



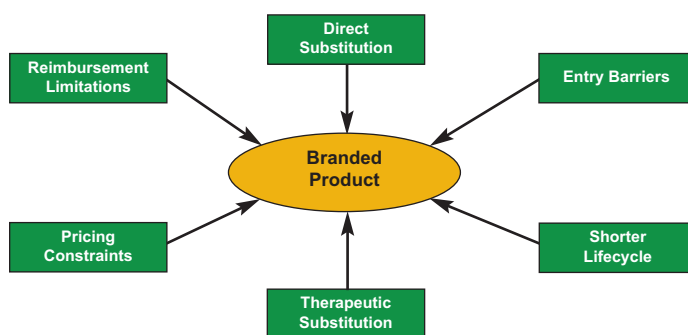
## Not Your Father's Generics

How a Rapidly Changing Global Generic Industry is Challenging Lifecycle Planning

### Introduction

Gone are the days when generic drugs impacted branded manufacturers only after their product's patent had expired. Increasingly innovators feel pressure from generics through Paragraph IV challenges that threaten to shorten the branded lifecycle. Generic manufacturers are making copies of complex products whose technical challenges previously presented high barriers to entry. The very presence today of a generic within a therapeutic area affects co-pay tiers, pricing, reimbursement, contracting, and the degree of therapeutic substitution. A variety of regulatory and payer initiatives frame these changes, but at the heart is an increasingly sophisticated, rapidly globalizing, well-capitalized, and aggressive generic industry. Understanding the trends, strategies and economics shaping the generic industry today has become critical to brand planning.

### Impact of Generics on Branded Products



Source: Putnam Analysis

### The Cost to a Brand

The hits taken by brands are growing. Driven by co-pay differentials, Lipitor loses 25% of its market share to generic simvastatin years ahead of its own patent expiry. Miscalculation of generic manufacturer psyche and incentives cost BMS an estimated \$600 million in its negotiations with Apotex on Plavix. New intravenous antibiotics now negotiate pricing facing the specter of generic Rocephin. In global markets the increasing use of cost effectiveness criteria relative to available generics in a category creates a hurdle for reimbursement. Failing to understand the depth of challenges which today's generic competitors pose can create unexpected and unpleasant surprises.

### The Generic Industry 2008 and Beyond: Global Integration

The generic industry has come a long way since the late 1990s. Then it often took six or more months post-patent expiry for a generic price point to drop to 20% of the branded. Today that can happen on the first day multiple generics are available. Through 2016, patents on drugs representing over \$140 billion in sales will expire. Driven by favorable legislation, healthcare cost containment pressures, and growing market acceptance, generic utilization is escalating across most developed pharmaceutical markets. Generic drugs now represent over 65% of all scripts filled in the U.S. Over 75% of the drugs listed on the FDA's Orange Book have generic counterparts. In Europe, where generic utilization varies widely, some central and eastern European countries now have utilization rates of as much as 70%.

As the generic industry expanded, it globalized. With Barr and Mylan moving into global markets through their acquisitions of Pliva, Matrix and Merck KGaA, Watson remains the only major formulator focused entirely on selling into a single market (U.S.). Indeed the U.S. market accounts for half or less of most leading generic manufacturer sales. Geographic diversification has been driven by low cost development and manufacturing in countries like India, a drive for global scale, and a desire to limit exposure in any one national market.

### Global Generic Utilization Rates - 2006

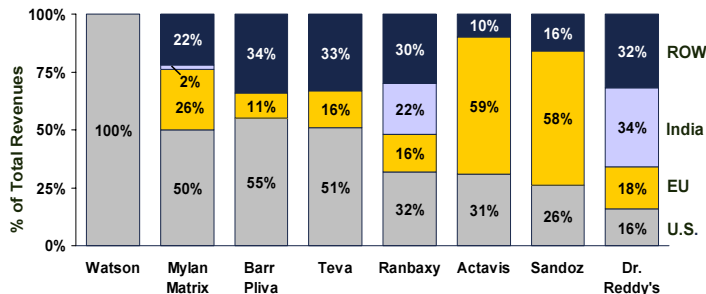
	Poland	UK	USA	Denmark	Germany	Turkey	Netherlands	Sweden	Hungary	France
% Share (Volume)	66%	66%	65%	56%	54%	51%	50%	44%	40%	17%
% Share (Value)	52%	26%	8%	20%	30%	33%	20%	14%	29%	9%

