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A report by Ernst & Young for IBEF

Market Overview

Indian pharmaceutical market set to grow by over 7 per cent to become a US$ 11.6 billion opportunity by 2009

With an estimated market value of US$ 8.2 billion (at consumer prices) in 2004, India accounts for a little under two per cent of the world market for pharmaceuticals and ranks as the fourth largest globally in terms of volume and the 13th largest by value.

Summary of the Indian Pharmaceutical Market in 2004

	2004
Market Size (US$ millions)	8,200
as % of total health expenditure	25.3
as% of GDP	1.3
as% of world market	1.6
Growth rate %	7.2
Per capita expenditure (US$)	8

Source: Epsicom

The Indian pharmaceutical market has been forecast to grow to as much as US$ 25 billion by 2010 as per Organisation of Pharmaceutical Producers of India (OPPI) estimates. However, Espicom's market projections forecast more modest but stable annual market growth of around 7.2 per cent, putting the market at US$ 11.6 billion by 2009.

Projected Pharmaceutical Market, 2004-2009

	Market (US$ millions)
2004	8,200
2005	8,790
2006	9,423
2007	10,102
2008	10,829
2009	11,609

Source: Epsicom

New product launches underlie market growth

The market has been growing between 6-8 per cent over the last two years, primarily driven by new launches and to some extent by volumes. In the last two years, more than 3,900 new products (largely branded generics) have been launched in India, contributing about US$ 355.6 million (million) worth of market value. While the Indian pharma majors launched more than ten products per year, global MNCs averaged one or two annually. In 2005, Indian companies controlled 70 per cent of the domestic market.

Chronic therapy segments witnessing rapid growth

While in developed economies chronic therapies account for more than two thirds of the market, in India, it is acute therapies that make up about 60 per cent of the market. However, with changing lifestyles and an aging population, sales of chronic therapies (i.e., diabetes, cardiovascular, etc.) are growing rapidly at almost 15-20 per cent p.a.

Therapeutic break-up of Indian market

Category	Value (Rsbn)	Value market share (%)	Value growth (%)	Volume growth (%)
Anti-infective	32.8	16.4	4	11
Gastrointestinal	21.8	10.9	8	9
Cardiac	20.7	10.3	18	15
Respiratory	20.4	10.2	9	6
Vitamins/minerals/nutrients	19.3	9.6	5	5
Pain/analgesics	19.1	9.5	8	9
Dermatologicals	10.8	5.4	8	4
Gynaecology	10.7	5.3	3	(1)
Neuro psychiatry	10.6	5.3	10	6
Antidiabetics	8.8	4.4	11	16
Opthologicals	3.5	1.7	18	16
Others	22.0	11.0	-	-
Aggregate	200.5	100.0	8	9

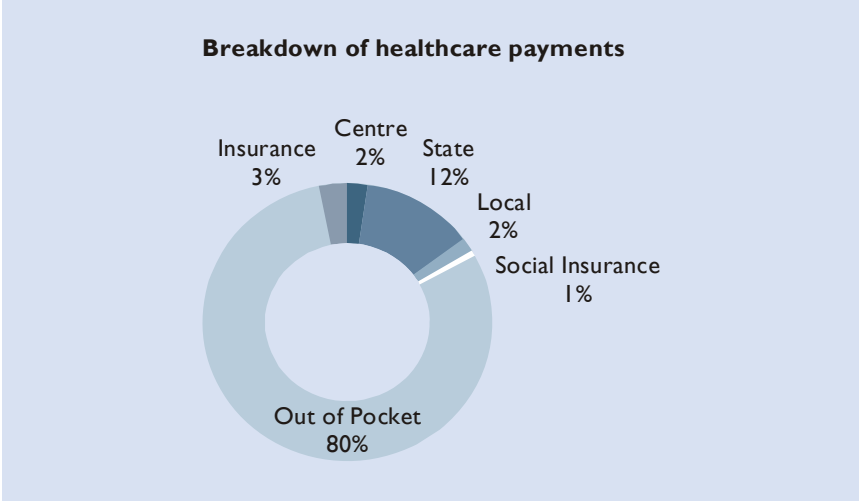
Source : CLSA Asia-Pacific Markets, BT

Among the top five therapeutic segments, gastro-intestinal and cardiac are experiencing both high volume and value growth. Opthologicals, cardiovascular, anti-diabetic and neurological drugs continue to top the growth list. The anti-infective, neurology, cardiovascular and anti-diabetic segments have witnessed a high number of new product launches in recent years.

Drug access and affordability to improve significantly

India's per-capita expenditure on drugs is about US$ 8 p.a. compared to US$ 170 in the US. This is because only about 30 per cent of |India's 1 billion citizens have access to modern medicine, most of whom reside in the cities.

Some 80 per cent of healthcare payments are borne by the individual in India, unlike the developed markets where only 10-30 per cent is borne by the individual.



Source: CLSA Asia-Pacific Markets

In India, with patients bearing the majority of the cost of healthcare, unless a new drug offers significant therapeutic benefit over existing drugs, price sensitivity is high. Presently, only a small segment of the population can afford expensive drugs. This partially explains why India is a high volume, low-price market. For example, GlaxoSmithKline (GSK) India contributes less than 2 per cent of the group's global revenue but 25 per cent of its overall volume.

The demographics of the country are gradually changing and disposable incomes are rising. The Indian pharmaceutical market has potential for tremendous growth with a burgeoning middle-class of around 300 million people that have higher healthcare expectations.

In the long run, affordability and awareness are expected to increase and about 35 million-45 million Indians are estimated to be able to afford the best medicines.

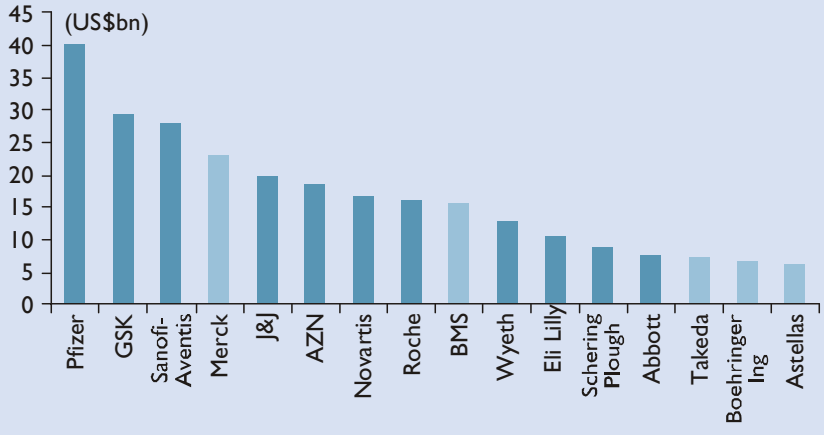
Key Opportunities

Marketing Opportunities

Post 2005, India is an exciting market for Big Pharma

Of the top 20 Big Pharma companies globally, 15 have an active presence in India.

Top pharmas with an active presence in India



Source: CLSA Asia-Pacific Markets

From January 2005, product patents came into force in India and under the new regime, any new drug patented after 1995 will receive patent protection in India as well.

