

# White Paper on Indian Pharma Industry Quest for Global Leadership



**ASSOCHAM**

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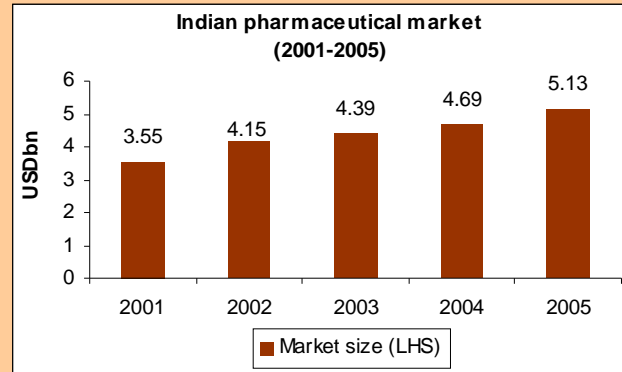
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## 1. Indian pharmaceutical market – At a glance

### 1.1 Market size

Indian pharmaceutical market has grown by 9.5% to reach USD5.13 billion in 2005. It accounts for about 1% of the global pharmaceutical market in value terms and 8% in volume terms. The pharmaceutical market has grown at a compounded annual growth rate (CAGR) of 9.7% during the last five years.



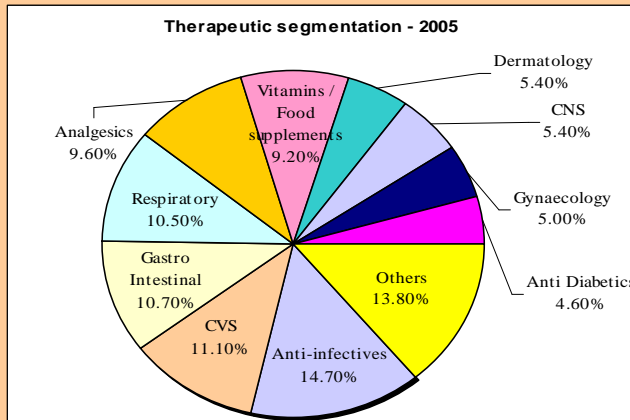
Source: Cygnus Research

Market growth during 2005 was primarily driven by a number of new product launches by both Indian and foreign companies. The Indian market started to attract a number of foreign players, with the implementation of product patents in January 2005. The FDI in pharma industry was USD172 million in 2005-06, growing at a CAGR of 62.6% during the period 2002-06.

### 1.2 Major segments

Anti-infective is estimated to be the major therapeutic segment accounting for 14.7% of the total pharma market in India. The major sub-segments within this category are Cephalosporins, Quinolones, Penicillin and Macrolides.

Cardiovascular drugs are the next major therapeutic segment contributing 11.1% of the total sales. The major sub-segments under this category include anti-hypertensives, statins and anticoagulants. Gastrointestinal and respiratory are the next leading therapeutic segments accounting for 10.7% and 10.5% in 2005-06.



Source: Cygnus Research

### **1.3 Industry trend**

- ✓ Indian Pharma companies are on a global acquisition spree, specially gaining importance in the global generics market
- ✓ The industry is witnessing significant growth in the Contract Research and Manufacturing Services (CRAMS) domain
- ✓ Indian companies de-risk their R&D by out-licensing their NCEs or spin off their R&D unit into a separate entity
- ✓ Indian companies are raising funds through FCCB, ADR to finance their overseas acquisitions
- ✓ The draft Drug Policy 2006 intends to bring additional 354 drugs under price control
- ✓ The strengthening IPR scenario in India drives MNCs to:
  - Launch their patent protected drugs in India
  - Invest in increasing their R&D presence in India

### **1.4 Outlook**

The Indian pharmaceutical market is expected to register a growth of 11% in 2006 to reach USD5.7 billion and expected to grow at a CAGR of 13.6% during the next five years.

## 2. India's global competitive strategy

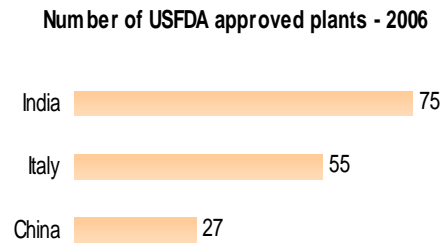
Indian pharmaceutical industry is expanding its presence across the globe through a lot of mergers and acquisitions and today, India is one of the most preferred manufacturing bases for the multinational companies. India is positioned competitively in the following areas.

