

# GENERICS SIZE UP MARKET OPPORTUNITY

While the market for original brands slowed in 2005, sales of generics have gone from strength to strength. Eva Edery, IMS Global Pharma Strategy, offers new insights on this growing sector.

A stringent focus on cost containment in the major world markets tempered global pharmaceutical growth in 2005, but saw sales in the generics sector grow strongly. As an increasing number of payers ramp up their efforts to encourage the use of generics, the sector is expected to maintain its growth lead over the original brands market to at least 2009. There are challenges ahead to sustain the momentum, but as new analyses from IMS reveal, the range of opportunities and potential rewards may be significantly greater than previously realised.

## Slower world market growth

World pharmaceutical market growth continued to slow in 2005, with audited sales growing at a rate of around 7 per cent to reach \$550bn. The USA, although still the dominant market, experienced a sharp decline in growth to just below 6 per cent, down from 18 per cent in 1999. Growth in the EU also slowed, although not as steeply. Among the top five European markets, which represent about 70 per cent of EU sales, Italy and the UK were the lowest growth performers at 0 per cent, reflecting increased cost-containment measures and, in the UK, the impact of price cuts imposed by the PPRS.

The world's second largest market, Japan, which has historically been a lower growth country but represents about 13 per cent of global sales, maintained its modest recovery in 2005 with growth of 5 per cent. Of particular interest is the fact that one third of that growth was driven by three main drug classes: angiotensin IIs, antihistamines and oncology therapies. A feature in Japan at the moment is the increasing number of new products originating from the USA and Europe, as access to this market continues to improve, albeit slowly. It is still the case that 39 of the current 92 global blockbusters have yet to be launched in Japan.

## US contribution declines

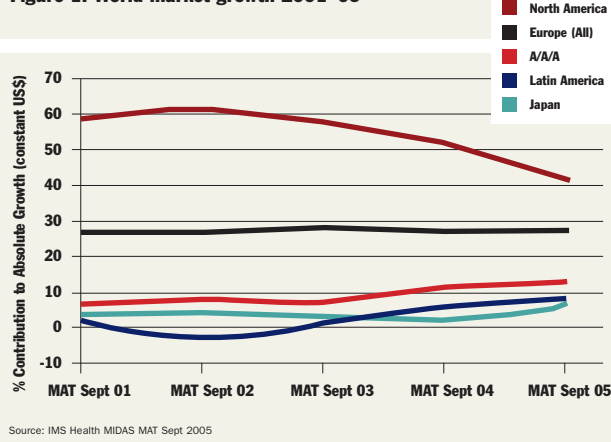
After historically driving the bulk of global pharmaceutical growth, North America's contribution to world growth has declined sharply in recent years, falling from 60 per cent in 2001 to around 40 per cent in 2005 (see Figure 1). Factors contributing to this trend include the failure of several recent launches to deliver on expectations in 2005 and the continued slowdown in the number of new chemical entities launched



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Figure 1. World market growth 2001–05



globally during the year (30, compared with 31 in 2004). In addition, reflecting the more risk-averse nature of the FDA was the much higher number of black box warnings issued in 2005 (45 versus nine in 2004) and the significant increase in time from application to approval (29 months versus 16 in 2004).

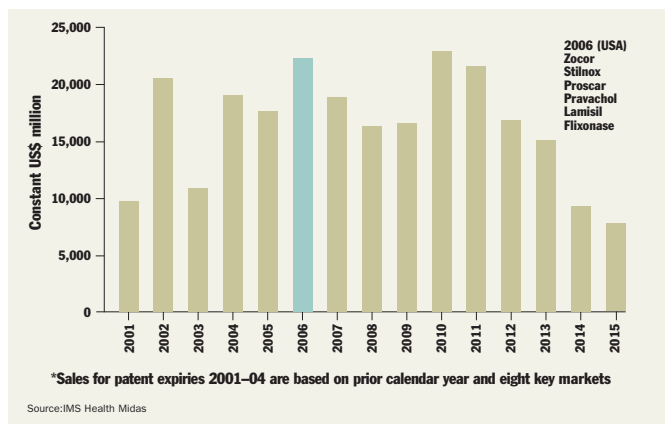
With the USA representing about 44 per cent of global sales, these events are significant for companies that do most of their business in this market, as seen in the lower than average growth achieved by five of the top ten pharmaceutical corporations in 2005. The EU, representing one-third of global sales, continued to drive 30 per cent of overall growth in 2005.

## Generics pivotal role

One of the primary factors in the slowdown of global growth in 2005 was the stronger role played by generics in major markets and their impact on originally protected brand sales, as national governments continued their efforts to drive down healthcare costs. Generics will continue to feature strongly among the key events anticipated in 2006, which will restrain total growth.