The introduction of product patents has renewed the interest of global pharmaceutical giants in India. Formerly cautious big pharma companies are now willing to launch new drugs to capitalise on this new market opportunity. Global pharma companies are expected to cumulatively launch 200-250 new drugs over the next 8-10 years, totaling an estimated cumulative value of US$ 3-5 billion. The new launches are expected to gather momentum by 2007, reaching critical mass by 2010.

Most large multinational pharma companies such as Pfizer, Novartis and Merck, with listed subsidiaries in India, also have 100 per cent-owned subsidiaries. Although the sales and marketing infrastructure lies with the listed company, many of these companies have plans to launch their new products through the 100 per cent subsidiaries of the parent. Several other Big Pharma such as Bristol Myers Squibb, Boehringer Ingelheim and Eisai, which did not have a local presence earlier, have recently forayed into India.

FDI in Indian pharma increases six fold in 2004

Drugs and pharmaceuticals figured among the top five sectors accounting for maximum Foreign Direct Investments (FDI) in India between April 2002 and December 2004. The sector has seen the maximum FDI inflow, amounting to US$ 340 million, in fiscal year 04.

The sector also saw the largest increase in FDI inflow among the major sectors, growing over six fold from a meagre US$ 60.7 million in 2003.

Big Pharma bank on earlier successes to launch patent–protected products in India

GlaxoSmithKline (GSK) is the number one prescription generator in India. It is ranked first by general/consulting physicians and general surgeons. 2 of top 3 and 3 of top 10 brands by prescription belong to GSK. With an overall market share of 6.5 per cent, the company has held a leading position in the Indian market for over last two decades. It enjoys the highest sales force among global MNCs in India. GSK's coverage spans over 9 segments, with top ranking in 8 out of 12 doctor segments. It is the leader in anti-infective, anti-inflammatory, analgesic, gastroenterological, anti-allergic and dermatological (corticosteroids) segments.

GSK India further plans to expand its Indian product portfolio by launching the following 4 products in the 2007-10 period.

Product	Segment	Expected launch year
Alvimopan	Post-operative Ileas	2007
Lapatanib (572016)	Anti-cancer	2008/09
406381	Pain management	2008
480848	Cardiovascular	2010

Source: Anand Rathi Securities Pvt. Ltd.

Aventis Pharma (Now Sanofi-Aventis), in 1999 was one of the very few big pharma subsidiaries in India to have initiated aligning its Indian operations with that of the parent. 3 of the parent's top 6 products and 6 of the top 20 products have been launched in India, including most of its parent's new products such as *Allegra*, *Clexane* and *Lantus*.

Aventis - Committed to India

Aventis's key product		Launched in India
Allegra	Anti-allergy	Yes
Clexane	Anti-clothing	Yes
Lantus	Long-acting insulin	Yes
Amaryl	Antidiabetic	Yes

Source: CLSA Asia-Pacific Markets

Core brands of Aventis Pharma in India continue to show robust growth, e.g. Cardace (12 per cent), Amaryl (16 per cent), Clexane (28 per cent) and Targocid (26 per cent). The share of strategic brands in Aventis' revenue has risen from single digit levels in 1998 to 36 per cent in 2004. The rising share of high margin products has resulted in material cost to sales declining from over 55 per cent to less than 45 per cent. About 20 per cent of Aventis India's turnover comes from exports and the company also has a play in outsourcing from India.

Novartis India plans to launch products in the cardiovascular, respiratory, cancer and metabolic segments from the global parent's pipeline. The first of the products is indicated to be launched in 2007 or beyond. 13 of the 30 phase III projects and 23 of the 52 phase II/III projects are in the above-mentioned segments indicated for an Indian launch.

Successful niche launches encourage Big Pharma

Several global pharma MNCs have been successful in launching niche products in India (these are not necessarily patent-protected patents)

Eli Lilly launched *Xigirs* in India at global prices. *Xigris* is used to treat sepsis and costs about US$ 6,800 per patient for a four-day course. It was launched in India in October 2002 at US$ 14,000 because of the 57 per cent import duty on the drug. After a cut in the duties, the drug is now priced at about US$ 7,000. It is targeted at hospitals and hence is marketed by Eli Lilly alone. Although sales are not publicly known, it is estimated that at least 1000-2000 patients are being treated in India annually with this drug, which translates into US$ 7million-15million in potential annual sales.

AstraZeneca has been very successful with the launch of its injectible anti-infective *Meropenem* in India. The product costs US$ 120/day and has achieved sales of about US$ 8million-10million in the two years since its launch.

Big Pharma licensing drugs for Indian market in a big way

A large number of companies in India have begun to tie up with foreign companies to in-license drugs. Among the Big Pharma, GlaxoSmithKline is the most aggressive in this area. Being the largest foreign company in the domestic market, it is positioning itself as a partner of choice for other foreign companies wanting to launch new products, but lacking a presence in India.

In-licensing deals

Partner	Details
Cadila	
Schering AG	10-year contract for sale and distribution of existing and new products in India.
Boehringer Ingelheim	10-year contract to manufacture and market existing products, line extensions.
Viatris Gmbh	10-year contract to manufacture and market respiratory device (MDPI).
Nicholas Piramal	
Ethypharm, France	Pain Relief & Fever indications market, especially for paediatric use.
Genzyme Corporation	Synvisc Viscose Supplementation - therapy for the local treatment of pain associated with osteoarthritis (OA) of the knee.
Eli Lily and Co.	Dobutrex - injectible drug in the Cardiovascular (CVS) therapeutic segment - registered Sales of Rs 63.4m in 2003.
Biogen Idec	Avonex® (Interferon beta 1a), a leading life-saving therapy for Multiple Sclerosis (MS).
Chiese Farmaceutici	Curosurf®, a lung surfactant for premature babies with Resiratory Distress Syndrome (RDS).
Minrad	Isofurane, Enflurane and Sevoflurane (Inhalation Anesthetics).
Laboratories Pierre Fabre	Manufacture and market a range of dermatology and dermo-cosmetic products in India.
Glaxo	
Farchim	Cetzine (Zyrtec)/Cetzine Les, Levoctirizine (Vozet).
Fujisawa	Cefspan, Cefizox.
Teva	Alpha D 3.
GNC-CCM	Calcium Citrate Maleate.
Novartis	Terbenafine (Lamicil).
Organon	Oral contraceptives.
Undisclosed Japanese company	Proton Pump Inhibitor.

Source : CLSA Asia Pacific Markets

Outsourcing & Offshoring Opportunities

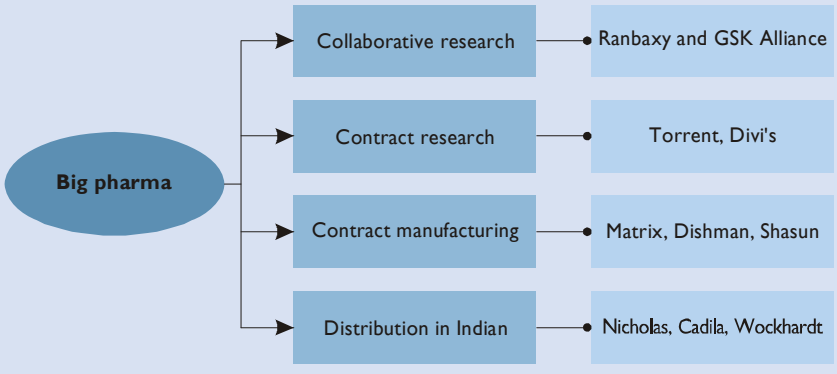
Globally, pharmaceutical outsourcing is on the rise with large global pharma companies facing the vagaries of pipeline surges and slowdowns, internal consolidation, and global expansion. Globally, contract manufacturing is estimated to be a US$ 30 billion opportunity, growing at 10-12 per cent p.a. while the contract research market is estimated to be US$ 6-10 billion growing at 16-18 per cent annually.