### 2.1 Emergence as the preferred manufacturing base

With strong chemistry skills, and high skilled manpower at cheaper cost, India is in a position to manufacture at a very low cost compared to pharma companies in the Western countries. This has triggered Western pharma companies to outsource their manufacturing activities to India. Other main factors that drive the Western companies to prefer India include –

#### 2.1.1 Highest number of US FDA approved plants outside US

India currently has the highest number of US FDA (Food and Drug Administration) approved plants (outside US) at 75, followed by Italy with 55, and China with 27. Industry estimates put that, Indian pharma companies have invested a combined capital expenditure of USD1 billion between FY2003 and 2005, a majority of which is in USFDA approved assets.



Source: Cygnus Research

#### 2.1.2 Increasing number of regulatory filings

Indian pharma companies are increasing the number of regulatory filings such as DMF and ANDA as these enable them to manufacture and market drugs in the regulated market such as the US and Europe. The total number of DMF (Drug Master File) filings in USFDA made by Indian companies has increased from 62 in 2001 to 265 in 2005, growing at a CAGR (Compounded Annual Growth Rate) of 44% during this period. Indian DMF filings accounted for 37% of the total DMF filings made with USFDA in 2005. Similarly, Indian companies account for a significant amount of ANDA (Abbreviated New Drug Application) filings made every year.

#### 2.1.3 Special Economic Zones (SEZ) to boost manufacturing

The new SEZ Act supports the export oriented approach of the Indian pharma industry as it offers tax incentives and other benefits for firms that manufacture products primarily for exports. Around 15 pharma SEZs have received approval from the SEZ board. The SEZ concept is aiding the Indian pharma industry to place itself competitively in the global arena.

## 2.2 Establishing global presence through acquisitions

Mergers and acquisitions are considered to be one of the main strategies by the Indian pharma firms for increasing their global presence, for expanding their product portfolio and acquiring new customers. The major acquisitions made by Indian pharma firms in the recent past include – Dr. Reddy’s acquisition of Betapharm (Germany) for USD574 million and Ranbaxy’s acquisition of Terapia (Romania) for USD324 million.

### **2.3 New patent regime attracting investments**

With the implementation of product patent regime in India on January 2005, MNCs are investing in launching new products in the Indian market and on setting up manufacturing facilities and R&D centres in India. For instance, Israel's Teva is developing an R&D centre at Noida near Delhi. Ferring Pharmaceuticals, a 100% subsidiary of Dutch major Ferring BV, is setting up a manufacturing unit in Mumbai for producing specialty proteins and hormones; Germany's Hexal AG is setting up a formulation plant in Bangalore.

## 3. Policy & Pricing Framework

### 3.1 Draft drug policy 2006

Draft Drug Policy, 2006	
Area	Policy
Drug Regulatory System	National Drug Authority would be constituted
	Several of the existing provisions of the Drugs and Cosmetics Act, 1940 would be amended
Intellectual Property Rights including Data Protection	Proper training to be imparted to the personnel
	The number of patent examiners to be further increased
	Full computerization would be undertaken
	Electronic filing of patent applications to be introduced
	An IP Cell to be set up in the Department of Chemicals and Petrochemicals
Clinical Trials and Drug Development	An early decision on data protection
	National Toxicology Centre to be made fully compliant with GLP norms
	Tax benefits available to R&D to be made applicable for Clinical trials too
	Clinical trial samples being imported into India to be exempted from payment of import duty
	Exemption from service tax for a period of 10 years upto 2015
Anti-Cancer and Anti-HIV/AIDS Drugs	Public-Private Partnership Programme
Drugs for Other Life Threatening Diseases	All such drugs to be identified and brought under the public-private partnership model
Patented Drugs	The patented drugs (formulations under product patent) that are launched in India after 1st January, 2005 would be subjected to mandatory price negotiations before granting them marketing approval
Excise duty relief	Excise duty is now levied on 60% of the MRP as compared to the ex-factory price earlier
Maximum Retail Price (MRP)	Concept of MRP inclusive of taxes would be made applicable to medicines sold in the packaged form
New Drug Price Control Order	A new Drug Price Control Order (DPCO) replacing the existing DPCO, 1995, would be issued under the Essential Commodities Act, 1955.
Bulk purchases by Government	Lower prices for bulk purchases by Government
Promotion of Generic Drugs	Public procurement and distribution of drugs would preferably be for generic drugs
	Quality certification would be provided free of cost to generic drug manufacturers
	No control on prices of generic drugs
Control on Pharmaceutical brands	No change should be permitted in the composition of a given brand
Strengthening of Pharma PSUs	A Pharma Development Fund would be created to help the pharma PSUs
Health Cess	A health cess of 2% for funding Schemes for the poor
Orphaned Drugs	Development of Orphaned Drugs by providing efforts made to further develop and launch several orphaned drugs in the market.
<i>Source: Department of Chemicals and Petrochemicals, Govt. of India, compiled by Cygnus Research</i>	

