology-derived products, especially in North America and Europe (see 'Has the IPO window closed? on p42). The biotech market enjoyed 17% growth in 2004, with more than 80% of the market held by just ten firms. Amgen continues to be the leading player, with 30% growth and five of the ten biotech blockbusters – Epogen (erythropoietin), Aranesp (darbepoietin alpha), Enbrel (etanercept), Neulasta (pegfilgrastim) and Neupogen (filgrastim) – in its portfolio. Regarding the industry's pipeline as a whole, the future looks bright – with 27% of active compounds being biotech-based. The only cloud on the biotech horizon in the near future is the availability of biogenerics, which could threaten 25% of biotech sales, but because of regulatory uncertainties this is unlikely to happen before 2008.

And although there is speculation as to the demise of the blockbuster, 2004 data will show the largest number of billion dollar-plus brands ever. Around 85 blockbusters are expected to account for 30% of global sales by year-end, up from 69 in 1993. There was also an increase in the number of brands achieving sales in excess of US$2 billion – about 40 in 2004, including Lipitor (atorvastatin), Zocor (simvastatin), and Zyprexa (olanzapine), compared with 25 the year before. The US continues to take the lead in blockbuster sales (see Figure 2) – it had a 70% share in terms of value and 50% in volume – highlighting the price premiums that exist for many blockbusters (at ex-manufacturer level).

Figure 2 – Global blockbuster sales by geographical region by value



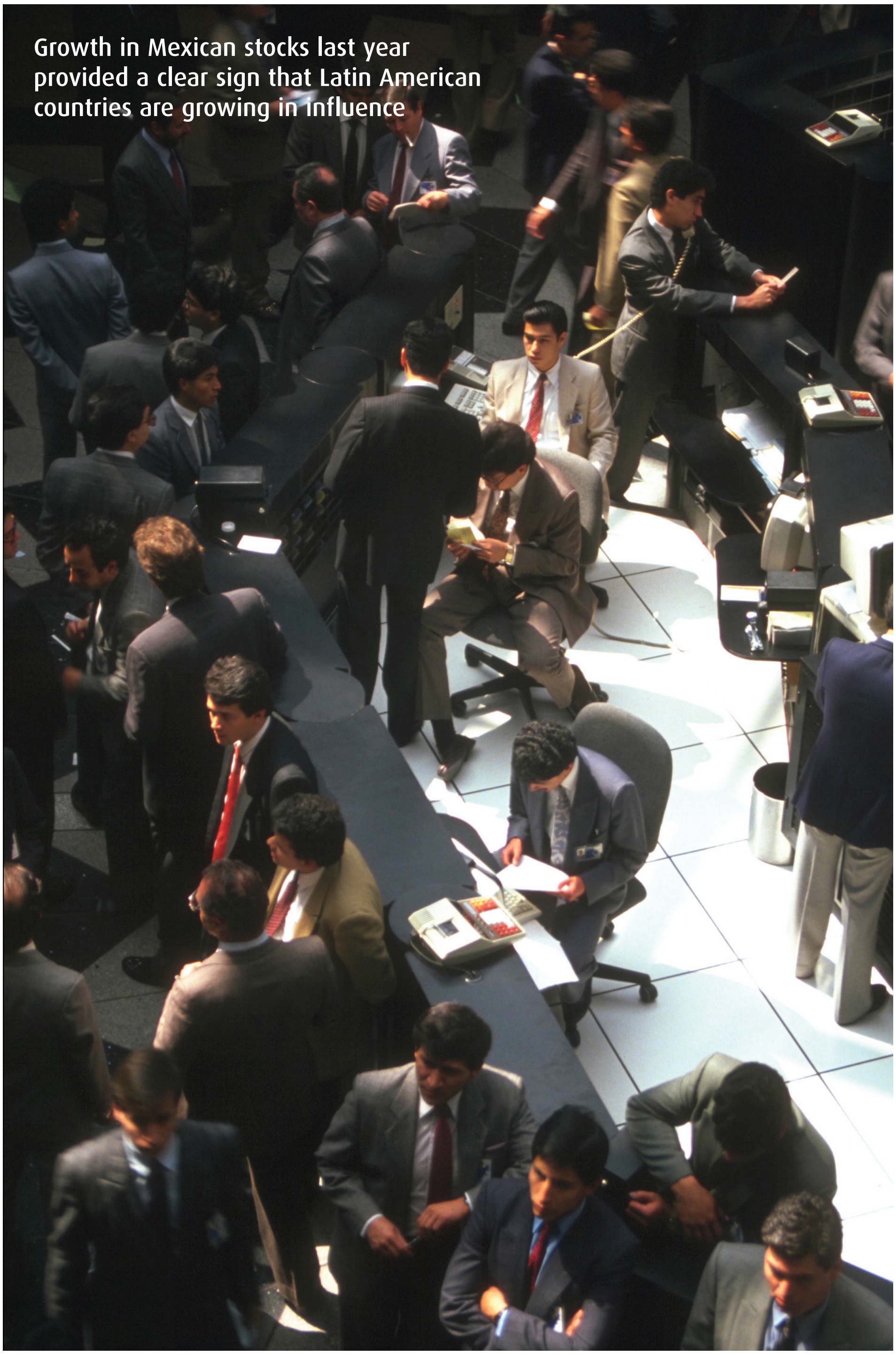
Source: IMS Health, MAT to September 2004