India's presence in the outsourcing and partnering plans of Big Pharma is becoming conspicuous

India is emerging as an alliance and outsourcing destination of choice for global pharma companies across the value chain. Companies such as Roche, Bayer, Aventis and Chiron are all executing plans to make India the regional hub for Active Pharmaceutical Ingredients (APIs) and supplies of bulk drugs. GSK has signed up a drug discovery alliance with Ranbaxy. Pfizer, Novartis and Eli Lilly and now GSK are all understood to be making India a global hub for their clinical research activities.

The growing traction in this regard is being driven by higher awareness about India. The emergence of multinational Indian companies such as Ranbaxy, Cipla, and Dr. Reddy's (DRL) as credible players in the global generics mart and the growing number of FDA approved plants and ANDA (Abbreviated New Drug Application)/DMF (Drug Master File) filings by Indian companies has brought India into the limelight as a cost-competitive supplier of quality pharmaceutical products. The change in the country's patent laws, transitioning from a process patent to a product patent regime, has also assuaged fears of intellectual property risk.

Big pharma partnering with Indian pharma



Source : CLSA Asia-Pacific Markets

India's value proposition…

India offers distinct economic advantages to large pharmaceutical companies who are looking to reduce their time-to-market on new products and save at the same time. These include:

- cost-competitive research base
- large and skilled workforce
- skills in process chemistry
- success in IT
- globally harmonised regulations
- cGMP compliance and FDA approved manufacturing facilities

These advantages, coupled with increased credibility and visibility, are bound to make India's share of the global outsourcing pie grow rapidly.

India's cost competitiveness is manifold

Indian pharmaceutical companies enjoy a considerable cost advantage over their western counterparts and the latter are generally able to provide a step down of 30-40 per cent in cost by a mere site transfer to India.

Contrary to popular perception, however, the Indian cost advantage extends well beyond low labour costs and ensures that the cost reduction process is a continuous process. The factors that drive India's cost advantage include:

Capital efficiency: Indian companies are able to reduce the upfront capital cost of setting up a project by as much as 25-50 per cent due to access to locally fabricated equipment and high quality local technology/engineering skills. Indian companies have been able to establish US FDA standard plants at approximately 50 per cent lower capital costs as compared to US or Europe based manufacturing units.

Lower filing costs: Generic filings require complex technical and legal documentation, which takes about 8 quarters. The cost of filing DMFs and ANDAs is at least 50-60 per cent lower for Indian companies as compared to their US or European counterparts.

Process engineering: The highly competitive local market and lack of pricing power force Indian companies to continuously work on the molecule even after a product is launched. This often results in gains in the form of improved yields and/or more cost effective manufacturing processes. The customer and supplier generally share such benefits in a pre-determined ratio, thus providing the benefit of continuous cost reduction.

Manpower cost advantage: India has a huge talent pool of skilled scientists, available at a fraction of the cost in developed countries such as the USA. Labour costs in India are around 1/7th the levels in developed countries and offer an obvious cost advantage.

India scores over China on several aspects…

While China also enjoys most of the cost advantages that India does, the latter scores over China in terms of advanced chemistry knowledge, regulatory capabilities and language skills. Industry analysts thus believe that the Chinese presence in outsourcing is likely to be restricted largely to intermediates and low end APIs, while Indian companies are likely to be present across the value chain.

Manufacturing Opportunities

Contract manufacturing has potential to generate US$ 1 billion by 2010

Globally, pharmaceutical manufacturing services are estimated to be worth US$ 25-30 billion and are set to grow to US$ 45 billion by 2010. Contract manufacturing is still a nascent industry in India with deals worth US$ 300 million concluded to date. It is a significant opportunity for Indian pharma and is estimated to generate US$ 1 billion in revenue in 2010. Cadila Healthcare, Shasun, Divi's, Matrix, Dishman and Nicholas Piramal are some of the key players in contract manufacturing in India.

Contract manufacturing deals in India

Company	Total outsourcing value (US$m)	Key outsourcing partner	Type of outsourcing
Nicholas Piramal	45	AMO, Allergan etc.	Contract manufacturing for API and formulations
Dishman	30	Solvay, GSK etc.	Contract manufacutring for intermeddiated and API
Shasun	30	Eli Lilly, GSK, Novartis	Contract manufacturing for API
Jubilant	25	Novartis	Contract manufacutring for intermeddiated and API
Divi's	15	Three of top 10 pharma	Custom chemical synthesis
Matrix	20	GSK	Contract manufacturing for API
Cadila	35	Altana, Zyban	JV structure for manufacturing on patent drug
Strides	15	Mayne	Injectibles manufacturing
Ipca	15	Astra Zeneca, European	Contract generics manufacturing of APIs
Others	50		
Total	285		

Source : Compnay Reports, CLSA Asia-Pacific Markets

Opportunities in both on and off-patent molecules

Growth in contract manufacturing is likely to be driven by increasing outsourcing of late-stage and off-patent molecules by big-pharma to compete with generics. On-patent molecules in highly competitive therapies e.g., proton pump inhibitors (PPI) may also be outsourced to improve the foreign company's ability to gain market share via aggressive pricing (e.g., Protonix).

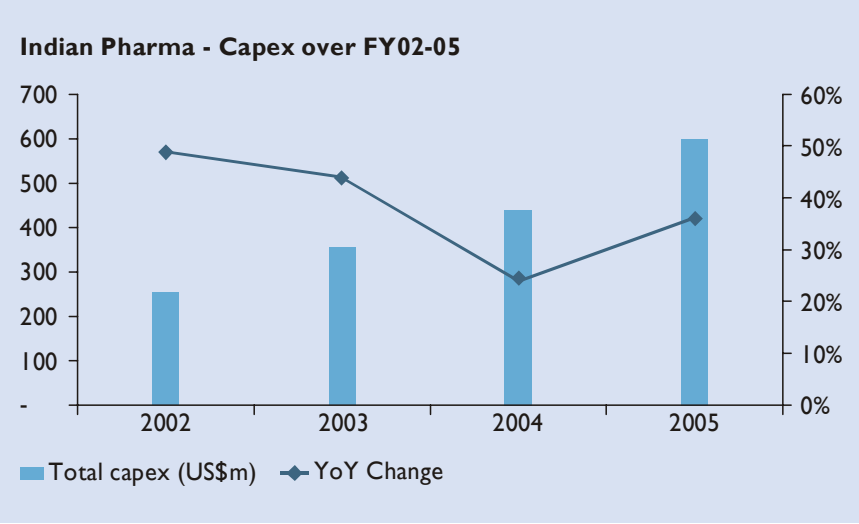
Case Study: Zydus Altana JV

Zydus Altana is a 50:50 joint venture between Cadila Healthcare and Altana AG set up in 1998 to manufacture and supply two intermediates for Altana's blockbuster product *Protonix* (pantoprazole). Protonix is a gastro-intestinal drug with global sales in excess of US$ 2 billion. The product is under patent till 2010.