### 3.2 Pricing scenario

#### 3.2.1 Current

- ✓ Currently 74 bulk drugs and the associated formulations are under price control. The prices are fixed and revised by the National Pharmaceutical Pricing Authority (NPPA).
- ✓ MRP, Inclusive of All Taxes, regime introduced since October 2, 2006.

- ✓ The price of formulations in India is fixed on the basis of the following formula on which a 4% value added tax (VAT) is imposed-

$$\text{MRP} = \text{Ex-factory Cost} + 100\% \text{ MAPE on Ex-factory Cost} + \text{ED} + \text{VAT} + \text{Other tax (If any)}$$

*MRP = Maximum Retail Price, MAPE = Maximum Allowable Post-manufacturing Expense (100%), ED = Excise Duty (16%) – With an abatement of 40% on MRP, VAT = Value Added Tax (4%)*

### 3.2.2 Future

- ✓ The formulae proposed for fixing equitable prices for bulk drugs and their formulations, include cost plus margins model, negotiated prices, differential prices, reference prices, and bulk purchase prices.
- ✓ The MAPE have been increased to **150%** from 100%, with an extra 50% for products of R&D intensive companies.
- ✓ Imported drugs would be allowed 50% margin on the landed costs.
- ✓ To avoid a sudden spurt in prices of the current list of 74 drugs under price control their MAPE will remain unchanged for one year.
- ✓ New patented drugs would be exempted from price control for 10 years post commercialization.

## 4. Industry partnership & alliances

Indian pharma companies are eyeing for mergers and acquisitions in expanding their geographical reach, and for product extensions. Similarly, they are looking out for alliances, especially in the research and development domain to de-risk their research activities and use the expertise of large companies. Indian companies are also partnering with overseas companies to launch their products in India.

### 4.1 Major M&A deals by Indian pharma companies

In India, pharma is one of the dynamic industries with lot of mergers and acquisitions on the roll. The recent high value acquisition was Dr. Reddy's acquisition of Betapharm, the second largest generics company in Germany for USD574 million. The acquisition has given way to Dr.Reddy's to establish a strong presence in Germany and access Betapharm's product portfolio. The other major acquisitions during 2005-06 are listed in the table below.

Major acquisitions by Indian companies - 2005-06			
Acquirer	Target	Value USD million	Date
<b>Generics</b>			
Dr. Reddy's	Betapharm (Germany)	574	Feb-06
Ranbaxy	Terapia (Romania)	324	Mar-06
Ranbaxy	Ethimed NV (Spain)	-	Mar-06
Ranbaxy	Allen Spa (Italy)	-	Mar-06
Aurobindo	Milpharma (UK)	13	Feb-06
Jubilant Organosys	Target Research Associates (US)	34	Oct-05
<b>Branded formulation</b>			
Sun Pharma	Able Laboratories (US)	24	Dec-05
	Valeant Pharma (2 facilities) (Hungary, US)	10	Aug-05
<b>Active pharmaceutical ingredient (API)</b>			
Dr. Reddy's	Roche's API Business (Mexico)	59	Nov-05
Matrix	Docpharma (Belgium)	263	Jun-05
<b>CRAMS</b>			
Jubilant Organosys	Trinity Laboratories (US)	20	Jul-05
Dishman	Solutia's Pharma services (US)	75	May-06
Nicholas Piramal	Avecia Pharma (UK)	17	Oct-05

Source: Cygnus Research

### 4.2 Out-licensing & in-licensing deals

In order to reduce the risk in new drug development, Indian pharma companies out-license their molecules under development to large companies which have enough financial strength to support their research activities and a strong marketing arm. Some of the major out-licensing deals made by the Indian companies include –

Major out-licensing deals by Indian companies			
Company	Licensed to	Molecule	Indication
Dr Reddy's	Novo Nordisk	DRF 2593	Diabetes
	Novo Nordisk	DRF 2725	Diabetes
Ranbaxy	Bayer	Cipro XR	NDDS