The leading therapy classes, accounting for approximately 30% of the global market, are shown in Figure 3. Although not yet represented in the top ten therapy class rankings, both oncology and rheumatoid arthritis have seen exceptional growth, resulting largely from the launch of innovative products, many from the biotech sector, such as Humira (adalimumab), Avastin (bevacizumab) and Erbitux (cetuximab).

Figure 3 – Leading global therapy classes

ATC code	Therapy class	Sales (US$billion)	Percentage global sales (US$)	Fixed-rate growth (%)
C10A	Cholesterol & triglyceride reducers	29.2	5.7	13.0
A2B	Anti-ulcerants	25.1	4.9	2.0
N6A	Antidepressants	20.1	4.0	4.0
N5A	Antipsychotics	13.6	2.7	14.0
M1A	Antirheumatic non-steroidals	13.4	2.6	9.0
C8A	Calcium antagonists, plain	11.4	2.2	2.0
B3C	Erythropoietins	11.2	2.2	12.0
N3A	Anti-epileptics	10.9	2.1	20.0
A10B	Oral antidiabetics	9.8	1.9	10.0
J1D	Cephalosporins	8.7	1.7	2.0
Total for ten leading Anatomical Therapeutic Classification (ATC) classes at Level 3		**153.4**	**30.0**	**8.8 (average)**

Source: IMS Health, MAT to September 2004



Growth in Mexican stocks last year provided a clear sign that Latin American countries are growing in influence

Innovation in 2004 was not confined to biotech, even though the number of new chemical entity launches was the lowest for ten years. Oncology, cardiovascular, central nervous system and metabolic diseases all benefited from the introduction of new products, which will add to the growing list of blockbusters in future years. Examples include Namenda (memantine), the Alzheimer's disease therapy from Forest Laboratories and Merz, and duloxetine, marketed by Lilly as Cymbalta for depression and by Lilly and partner Boehringer Ingelheim as Yentreve/Ariclaim for stress urinary incontinence (see 'Does lack of launches spell end of expansion?' on p24).

Company performances over the year were variable, exemplified by the underperformance of the pharma sector in most of the world's leading financial indices. It has also become a feature of recent years that the largest companies are growing at a lower rate.

Interestingly though, despite all of the mergers in recent years, including the Sanofi-Aventis deal at the end of 2004, the top ten corporations still account for less than half of the global pharma business (see Figure 4).

So was 2004 a watershed in the evolution of the pharma industry? The critical events were challenges to the core methods used to test compounds and to produce rigorous clinical data, taking into account both benefits and risks, and increasing acceptance by all key players – payers, providers and patients – that generics are acceptable substitutes. But proven innovation last year demonstrates that, at its best, the industry continues to have a record of which it can be proud.

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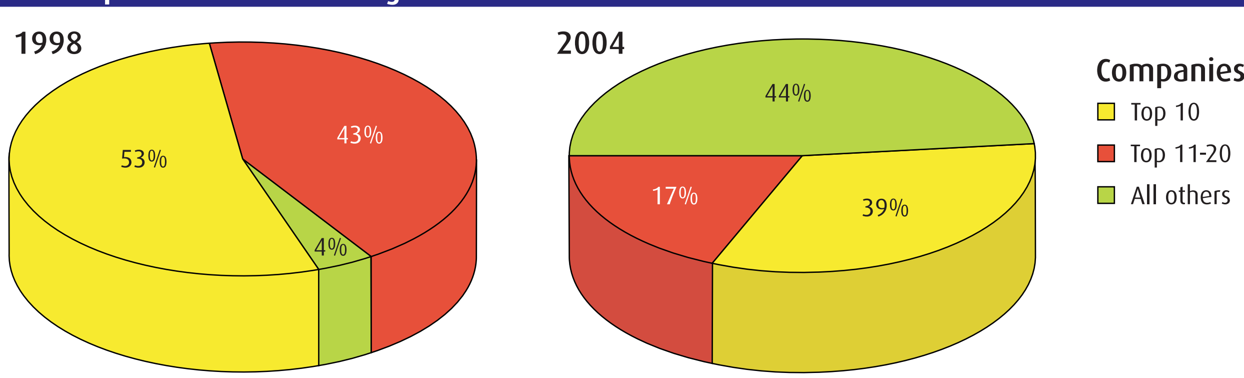
Figure 4 – Corporate contributions to growth



Source: IMS Health