Over the last three years, Cadila Healthcare has expanded its cumulative capacity for manufacturing the intermediates from 60 tons to 90 tons and further to 112 tons. Cadila Healthcare services an estimated 60 per cent of Altana's global sales. In the very first year of operations (fiscal year 03), the joint venture reported a turnover of US$ 24.4 million and profits of US$ 17.1 million, which grew further to US$ 33.3 million and US$ 26.7 million respectively in FY04.

Significant capacity in industry to meet demand for manufacturing services

There has been a significant capacity build-up in the generics industry across the globe. The most aggressive increase in capacity has come in India: aggregate capital expenditures of the fifteen largest generics companies more than tripled between 2000 and 2004. Not only did large companies step up their investments, but second and third tier companies have also made heavy investments to service planned forays into the regulated markets.

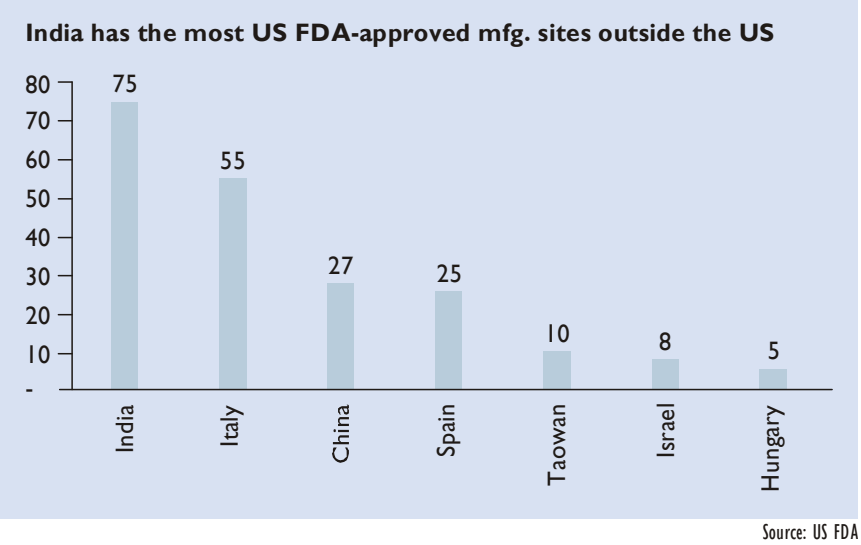


Source: Company Annual Reports; Citigroup Investment Rescearch.
This includes - Ranbaxy, Reddy, Cipla, Sun Pharma, Wockhardt, Cadila, Jubilant, Matrix, Glenmark, Auribindo, Nicholas and Biocon

Indian pharma companies have undertaken combined total capex of over US$ 1 billion between FY03 and FY05, and the net fixed assets of Indian pharma companies have grown by 50 per cent to US$ 1.6 billion during this period.

India tops in number of USFDA approved plants outside the US

Most of the capex has been in USFDA-approved plants in anticipation of the large wave of patent expiries in 2006. There has also been a surge in the number of plants receiving USFDA approval in India.



Source: US FDA

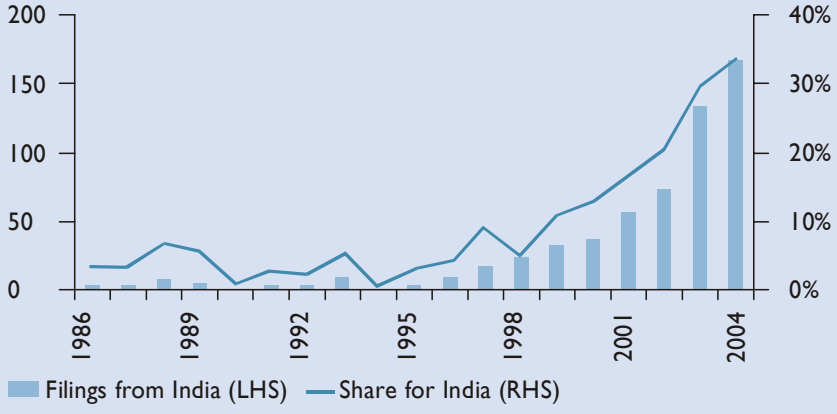
India tops in global DMF and ANDA filings

Indian companies have been at the forefront, both in terms of DMF and ANDA filings with approximately 35 per cent share in DMFs and about 25

per cent share in ANDAs. Over the last two to three years, several second/third tier Indian companies have aggressively scaled up their ANDA/ DMF filings in the US market.

The proportion of DMF filings from India was at 34 per cent in 2004 from 3 per cent in 1995 and 13 per cent in 2000. This trend is likely to continue as more small Indian companies look to file DMFs in the US.

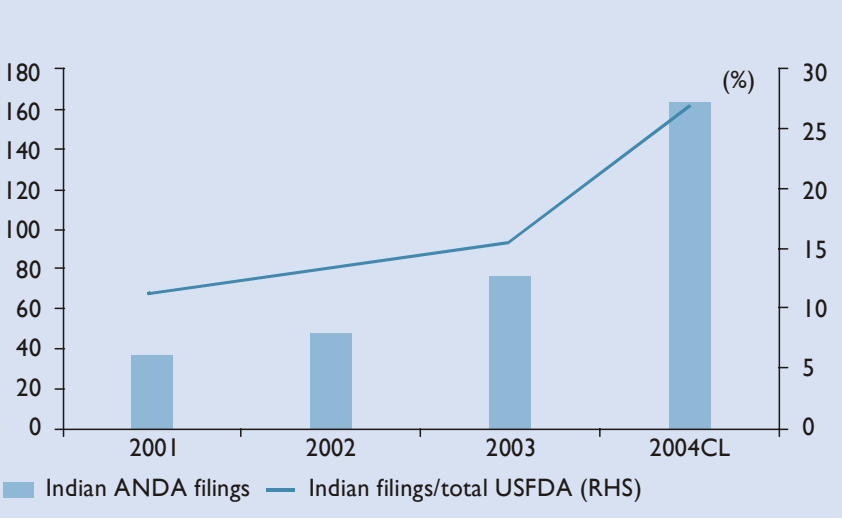
Increasing number of DMF filings from India



Source: US FDA

Indian companies accounted for 38 per cent of the DMFs filed during the June 2005 quarter with the US FDA, largely in line with trends seen over the past two years. The growing number of small players opting to file for DMFs (20 firms accounted for the 65 DMFs filed) hints at a widening manufacturing base.

Indian companies filed more than an estimated 150 ANDAs in 2004 accounting for over 25 per cent of global ANDA filings, compared to only about 30-35 in 2000.