	Schwarz	RBx 2258	BPH
Torrent	Novartis	Age Breaker	Diabetes
Glenmark	Forest (For North America)	GRC 3886	Asthma/ COPD
	Tejin (For Japan)	GRC 3886	Asthma/ COPD
<i>Source: Citigroup Research</i>			

Indian companies also enter into in-licensing of products or technology from other companies. Some of the in-licensing deals made by Indian companies in the recent past include –

- ✓ Ranbaxy's in-licensing agreements
  - With Janssen-Ortho Inc for marketing 2 products in the Canadian market
  - Invagen Pharmaceuticals Inc for anti-epileptic drug zonisamide in the US market
  - Eurodrug Laboratories for Doxophylline in the Indian market
- ✓ Nicholas Piramal's in-licensing agreement
  - With Ethypharm, France, for licensing of technology for Paracetamol flash tablets
- ✓ Lupin's agreement
  - With ItalFarmaco's Enoxaparin Sodium Injection for marketing in India.

## 5. CRAMS and Clinical trials

### 5.1 CRAMS market scenario

Over the last few years, the pharmaceutical industry has seen large companies use ‘downsizing’ strategies more and concentrating their resources on core skills. As industry margins come under increasing pressure, companies could begin the outsourcing aspects of their development, manufacturing or marketing processes so as to concentrate on their core specialties.

In 2005, CRAMS market in India was valued at USD532.10 million, of which contract manufacturing accounted for 84% of the total market, while the remaining 16%

Segment	Contract Research*	Contract Manufacturing
Indian Market (2005)	USD 87.1 million	USD 445 million
Growth rate over previous year	45%	48%
<i>Source: Cygnus Research, *excluding clinical trials</i>		

was accounted by contract research (excluding clinical trials). Both the segments of CRAMS have registered a robust growth rate of over 40% in 2005 over the previous year.

### 5.2 Recent CRAMS agreements

Indian companies are proving better at developing APIs than their competitors from target markets and that too with non-infringing processes. Indian drugs are either entering into strategic alliances with large generic companies in the world of off-patent molecules or entering into contract manufacturing agreements with innovator companies for supplying complex under-patent molecules.

Major CRAMS agreement by Indian companies			
Indian Company	Outsourcing partner	Outsourcing value (USD million)	Outsourcing Type
Nicholas Piramal	AMO, Allergan etc.	45	Contract manufacturing for API and formulations
Cadila	Altana, Zyban	35	JV structure for manufacturing on patent drugs
Shasun	Eli Lilly, GSK, Novartis	30	Contract manufacturing for API
Dishman	Solvay, GSK etc.	25	Contract manufacturing for intermediates and API
Jubilant	Novartis	25	Contract manufacturing for intermediates and API
Matrix	GSK	20	Contract manufacturing for API
Divi's	Three of top 10 pharma	15	Custom chemical synthesis
Strides	Mayne	15	Injectibles Manufacturing
Ipca	Astra Zeneca, Europe	15	Contract generics manufacturing of APIs
<i>Source: Compiled by Cygnus Research</i>			

### 5.3 Clinical trials

In 2005, the industry for clinical trials in India was USD100 million. This market is growing at an accelerated pace. India offers a lot of advantages in the clinical trials domain such as cost advantage compared to Western

Cost of clinical trials in US vis-à-vis in India		
Study	Average US cost (USD million)	Indian Cost
Phase I	20	50% less than the average cost in US
Phase II	50	60% less than the average cost in US
Phase III	100	60% less than the average cost in US

*Source: Taken from Pharmabiz*

countries. For instance, the average cost of conducting a Phase I trial in the US is USD20 million, while it costs only USD10 million in India.

### 5.4 Advantages offered by India in CRAMS and Clinical trials domain

#### 5.4.1 Cost saving

Today, the cost of hiring a medicinal chemist in the US is very high, approximately USD250,000-300,000 per year. The US pharma industry employs roughly 50,000 chemists. According to industry sources, Indian discovery research outfits charge global pharma companies around USD60,000 per chemist which is roughly one-fifth of what the pharma companies pay abroad. And while it is difficult to pin down an average pay for chemists in India for doing a similar work, conservative estimates suggest it to be around Rs1 million per annum (USD20,000). Beside, the Indian company is also reimbursed the costs of all consumables. So, it is a win-win situation- the overseas pharma saves about 50% cost and the Indian company makes it about 50% margin.