	Japan	Belgium	Brazil	Spain	Portugal	Switzerland	Italy	Austria	Finland	Ireland	Greece
% Share (Volume)	17%	14%	12%	12%	10%	10%	8%	8%	6%	4%	2%
% Share (Value)	7%	10%	9%	8%	17%	4%	4%	6%	2%	1%	1%

Source: GPha, BMI Generics Forecast, Verispan, IMS, Putnam Analysis

## Global Sales Breakdown of Leading Generic Manufacturers (2006)



Source: Corporate Financial Reports and Filings 2006

Indian manufacturers such as Ranbaxy and Dr. Reddy's Labs validated their ability to compete in highly regulated Western markets by first serving their domestic markets. They next expanded into major semi-regulated markets, often referred to as the BRIC countries (Brazil, Russia, India, China). As these companies grew into generic industry leaders, BRIC and domestic markets have remained significant sources of revenue. They have been steadily increasing their U.S. presence through both persistence and acquisition.

While North America currently accounts for the majority of the generic industry's finished product facilities, formulation is increasingly an ex-U.S. activity. Eastern Europe and India are the preferred locations for API (Active Pharmaceutical Ingredient) manufacturing where opportunities to secure substantial cost and tax advantages can be realized. Even Watson, focused on difficult to manufacture specialty products for the U.S. market, has acquired manufacturing operations in the developing world.

### Offshore Economics

The benefits of "offshoring" manufacturing are compelling. An Indian scientist or chemist usually costs about 20-30% of a U.S. counterpart. Low cost labor benefits extend into other areas such as API production, which on average costs 5-10% of sales versus 25-30% of sales for a European-based manufacturer. Plant and capital equipment are estimated to be approximately 25% of U.S./EU costs. Local government competition for manufacturing plants results in tax breaks and infrastructure benefits (e.g., free electricity) for manufacturers considering an Indian location. Similar benefits are experienced by companies operating in East Europe, China and Israel.

In the face of such economics, generic companies can sell their products at 70% or more discount to the branded price and still make a profit. Supported by a growing base of U.S./EU regulatory expertise, a rich talent pool, manufacturing experience in local and BRIC markets, and English as a common language, the importance of India and other low cost locations will continue to grow.

GSK, Merck, Pfizer, Lilly, and Sanofi-Aventis are some of the industry leaders that have moved to take advantage of these economics by investing in India and other high skill/low cost environments. Involvement ranges from contract manufacturing and development to R&D joint ventures with well-established local pharmaceutical companies. In addition, major Western companies are establishing their own individual R&D operations in the region. Sanofi-Aventis' opening of their own pharmaceutical development center in Goa, India is a prime example. Economics and expertise provide a compelling argument for this strategy.

### Manufacturing Locations of Major Generic Suppliers

Company	API Facility Location	Formulation Facility Location
Teva	<ul style="list-style-type: none"> <li>▪ Israel</li> <li>▪ Europe</li> <li>▪ Canada</li> <li>▪ India</li> <li>▪ Latin America</li> <li>▪ United States</li> </ul>	<ul style="list-style-type: none"> <li>▪ Israel</li> <li>▪ Europe</li> <li>▪ Canada</li> <li>▪ Latin America</li> <li>▪ United States</li> </ul>
Sandoz	<ul style="list-style-type: none"> <li>▪ Argentina</li> <li>▪ Europe</li> <li>▪ India</li> <li>▪ United States</li> </ul>	<ul style="list-style-type: none"> <li>▪ Argentina</li> <li>▪ Europe</li> <li>▪ India</li> <li>▪ United States</li> </ul>
Barr	<ul style="list-style-type: none"> <li>▪ Croatia</li> <li>▪ Czech Republic</li> </ul>	<ul style="list-style-type: none"> <li>▪ Croatia</li> <li>▪ Czech Rep.</li> <li>▪ Poland</li> <li>▪ United States</li> </ul>
Mylan	<ul style="list-style-type: none"> <li>▪ China</li> <li>▪ Europe</li> <li>▪ India</li> <li>▪ South Africa</li> </ul>	<ul style="list-style-type: none"> <li>▪ China</li> <li>▪ Australia</li> <li>▪ Europe</li> <li>▪ India</li> <li>▪ United States</li> </ul>
Dr. Reddy's	<ul style="list-style-type: none"> <li>▪ India</li> <li>▪ China</li> <li>▪ Mexico</li> </ul>	<ul style="list-style-type: none"> <li>▪ India</li> <li>▪ China</li> <li>▪ Mexico</li> <li>▪ UK</li> </ul>
Ranbaxy	<ul style="list-style-type: none"> <li>▪ India</li> </ul>	<ul style="list-style-type: none"> <li>▪ China</li> <li>▪ India</li> <li>▪ Ireland</li> <li>▪ Nigeria</li> <li>▪ United States</li> </ul>