Source: CLSA Asia-Pacific Markets

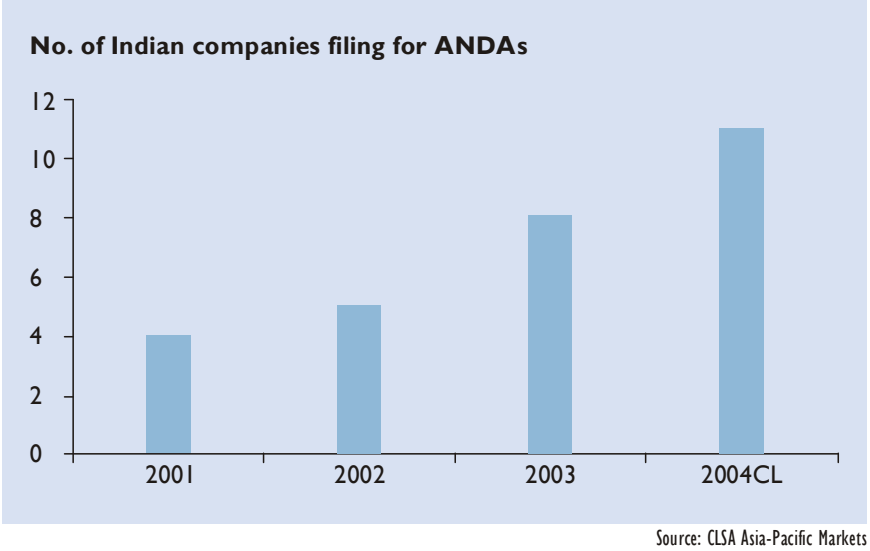
In the last three years, Indian companies have ramped up their ANDA filings in the US. The ANDA filings by a group of 9 large Indian companies increased from 24 in year ended March 2002 to about 144 in the year ended March 2005. Moreover, most of these companies have individual targets of filing over 20 ANDAs annually.

Ramp-up in the number of ANDA filings from India

Company	FY02	FY03	FY04	FY05	Pending approval
Ranbaxy	15	25	25	29	60
Sun Pharma	1	3	6	22	24
Dr Reddy's	6	14	13	13	45
Glenmark	-	-	-	7	5
Cadila	-	-	12	13	20
Orchid	-	-	-	18	17
Lupin	2	3	-	14	15
Aurobindo	-	-	2	22	28
Wockhardt	-	1	6	6	14
Total	**24**	**46**	**24**	**144**	**230**

Source: HSBC Securities & Capital Markets

In addition, a number of smaller Indian companies are also looking to ramp up their ANDA filings from a low base.



Source: CLSA Asia-Pacific Markets

Several Indian companies come to the fore as preferred contract manufacturing partners

Emerging Indian companies such as Divi's, Suven, Matrix and Nicholas Piramal are partnering large global pharmaceutical companies in custom chemical synthesis and contract manufacturing.

Divi's Laboratories

Divi's provides custom synthesis services to innovators and is currently working on 75 products with top 20 innovator companies. Divi's has positioned itself as an IPR adherent. Divi's is focusing on future generics – products that are to go off patent in the coming years and has made 19 DMFs to date. Divi's would be supplying APIs to generic companies for these products, when they go off patent. The company shall not be tying up with a Para IV challenger, given its strategy of respecting IPR.

Matrix Labs

Matrix has filed 46 DMFs to date, of which 31 were filed in FY05 itself. The company intends to position itself as an integrator with innovators and generic companies for outsourcing contracts. It expects its CRAMS (Contract Research and Manufacturing Services) business to grow from 10 per cent of its revenues currently to about one third of revenues in 3-4 years. The company has also taken a 60 per cent stake in a China based company – MCHEM Pharma Group and a 22 per cent stake in Belgium based Doc Pharma for US$ 263 million to get direct access to the highly fragmented market in Europe. It has a profit sharing agreement in the US for 20 products, which it will manufacture. It has two joint ventures in the EU for eight products.

Suven Life Sciences

Suven Life Sciences has been an adherent of IPR and offers services to innovator companies in the drug discovery space. Despite its small size, it has filed 28 patents in the CNS (Central Nervous System) segment, which is considered to be one of the most complex segments to work upon.

The company gets 75 per cent of its business from CRAMS and the remaining through drug discovery support. In the CRAMS segment, it manufactures intermediates to be used by innovators in clinical trials. The company expects this business to grow by 25 per cent.

Suven offers a host of services—from lead development to clinical trials. It has already started clinical trials for two molecules and expects to start another four soon. This segment is expected to grow at 15-20 per cent. Suven has worked on 275 projects for several global pharma majors and is currently working on more than 40 projects.

Nicholas Piramal India Ltd (NPIL)

NPIL has a presence across the value chain from chemical synthesis to formulations. It has USFDA certified facilities and proven success in niche

segments like inhalation anaesthetics. Its clear strategy of non-infringing business model gives it an edge over the other generics companies.

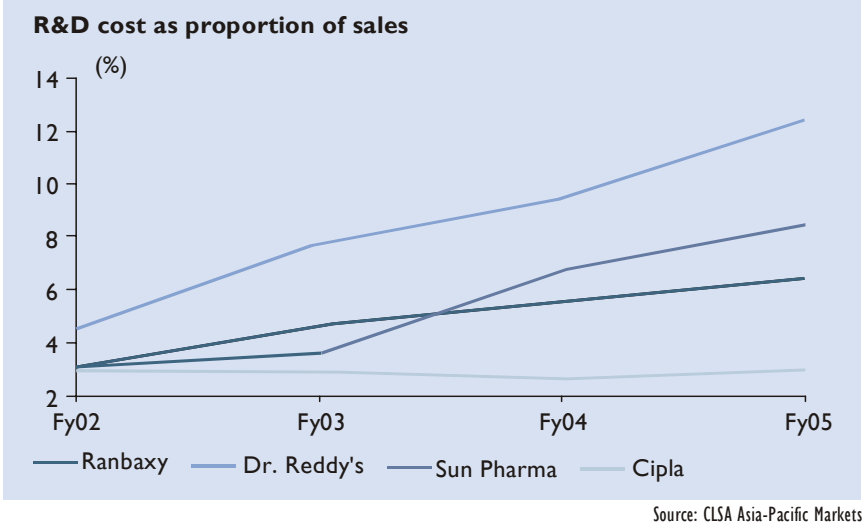
It has already announced contracts worth US$ 50 million and is likely to soon announce two more contracts worth about US$ 30 million. It has a target of inking 3-4 deals per year. It is also anticipating this new line of business to make up around 50 per cent of its total revenues over the next 4-5 years.

Innovation Opportunities

Licensing Opportunities

While generics will continue to be the key revenue earner for the Indian pharmaceutical industry in the near term, several leading companies are ploughing back earnings into R&D and are migrating into a new growth orbit for the long-run. India will emerge as a source for global drug candidates over the next five to seven years and proprietary products will drive long-term growth.

Indian pharma companies scaling-up investments in innovation



Source: CLSA Asia-Pacific Markets

In absolute terms, R&D budgets in the Indian pharma industry have risen several times over in the past three years. Ranbaxy's have increased by four times to US$ 75 million, Dr. Reddy's three times to US$ 55 million and Sun Pharma's five times to US$ 24 million.

The major domestic manufacturers are currently investing between 6 and 10 per cent of turnover in R&D, some of which is on New Chemical Entities (NCEs) as they strive to compete in the research-driven global

marketplace. Dr. Reddy's has the highest R&D investment in the Indian pharmaceutical industry as a proportion to sales at 12.5 per cent. Sun Pharma has been very aggressive in the recent past, with R&D rising to 8 per cent of net sales.