#### 5.4.2 Improved skills to face international competition

The future in this space belongs to the one who will not only grab the opportunity with both hands, but also play the game well. Like the IT and the software wave, and the earlier generic pharma wave, Indian discovery services companies have the opportunity to make it to the global scheme of things. Time will tell which of the niche players will consolidate to become fully integrated discovery companies and which of the Indian companies, if any, will become global players. Indian scientists are exposed to the outsourcing environments, improved confidence to face international challenges. This directly attracts international players to the Indian market.

#### 5.4.3 Already existing strong manufacturing base

India's manufacturing clout has become a massive threat to the Western generic firms. The freedom to manufacture generic versions of patent protected drugs using non-infringing processes has also given them a head start in developing new methods of production and getting them to the market very rapidly.

#### 5.4.4 Strong marketing and distribution network

Many of the Indian mid sized pharmaceutical companies have extensive marketing and distribution network facilitating the business of contract research and manufacturing services.

#### 5.4.5 Rich biodiversity

The huge patient population offers vast genetic diversity, making the country an ideal site for clinical trials. The advantages offered by India over the Western countries are listed in the table below.

Advantages offered by India in clinical trials		
	Western Countries	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

Source: IBEF

Number of pharmaceutical companies has successfully used clinical trial data generated from India for US FDA New Drug Application

US FDA New Drug Application data generated from India	
Drug Company	Molecules Researched
Alcon	Vegamox
AstraZeneca	Merenem
Cangene	Hepatitis B Vaccine
Eli Lilly	Alimta Gemcitabine (breast cancer) Cialis (erectile dysfunction) Xygris (Septicemia)
Glaxo	Lamictal
Janssen	Resperidal
Novartis	Tegaserod
Pfizer	Voriconazole
Roche	Peg-Interferon
Santen	Quixin
Wyeth	Influenza A Vaccine

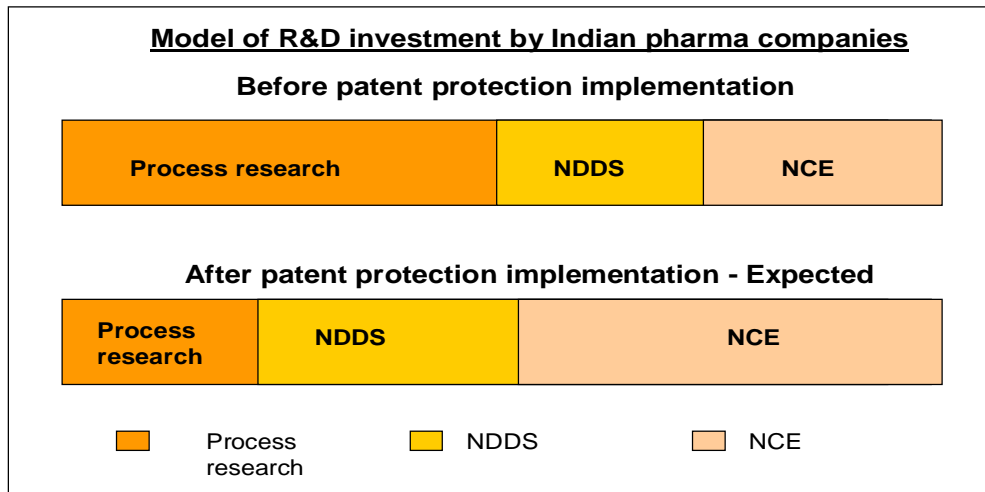
Source: Pharmabiz

## 6. Drug discovery & development

With the implementation of product patents in India in January 2005, investing in R&D became inevitable for the Indian pharma companies, to compete globally and survive in the long run. The benefits reaped by a few companies such as Ranbaxy and Dr Reddy's in the R&D field have attracted others to follow. Most of the Indian pharmaceutical companies including Cipla, Lupin, Wockhardt, Nicholas Piramal and Torrent are actively involved in R&D activities.

### 6.1 Shifting R&D investment model

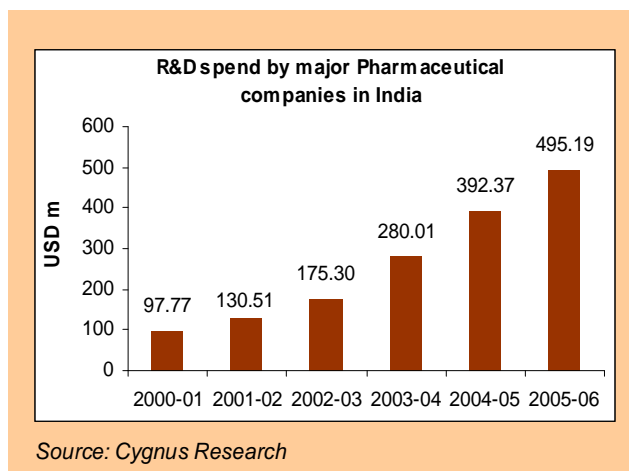
The model of R&D investment by Indian companies is shifting from core process research to new drug development and novel drug delivery systems (NDDS). For instance, Ranbaxy has out-licensed its NDDS to Bayer for the development of Cipro XR formulation.