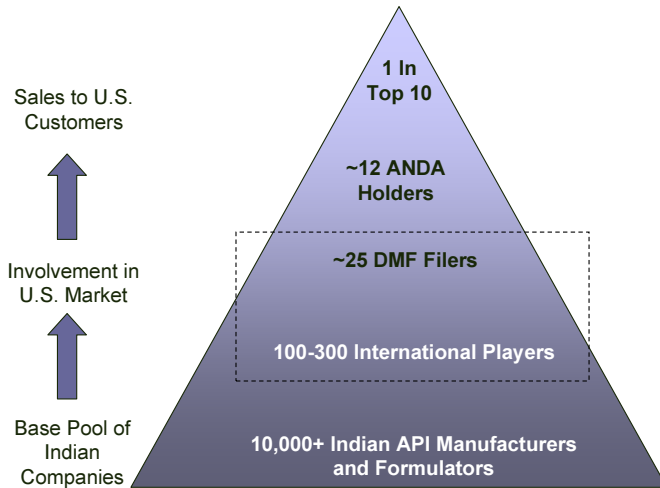
■ Developing Market Location

Source: Annual Reports, Investor Presentations, News Releases

### Just the Tip of the Iceberg - India Rising

While the number of Indian applications is rapidly increasing, in the U.S. today the vast majority of ANDA and DMF (Drug Master File) filers are still U.S. generic companies; 12 Indian manufacturers were responsible for 11% of the ANDAs filed between 2000 and 2006. This means that India's current impact on the generic market is arising from either large established players like Mylan, Barr and Sandoz extending into the Indian market or from a small handful of Indian suppliers who are starting to succeed in the U.S. (and EU) markets. However, there is an enormous amount of untapped generic manufacturing potential in India.

## Distribution of Indian Companies by Level of Involvement in the U.S. Markets (2000-2006)



Source: FDA, Putnam Interviews

One Indian generic manufacturer told us that “it is easier to open a generic drug company than a restaurant in India.” While this may be a bit of an overstatement, the Indian pharmaceutical industry is flourishing in many respects. There are currently more than 20 Indian-based generic companies operating internationally, and more than 100 FDA-approved plants, the largest number in any country outside of the U.S. Not including recent foreign investment interest in new facilities, as many as 300 existing domestic plants in India are selling generic drug products internationally that, with some investment, have the potential to serve Europe and the U.S. Both branded and generic manufacturers should continue to brace themselves: direct competition from Indian generic companies appears to be just beginning.

## **China in the Wings**

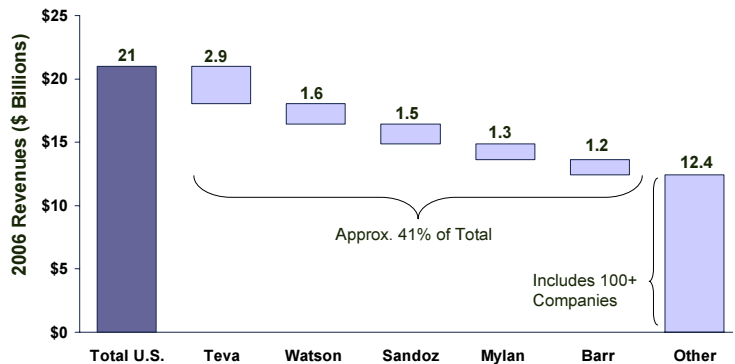
China is already a major player in the global generic markets, albeit a less visible one. Substantial amounts of API utilized by leading U.S. generic competitors are now made in Chinese factories. Current estimates of the number of FDA-approved manufacturing facilities in China range from 30 to 50. As substantial as the Indian economic advantage is, China holds the potential for even greater leverage. The lack of regulatory reliability and transparency in addition to well-publicized contamination incidents with some Chinese products will slow their emergence in the finished product markets. However, it is worth noting that the first finished dose Chinese generic was approved by the FDA in 2007.

## **Consolidation and Expansion**

Despite the consolidation that has occurred, the generic industry remains rather fragmented. Over 100 companies account for 60% of the revenue in the U.S. Additionally, the number of competitors holding ANDAs has dramatically increased.