Evolving Indian R&D pipeline

Indian pharma companies started taking initiative in drug discovery research in the late 1990s. The Indian pharma R&D pipeline has been evolving over the years. The pipeline is in the early stages and is likely to take two to three years to reach critical mass. Several NCEs are in human clinical trials.

Drug discovery pipeline of Indian pharma

	Pre-clinical	Phase I	Phase 2	Phase 3
Ranbaxy	5	3	2	
Dr Reddy's	5	2	1	
Wockhardt			1	
Nicholas Piramal			1	
Lupin			2	
Orchid	2	1		
Torrent	19			
Glenmark	1	1		
Dabur	29	1	1	
Total	**64**	**12**	**4**	**0**

Source: HSBC Securities & Capital Markets

Given their limited balance sheet sizes, Indian R&D is not yet ready for a start-to-finish model for NCE research. Indian companies are adopting a collaborative approach, especially involving out-licensing of lead compounds, as the preferred route.

Despite the late start, the companies have had some successes with several out-licensing deals.

R&D licensing deals by Indian companies

Indian Firm	Partner	Molecule
Dr Reddy's	Novo Nordisk	DRF 2593 (Diabetes)
	Novartis	DRF 4158 (Diabetes)
	Novo Nordisk	DRF 2725 (Diabetes)
Ranbaxy	Bayer	Cipro XR (NDDS)
	Schwarz	RBx 2258 (BPH)
Torrent	Novartis	Age Breaker (Diabetic)
Glenmark	Forest (For North America)	GRC 3886 (Asthma/COPD)
	Tejin (For Japan)	GRC 3886 (Asthma/COPD)

Source: Citigroup Research

Indian pharma companies have entered into about eight out-licensing deals to date with global majors. These highlight the potential of innovation in India and suggest that out-licensing deals from India will increase.

Case Study: Glenmark-Forest Labs & Teijin Pharma

Glenmark's out-licensing deal with Forest Labs for a novel compound for asthma (GRC 3886) proves that innovation does not require large R&D budgets and that India is emerging as a global discovery hub (like Japan in the 80s and 90s). This is the biggest licensing deal in Indian pharma history, with US$ 190 million in phased milestone payments and 15 per cent of sales in royalties if the product hits the market. Glenmark will also supply the API for the product to Forest Labs. Glenmark has entered into a similar arrangement for the Japanese market with Teijin Pharma, in a deal worth US$ 53 million. Glenmark is expected to sign an agreement for the European market in FY06 for about US$ 100 million. The molecule will advance to Phase 2 trials in late FY06. If things are on course, this product may hit the market by 2009-10, with total value set to reach US$ 2-3 billion.

Contract Research

Indian contract research industry growing at 40-50 per cent

The Indian contract research Industry has grown tremendously over the past few years. It has witnessed the emergence of several CROs in the area of drug discovery & development over the last decade.

New technologies such as toxicology assays for lead validation, and pharmacogenomic screening in early clinical development are being applied to address development bottlenecks. This has led to the emergence of specific areas for outsourcing: ADME/Toxicology, Drug discovery research and Process chemistry.

Contract research (excluding clinical trials players) in India is estimated to be growing at 40-50 per cent per annum.

Strong chemistry skills and cost-competitive operations driving Big Pharma to offshore / outsource R&D to India

Indian pharmaceutical companies are extremely strong in chemistry driven drug discovery research activities such as organic synthesis, medicinal chemistry, process chemistry and analytical chemistry etc. India combines these strengths with low cost of operations, competent scientific workforce and expertise in IT to offer a strong value proposition to global pharma companies.

Recognising the capabilities of Indian companies in chemistry driven R&D activities and the attached cost advantages, several Big Pharma companies are outsourcing their R&D processes to India. Some have their own dedicated research and development centres in the country. For instance Pfizer, Novartis, Astra Zeneca and GSK have already established their own infrastructure to conduct offshore research in India.

Others typically pursue discovery related activities in a partnership mode and activities such as ADME, Toxicology, Custom Synthesis, Process Chemistry etc are outsourced on a fee-for-service arrangement model.

Emergence of Service Providers

Emerging global opportunities in the areas of R&D outsourcing have driven several Indian companies to redefine their businesses models and branch out into offering contract research services. A number of niche service providers have emerged in the recent past that bring with them a wide spectrum of offerings to cover gaps in capacity, optimise the costs, widen the skill base of the partner and enhance the drug development pipeline.

Quite a few Indian CROs have expanded the width of their service portfolio for innovator companies in the area of drug discovery & development. Several of these CROs have emerged as preferred partners for international companies to pursue R&D projects.

Case Study: AstraZeneca

Astra Zeneca is one among the few Big Pharma companies in India which are pursuing both captive and outsourced R&D.

Captive R&D Operations

AstraZeneca has a captive research facility at Bangalore, India, which focuses on research in the area of "Developing World Diseases Medicine". The current focus of the Centre is on discovering new treatments for tuberculosis.

The Indian facility is an integral part of the global organisation, with a mission to discover new drugs for the treatment of infectious diseases for the developing world. The Indian R&D centre, one of AstraZeneca's nine global R&D centers set-up exclusively to conduct research on tuberculosis (TB) and other infectious diseases, was the third to be established after those in Sweden & US.

The Indian R&D Centre was established with an investment of US$ 10 million and it is proposed to be ramped up further with an investment of

another US$ 35 million which would be incurred on laboratory equipments and operation costs over the next five years. The scientists in Bangalore work closely with AstraZeneca genomics and infection research centres in Boston, USA, to develop improved diagnostic tests, identify new treatment targets and uncover more effective therapies.

Presently, around 75 scientists are working at Astra Zeneca's Bangalore facility. The company is planning to expand this team to 150 in the near future.

Outsourced R&D

The Company has so far outsourced over US$ 2.2 million worth research to Indian service providers. In areas of chemistry, AstraZeneca has been outsourcing activities such as process R&D and intermediaries to Syngene and Strides Arcolabs for shortening drug discovery. Avesthagen and Bangalore Genei have been supporting research programmes focusing on developing proteins and building a genomic library.

Bangalore Genei is further supplying restriction enzymes critical to the research activity being conducted by AstaZeneca. Strand Genomics, Genotypic Technologies and SysArris Software have been handling a part of the process integration and informatics applications, respectively.

Toxicology services in India – a US$ 20-22 million opportunity

With more companies focusing on NCE research the demand for pre-clinical studies in India is estimated to increase substantially in the coming years. The current size of the toxicology business in India is estimated to be in the range of US$ 20-22 million.

The need to conduct pre-clinical studies is driving companies to either set-up their captive R&D facilities or form alliances with the Contract Research Organisations (CROs).

Enhanced biomedical infrastructure and competitive costs in recent years are driving the growth of this industry in the country. Today, Indian CROs are capable of offering international clients complete pre-clinical solutions at one place.

Indian toxicology companies offer a wide range of services, which include dossier preparation and regulatory summaries, product registration, product defence etc and have the capabilities to undertake studies in line with various international regulatory guidelines such as OECD, EC, EU and EPA/ OPPTS.