In the USA, these include the introduction of Medicare Part D legislation, which is important for the general pharmaceutical market, and a significant opportunity for generics since Medicare will more aggressively promote their use. In

**Figure 2. Value of patent expiries 2001–15**



Europe, intensive competition among generics and increased government pressure to prescribe generically will be key.

The most significant factor for generics in 2006 is the number of products that are due to lose patent exclusivity, especially in the USA (see Figure 2). The year is expected to be the biggest yet in terms of high-profile patent losses, with six \$1bn drugs affected: Zocor (simvastatin) (the largest, with sales of \$4bn in the USA), Zoloft (sertraline), Ambien (zolpidem), Pravachol (pravastatin), Lamisil (terbinafine) and Zofran (ondansetron). Overall, an estimated \$23bn in products will be at risk, \$18bn in the USA. Looking further ahead, 12 of the 35 leading molecules may lose protection by 2009, yielding a total exposure of \$72bn at 2004 sales values.

Zocor is one of the key drivers of this market opportunity and raises an important issue for the generics market in terms of whether generics will not only take sales from the original branded products, but also from other molecules within the class. This potential for class cannibalisation presents a huge opportunity for generics. It has provided increased potential for the sector in Europe, as demonstrated by simvastatin's performance in Germany, which took share from other brands, such as Lipitor (atorvastatin). Should the same effect be observed in the USA, both Lipitor and Crestor (rosuvastatin) will face significant challenges. IMS expects a similar effect with the angiotensin IIs, once Cozaar (losartan) loses protection.

The concept of class cannibalisation is a particular feature of classes with current gold standards and low brand differentiation. In the case of Fosamax (alendronate), which is now unprotected in the UK and Germany, but is not considered a gold standard within the class, no cannibalisation has been seen so far. However, it will be important for manufacturers assessing any market for generics to look beyond the size of the original molecule to the potential for the entire class.

**Generic exposure in strategic classes**

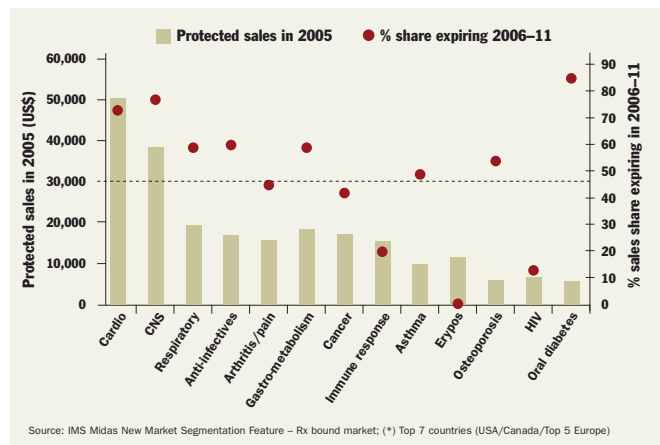
Generic exposure in strategic classes places \$123bn–135bn of sales at risk from 2006–11 in the top seven markets (see

Figure 3). Among those at highest risk going forward are cardiovascular (which stand to lose patent protection on products accounting for about 70 per cent of sales in 2011) and the CNS and respiratory classes. Over 80 per cent of oral antidiabetic sales are also at risk during the same period. This is significant for companies operating in these markets, and they will need to look carefully at strategies for protecting and maximising the value of their brands and addressing the upcoming challenges.

**Follow-on biologics**

Follow-on biologics, already marketed in China, Eastern Europe, India and South America, are expected to enter key strategic markets in Europe by 2008. Insulins, epos and human growth hormones (HGHs) might enter the market earlier. Omnitrope (recombinant HGH; Sandoz) is already moving closer with its recent CHMP recommendation in Europe. Given the highly cautious approach of the FDA at this time, follow-on biologics are unlikely to reach the US market before 2010, although this could change pending increased pressure from Medicare as it becomes more aggressive in managing down costs and seeking financial savings from pharmaceuticals.

**Figure 3. Generic exposure in strategic classes 2006–11\***



Follow-on biologics are a potential source of sizeable future income for the generics industry, with profit levels likely to be higher than those of traditional generics. The cost and complexity of the manufacturing process for these products will understandably limit intense competition. The marketing of follow-on biologics is expected to resemble the marketing of branded products, and thus marketing costs are likely to increase. Key players include a mix of large and medium-sized companies, such as Teva, Sandoz, BioPartners, Cangene, GeneMedix, LG Chemicals, Pliva, Rein Biotech, Roemmers, SciGen and Stada.