Source: Cygnus Research

### 6.2 Increasing R&D spend of Indian companies

The major pharmaceutical companies in India are the main R&D investors of the industry. The R&D spend (capital and current) of these major companies has grown at CAGR of 38% during the period 2000-01 to 2005-06. In 2005-06, the R&D expenditure of 50 major companies totalled USD495.19 million growing at a rate of 26% over the previous year. The higher growth rate is attributed to product patent implementation in the country in January 2005.



### **6.3 Establishment of R&D centres by MNCs in India**

The escalating R&D cost in the Western countries has driven the pharma companies in those countries to look out for destinations where R&D activities can be done at a low cost. Western firms are establishing their R&D centres in India to reap the benefits offered by the sub-continent such as rich talent pool, which is available at low cost compared to the Western countries. For instance, the Canada-based Apotex Corporation and US-based Sigma Aldrich are setting up an R&D centre in Bangalore; Israel's Teva is developing an R&D centre at Noida near Delhi.

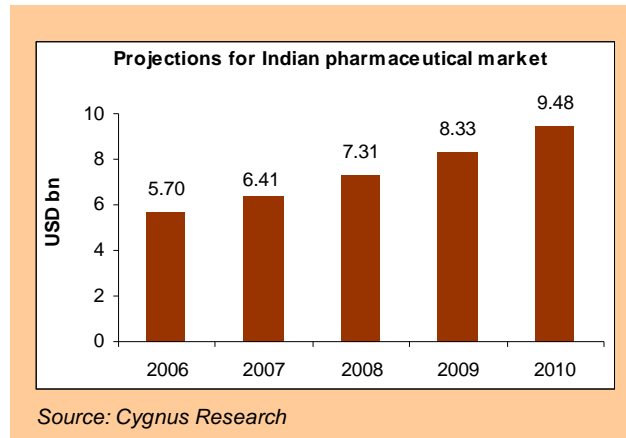
## 7. Data exclusivity issues

- ✓ Data exclusivity (DE) provides protection to an innovator's tests and clinical trial data for a certain period of time
- ✓ This data cannot be relied upon by another company to seek marketing authorisation of the same drug
- ✓ The time duration for DE varies with countries
  - Five years in USA,
  - Six years in China and
  - Upto ten years in EU members.
- ✓ Current TRIPs (Trade-Related Aspects of Intellectual Property Rights) regulations do not include data exclusivity clauses
- ✓ Hence India is not obligated to add this new clause to their Drugs and Cosmetics Act
- ✓ Pharmaceutical companies suggest that more product introductions, R&D and clinical trial businesses will come to India only if DE norms are in place
- ✓ But there are apprehensions that DE implementation in the country might lead to monopoly in the drug industry and in turn harm the accessibility and affordability of drugs.

## 8. Future Outlook

### 8.1 Pharma industry

The Indian pharmaceutical market is projected to grow by 11% in 2006 to reach USD5.70 billion. The market is expected to grow at a CAGR of 13.6% during the period 2006 to 2010 and reach a market size of USD9.48 billion. The growth of the market is expected to be largely driven by new product launches, especially new



branded drugs by foreign firms and the growth rate is expected to reach its peak by 2009, after which it is expected to stagnate with fewer new product launches.

### 8.2 CRAMS and Clinical trials

Industry estimates put that the clinical trials market in India will be USD200 million by 2007 and USD1 billion by 2010. The contract manufacturing market is expected to reach USD900 million by 2010 with the growth primarily driven by increasing number of USFDA plants in the country and rise in DMF and ANDA filings by Indian pharmaceutical companies.

### 8.3 Future trends

Some of the major trends that are expected in the future include – mergers and acquisitions in the industry; new product launches by MNCs and Indian companies; in-licensing of patented products by Indian companies to launch them in the Indian market and increase in the number of contract research organizations. The industry will also face stricter regulatory norms in order to maintain its competitiveness in the global space.