Toxicology players in India are focused on delivering high quality services. They follow stringent Standard Operating Procedures (SOPs) in the conduct of their operations and adhere to Good Laboratory Practices (GLPs) for all testing programmes. Most players are affiliated to independent Institutional Animal Ethics Committees (IAECs) which meet regularly to approve experiment protocols. Leading companies have received a wide range of national and international quality accreditations for their facilities and processes.

Established toxicology players have invested considerably in technically advanced facilities (such as barrier maintained units) and skilled, trained and experienced human resources to enhance their capabilities to cater to the needs of their international clientele. Their laboratories and facilities are well equipped and are at par with international standards. Most of the leading players such as Jai Research Foundation, Advinus Therapeutics, INTOX (Institute for Toxicology Studies) Pvt. Ltd. and Vimta Ltd. etc offer GLP compliant animal studies.

Animal studies conducted by Indian CROs are mostly on rats, mice, rabbits, hamsters but rarely on large animals (dogs and primates). The Indian regulations that govern studies on large animals are still evolving. There are several animal house facilities in the country, including those in research institutions, public & private pharmaceutical companies, universities, medical and veterinary colleges etc.

Government providing infrastructure support for pre-clinical research

The Government is taking certain initiatives to set-up world-class infrastructure for pre-clinical research for vaccine and drug development in the country. The Indian Council for Medical Research (ICMR), the country's apex biomedical research organisation, is looking forward to tap opportunities in this space. ICMR is setting up two large facilities, one in Mumbai and the other in Hyderabad.

The first is a Primate Research Facility in Mumbai with technical and financial assistance from the National Institute of Health, USA. The facility will be set-up on a 25-acre land with an investment of US$ 16.7 million. The facility is proposed to house 7500 breeding stocks. The centre has so far received a grant of US$ 3 million from the US and US$ 4 million from the ICMR.

The International Animal Resource Facility to be set up at Shapoorji Pallonji Biotech Park, Hyderabad is also an ICMR initiative. The Government of Andhra Pradesh (GoAP) has already allocated 100 acres of land for the Animal Resource Facility at the Biotech Park in Genome Valley. The Department of Biotechnology is providing US$ 4.4 million for this initiative. The facility to be set-up would be of international standards with animal

testing facilities, hi-tech equipment, a strong technical board and ethical committee. The facility will house primates, horses, cats and beagle dogs and is expected to be completed in the next 2-3 years.

Collaborative Discovery Research

In due acknowledgement of the emerging drug discovery skills of research based Indian pharmaceutical companies, a number of big pharma are opening up to the idea of collaborating with them to develop NCEs for global markets.

GSK and Ranbaxy, India's largest pharmaceutical company, have entered into a drug discovery and clinical development tie-up covering a wide range of therapeutic areas. Ranbaxy will identify potential drugs and develop them in initial stages, while GSK will take care of the later stages. GSK signed this agreement despite Ranbaxy's challenge to its blockbuster products - Ceftin, Augmentin and Valtrex, in the US market.

In another instance of a leading global pharma company tying up with an Indian company for research, AstraZeneca has tied up with Torrent Pharmaceuticals Ltd for research aimed at discovering a drug for the treatment of hypertension. Under the agreement, the partners will fund the research jointly. It involves success-based milestone payments to Torrent and royalties on the drug after commercialisation. Torrent would also get co-marketing rights for the product for the country.

Clinical Research

India to capture US$ 250-300 million or 10 per cent of global clinical trials by 2010.

India is emerging as a favoured global destination for global drug development companies as it offers all the enabling factors for accelerated clinical research activity. Recent changes in India's healthcare policies and a maturing regulatory environment have significantly brought down the risk of shifting more clinical research from the developed countries to India.

The clinical research industry in India is presently estimated at over US$ 100 million. Increasing compliance with ICH-GCP protocols and a growing body of trained and experienced investigators is enabling India to become a viable destination for global studies. India is expected to capture about 10 per cent of the global clinical research market within the next five years and is projected to reach a size of around US$ 250-300 million by 2010.

Several Big Pharma and international CROs make India a clinical research hub

Several big pharma companies have been conducting their clinical development activities in India for the last 5-10 years. Encouraged by the promise of early initiatives, they have been scaling up their investments aggressively by setting up dedicated clinical research teams/divisions to initiate and monitor pivotal clinical studies. Apart from local registration trials, Big Pharma companies are now also contributing patients from India for multicentric global trials of drugs for FDA/EMEA submissions.

For instance, GSK is carrying out clinical trials for the parent company in India. Currently nine clinical trials are in process, of which eight are Phase 3 trials and one is a Phase 2b trial. A total of 700 patients have been recruited for the trials.

Quintiles was the first foreign CRO to establish its operations in India in 1997. Several other global CROs followed suit and declared India as a preferred clinical research location for their global operations. Most CROs have chosen to enter India through the alliance route. Seven of the Top 10 global CROs have a presence in India to benefit their global clients with expanded geographic reach and faster recruitment of subjects. Several smaller international CROs have also set up their operations in India, sensing the potential opportunity.

Case Study: Quintiles Success Story

Quintiles chose the joint venture route to enter India in 1997 but soon bought out its partner's stake to become a 100 per cent subsidiary of Quintiles Transnational. The Company has grown from a two employee, single location operation to an outfit of more than 850 employees in three locations and has plans to double its numbers by 2010. It now offers its full portfolio of services for Phase I-IV clinical studies in various therapeutic areas. 15 of the top 20 global pharma companies have worked with Quintiles in India. The Company has so far undertaken about 130 international studies in India involving more than 600 sites and 20,000 patients covering a wide range of therapeutic areas including oncology, psychiatry, neurology, anti-infectives, gastroenterology, ophthalmology, endocrinology and cardiology. The company has conducted several pivotal studies for submission of data to US and European regulatory authorities. In 2003-04, the Indian subsidiary's revenue increased to US$ 13.5 million as against US$ 8.3 million in 2002-03. Quintiles, India is believed to be one of the most profitable subsidiaries (by operating profit margins) of Quintiles Transnational.

Emergence of domestic CROs

The growing clinical research opportunity has ushered in a number of domestic players in the sector. These are a mix of standalone CROs and

those which are offshoots of domestic pharmaceutical and biotech companies. The leading Indian CROs today have capabilities to conduct trials in strict compliance with international quality standards such as ICH-GCP, which has made potential sponsors and partners confident of their quality and competence to participate in global studies.

Key factors contributing to India's attractiveness as a global clinical research hub

Offshoring clinical development to India has now become a strategic imperative for most global pharmaceutical companies and international CROs. The key contributory factors include the relatively faster rate of recruitment of subjects and the significant cost advantage which facilitate affordable drug development research. Further, improved medical infrastructure, increased awareness of ICH –GCP requirements and the growing pool of English speaking research investigators have also contributed. Global regulatory harmonisation through the recent amendments to the Patent Act and the approval for conducting concurrent Phase II and III trials have further reinforced the Government's commitment to create a favourable environment for conducting clinical research in India. Improving human subject protection and increasing international acceptability of Indian data are further adding to India's appeal as a preferred clinical outsourcing destination.