From 1995 to 2005 the number of generic manufacturers authorized to market products in the U.S. more than doubled. The majority, however, market fewer than ten products. Historically, two to four generics would typically compete for share immediately following a patent expiration. However, recent cases, such as Rocephin, have seen as many as 32 generics enter the market. In the case of Ambien, pre-expiration competition was so intense that several ANDA holders declined to launch because they could not garner sufficient share to break even.

## Leading U.S. Generic Manufacturers by U.S. Revenues (2006)



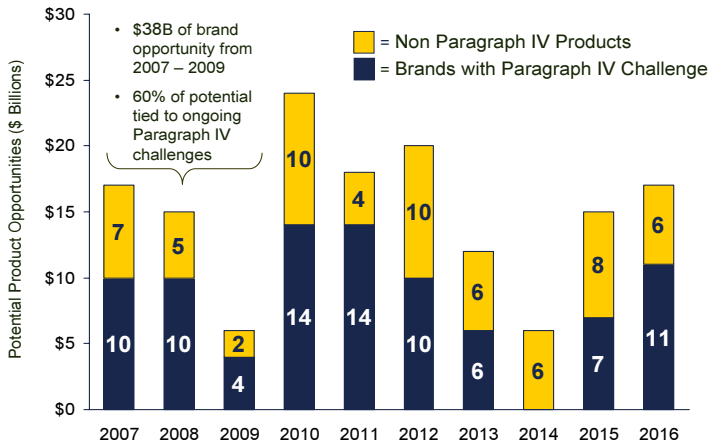
Source: Corporate Financial Reports and Filings 2006

Faced with an oversupply of companies marketing a particular product, generic companies seek to grab share early and follow price points down hoping to outlast the competition. Achieving their minimal target market share for a product enables a generic manufacturer to sell out their planned capacity and minimize unit costs by maximizing utilization of their manufacturing plants.

## **Evolution**

Seeking relief, generic manufacturers are increasingly moving into areas that have some barriers to entry. We have identified three strategies being pursued by generic manufacturers that seek to limit the competitive intensity they face: Paragraph IV challenges; generics with barriers to entry; and proprietary products.

## Potential Estimated Generic Product Opportunity through 2016



Source: CIBC World Markets, November 2006

### Paragraph IV Challenges

The Hatch-Waxman Act contains a provision which rewards generic companies that successfully challenge the patent for a branded product with 180 days of market exclusivity. This process is known as a Paragraph IV filing. During this six-month exclusivity period the generic typically gains substantial market share selling product at a 20%-30% discount relative to brand. Even facing an authorized generic, the profits during this period are significant compared to those once multiple generics enter the market. The profits associated with this strategy have spawned a host of challenges to branded patents extending to 2016 and beyond.

### Generics with Barriers to Entry

As generics seek to escape the competition associated with “commodity” generic and blockbuster products, some have

focused on products previously considered unlikely targets. Companies like Aurobindo have developed highly-automated, state-of-the-art penicillin facilities, Biocon is ardently pursuing fermentation products and biologics, and industry goliath Teva’s API division has expertise in many specialized technologies, such as fermentation processes, high-potency APIs, and peptide-based APIs. Former barriers to entry ranging from possible legal / liability exposure, difficult manufacturing processes, new formulations, stringent tracking requirements, or specialty distribution needs are now being viewed by some generic companies as potential havens from the generic “hordes.”

### Proprietary Products

The ultimate escape from generics is of course proprietary products. The tremendous growth and profits of recent years have produced strong cash flows and a stronger financial base for generic houses. This is being leveraged into potential proprietary drugs to complement strong generic positions. Many generic companies are investing in internal drug discovery and development as well as R&D alliances to seek higher-margin revenue streams. Teva now spends over \$500 million annually on R&D with close to 10% of revenues and an estimated 20% of gross profits coming from Copaxone and other branded products. Dr. Reddy’s has created a stand-alone R&D unit with outside investors to spur the development of proprietary products and Ranbaxy looks to follow suit. Generic companies which can innovate, develop, promote, and are backed by a low cost structure, as well as a culture of generic efficiency, will realize success on a broad scale.

### Conclusion

Faced with these changes and challengers, lifecycle planning has become more complex. Assumptions concerning product vulnerabilities must be reexamined. New competitors may also mean new opportunities for collaboration. A superior understanding of the motivations and strategies of the new competitors can result in better contingency planning.

### About Putnam

Putnam Associates is a premier strategy consulting firm headquartered in Boston and serving the pharmaceutical, biotechnology, diagnostics, and medical device industries on a global basis. Two decades of experience and focus in our industries enable us to create significant value for our clients. Creative and disciplined strategy development processes blend with deep market knowledge for one purpose: to help our clients succeed.

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