Regulatory procedures are expected to affect whether follow-on biologics will compete in the market in a similar way to traditional generics, '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. Regulations for follow-on biologics are being debated at the disease-specific level and procedures for filing will likely differ according to the therapy area and nature/complexity of the molecule. Initially, 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 trends to watch in this area include the vulnerability of HGH and insulins, two product categories that may enter the follow-on biologics arena earlier than others. Some of the big players, such as Novo Nordisk, Lilly and sanofi aventis, have launched new products in diabetes and big challenges may ensue should follow-on biologics come sooner than expected. The impact of a follow-on biologic insulin in Poland on Novo Nordisk and Lilly brand sales has been seen. It is possible that some R&D players with biotech expertise, such as J&J and Schering Plough, may launch follow-on biologic brands as a means of sourcing additional growth.

### Specialist key

A key recent trend noted by IMS is the rise of the specialist-driven market, sectors for which specialists make the majority of prescribing decisions within the dynamic market, either in the office or hospital setting. This observation is based on an analysis of the 'dynamic market': the sum of new patients, switches and add-on decisions.

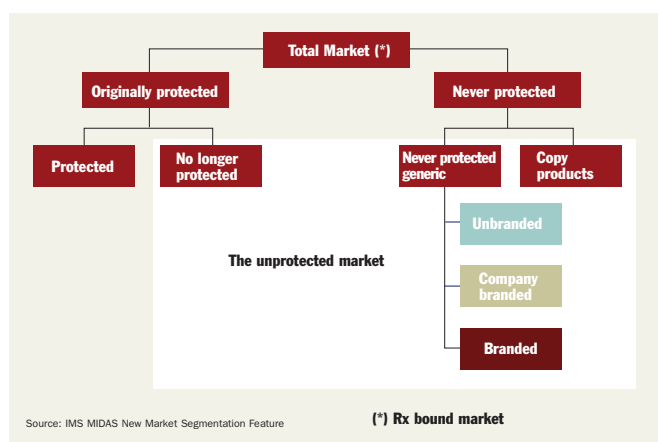
Specialist-initiated products have been growing much faster than those initiated primarily by general practitioners, and in 2005 they accounted for 40 per cent of the blockbuster drugs. IMS expects their dominance to increase and to drive most of the growth through 2009. This is a new opportunity for generics, although one that might require a different marketing approach.

### Sizing the opportunity

With so many new opportunities on the horizon for generics medicines, there is a pressing need for more sophisticated insights on the size, composition and performance dynamics of the market. To date there has been no standard way of measuring and quantifying the total generics opportunity, or indeed a standard way of actually defining the generics market. The classification and structure of available data have limited efforts to accurately identify the branded generics market, leading to sizing estimates mostly based on unbranded generic sales. The net result has been a sector valued on an incomplete picture of its components.

In order to improve the reporting, analysis and comparison of generic and original brand sales in different countries, IMS has developed a fundamentally new way of codifying the international generics market, making it possible to differentiate between original brands and branded generics, a unique advance in understanding the total unprotected market and providing a comprehensive view of its structure across the major countries (see Figure 4). Within originally protected brands, this includes the ability to analyse the performance of still protected versus

Figure 4. New segmentation of the protected and unprotected market



no longer protected brands, the impact of new generics on sales of no longer protected original brands, and assessments around the success of R&D strategies in protecting original sales with line extensions, new delivery formulations or the launch of authorised generics prior to the legal protection expiry date.

### New insights

Based on the new classification, IMS estimates that the unprotected market (which includes no longer protected original brands, generics and copy products) is worth \$98bn in the top seven markets (see Figure 5). This represents approximately 25 per cent of the global market. Preliminary analyses suggest a much larger, more competitive generics sector than previously recognised, with generics estimated to account for about half of the penetration in value and around 56 per cent in volume.

In value terms (at ex-manufacturer prices) generics are now estimated to be worth around \$48bn in the top seven markets (see Figure 6), representing about 78 per cent of global generics sales. This is significantly higher than previous estimates, which were based primarily on the unbranded generics market.

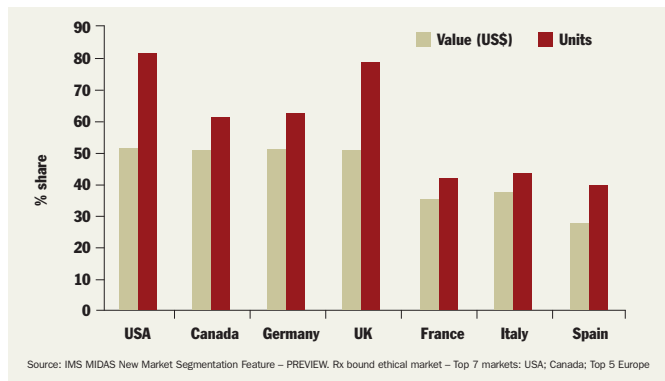
Generics have been growing at a rapid pace for a number of years and continued to show double-digit growth in 2005 at 13 per cent compared with just 5 per cent for original brands (see Figure 7). Higher growth for generics of 15 per cent can be observed in the USA, compared with 10 per cent in the top five in Europe, reflecting the faster penetration of these products in the USA.