	Western Hemisphere	India
Patients with urban lifestyle diseases	High	Very High
Patients with tropical diseases	Low	Very High
Speed for recruiting patients	Low-Medium	Very High
Speed for conducting a trial	Medium	High
Return rate of patients	Medium	Very High
Pool of qualified personnel	Very High	High
Heterogeneous population mix	High	High
Adherence to ICH quality guidelines	High	High
Availability of technology to streamline trials	Medium	High

Indian CROS becoming attractive international acquisition targets

The trend towards CRO acquisitions is accelerating as several international pharma companies are said to be considering India for such strategic investments. In September 2003, US-based information technology services company, iGate acquired a 95 per cent stake for US$ 1.5 million in Diagnosearch, an Indian company focused on early phase clinical trials and clinical data management with sales of US$ 680,000.

In a recent deal, Actavis, an Iceland-based US$ 600 million generic drug major with a strong focus on research and development, acquired Lotus Laboratories, one of India's leading CROs, in a Euro 20 million (US$ 25.52

million) all-cash deal in March, 2005. The deal value was over four times Lotus Labs' sales of US$ 6.4 million in 2004-05.

ANDA Research

Several Indian generics companies have focused on ANDA research, since it involves less risk compared to NCE research. Since the competitive landscape in the global generics market is worsening, cost control has become crucial. An analysis of the R&D productivity helps assess the cost advantage that Indian companies have in developing ANDAs.

R&D Productivity

	R&D spend in generics 2004 (US$m)	ANDAs filed	US$m/ANDA
Teva	247	53	4.7
Mylan	69	17	4.1
Alpharma	**81**	**10**	**8.1**
Ranbaxy	39	29	1.3
Dr. Reddy's	33	13	2.5
Cadila	**17**	**12**	**1.4**

Source : Annual reports, CLSA Asia-Pacific Markets

The comparison between Alpharma and Cadila Healthcare is interesting. Alpharma filed 10 ANDAs in 2004; spending about US$ 81million in R&D. Cadila (a new entrant from India) filed 12 in the same year and spent just US$17 million.

Case Study: DRL-IVF Deal

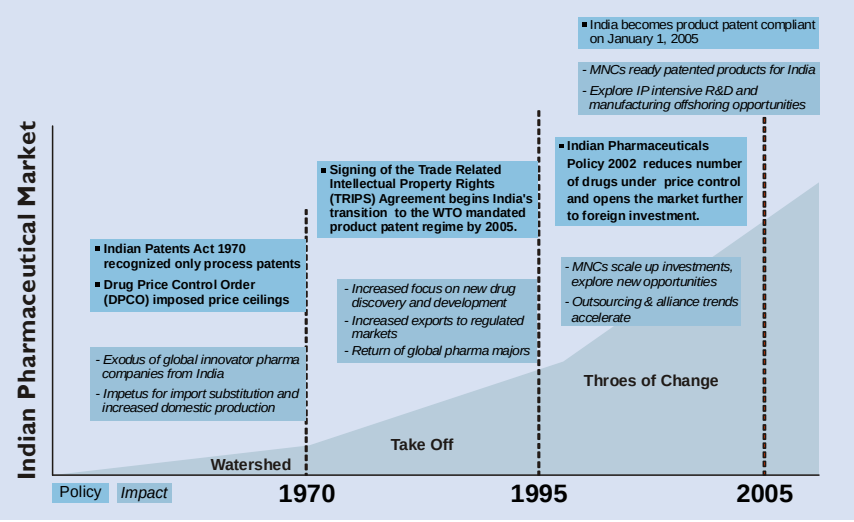
Dr. Reddy's Laboratories (DRL), one of India's leading pharma companies, sealed an agreement with ICICI Venture Funds (IVF), India's leading private equity company, for developing and selling products through the ANDA route.

The deal valued at US$ 56 million was a first-of-a-kind deal for the Indian market and is structured such that IVF will fund 50 per cent of all expenses incurred by DRL for development, registration and legal costs related to commercialisation of ANDAs over 2004-05 and 2005-06. The deal specifies the number of ANDA filings DRL has to make in the U.S. market. In return, IVF gets royalties for a five-year period after each molecule goes on sale in the U.S. IVF plans to stay invested until 2010, at which time it will decide its future course of action. DRL has right of first refusal should IVF choose to exit at that stage.

The IVF-DRL deal is being viewed as the beginning of a trend. DRL has structured a similar model for its innovation activities as well.

Policy Initiatives

Summary of evolving policy scenario



Recent policy changes in the Indian pharmaceutical market

The Patents (Third Amendment) Act. 2005

- Extension of product patent protection to all fields of technology (i.e., drugs, food and chemicals);
- Deletion of the provisions relating to Exclusive Marketing Rights (EMRs) (which would now become redundant), and introduction of a transitional provision for safeguarding EMRs already granted;
- Provision for enabling grant of compulsory licence for export of medicines to countries which have insufficient or no manufacturing capacity, to meet emergent public health situations
- Modification in the provisions relating to opposition procedures with a view to streamlining the system by having both pre-grant and post-grant opposition in the Patent Office
- New proviso to circumscribe rights in respect of mailbox applications so that patent rights shall be available only from the date of grant of patent, and not retrospectively from the date of publication.
- Strengthening the provisions relating to national security to guard against patenting abroad of dual use technologies
- Clarification of the provisions relating to patenting of software related inventions when they have technical application to industry or are in combination with hardware
- Rationalisation of provisions relating to time-lines with a view to introducing flexibility and reducing the processing time for patent applications, and simplifying and rationalising procedures

Notification of revised Schedule Y of the Drugs & Cosmetics Act, 1940

- Companies permitted to conduct Phase II-IV trials concurrently in India and overseas
- For new drug substances discovered in other countries, Phase I data generated outside India is mandatory for permission to conduct Phase II trials or to repeat Phase I trials in India
- Post Marketing Surveillance (PMS) study made mandatory in respect of new drugs

Amended Schedule M (Good Manufacturing Practices) of the Drugs and Cosmetics Rules

The Ministry of Health & Family Welfare has amended the Good Manufacturing Practices (GMP) outlined in Schedule M of the Drugs and Cosmetics Rules, to provide a fillip to India's growing global competitiveness in pharmaceutical manufacturing. The provisions in the modified regulations are now applicable to all pharmaceutical manufacturers from July 1, 2005

Stringent measures for makers of spurious drugs

- The Drugs and Cosmetics (Amendment) Bill, 2003 proposes levy of stringent penalties on manufacturing of spurious drugs. The Bill would make related offences non-bailable.

Creation of Pharma R&D Fund

- Government of India has created a Pharma R&D Fund with a total corpus of US$ 33.3 million. The Fund will act as a grant for public institutions and a loan to industry

Concessional Industrial Package:

The Government of India announced a Concessional Industrial Package in 2003 for certain hilly states in the country with the objective to promote industrial investment in these states**.** The Package offers 100 per cent excise exemption, among other fiscal incentives, for manufacturers in specified industries and this has encouraged a large number of pharmaceutical companies to expand capacities and set up new production facilities in these states.

Other recent Government interventions include setting up of the Indian Pharmacopoeia Commission and creation of Pharmaceutical Export Promotion Council (Pharmexcil).

CONTACT FOR INFORMATION

Information on the market and opportunities for investment in the pharmaceuticals sector in India can be obtained from the Confederation of Indian Industry (CII), which works with the objective of creating a symbiotic interface between industry, government and domestic and international investors.

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