Within the generics sector, the new classification reveals significant disparities in performance between the different segments of the market, with stronger growth over time apparent in the unbranded sector. Unbranded generics continue to outpace sales of those that are branded.

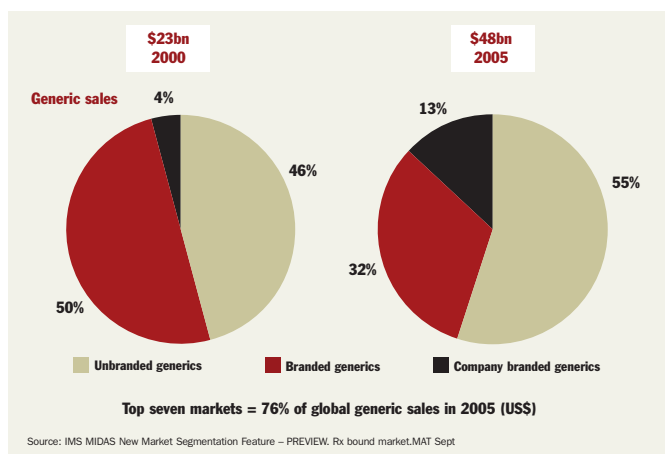
Share in value for branded and unbranded generics is highest in the UK, at around 24 per cent in 2005 (excluding discounts), followed by Germany and Canada. The UK is also highest

in volume with 64 per cent share (as measured in units of tablets, ampoules, etc). Penetration in value is lower in the USA, at around 11 per cent, reflecting the much wider price differential between brands and generics in this market.

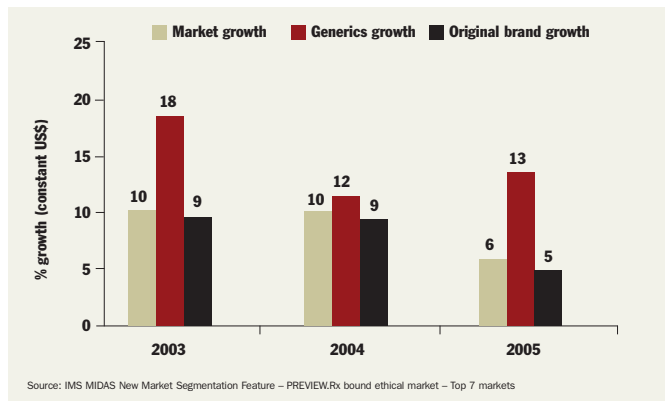
**Figure 5. Value of unprotected market**



**Figure 6. Generics value in top seven markets, 2005**



**Figure 7. Generics vs market and original brand growth 2003–05**



Questions remain around poorer generic penetration among the no longer protected products. This may be attributed to the lack of exciting opportunities, manufacturing difficulties, or the fact that the original R&D manufacturers employed a more effective strategy to protect their original brand or to convert some patients from that brand to a follow-up product or release form. Examples include Glucophage (Glucovance and Glucophage XR) and Astra Zeneca’s conversion of patients from Losec to Nexium to protect as much of the business as they could.

**Learning from experience**

To better understand the conclusions that may be drawn from past generics events, IMS has conducted analyses exploring the generic penetration of various molecules in different markets. These assessments reveal highly scattered generic erosion curves, reflecting the distinct characteristics of individual molecules in terms of indication (chronic or acute), formulation, supply issues and potential for class cannibalisation. Time to peak is also variable in different markets, from nine months in the USA to 27 months in Germany. Identifying and evaluating analogues will be important in developing models for determining generics potential.

To date, IMS has tested several variables for their potential impact on generic penetration, including revenues prior to patent expiry, the number of generics players, manufacturing complexity, number of formulations available for the same molecule, first generic to market in class, high generic prescribing and product indication. These have resulted in the identification of some initial commonalities. Collectively, these findings raise important questions about the need for different strategies to win market share in this increasingly complex environment.

**Further growth potential**

Looking ahead, IMS expects the generics market to grow at a CAGR of 14–17 per cent to 2009 (at ex-man price level US\$), double the rate of the overall predicted market average growth rate of 6–9 per cent, bringing its global share of sales by value to 18 per cent in the top seven markets up from its 13 per cent share.

Several factors could derail this forecast: the approval of follow-on biologic regulation for insulins before 2008: faster generic class cannibalisation than has been seen in the past with therapy gold standards going off patent; more patent challenges bringing forward the launch of generic versions; more intense competition among generics players, including the expanding role of Indian manufacturers; and stronger efforts by Medicare to encourage the use of generics amid clear indications that some branded products will be removed from the Medicare formulary. Equally, in terms of downside potential, some R&D companies have already been successful in defending their original brands from generic penetration, as in the court cases won by Pfizer for Lipitor, or through formulation rollovers. **END**