Project Completion Report

Pharmaceutical Sector in India

Implemented by

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PI, DST-ASPIRE Project

Administrative Staff College of India
Leadership through Learning

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Academy for Science, Policy Implementation and Research (ASPIRE)

ASPIRE was launched in 2010 by Department being incubated in project mode at the Administrative Staff College of India (ASCI), Hyderabad. It aims to provide a common platform for interconnecting and enhancing competencies in policy development and implementation emphasizing Science Technology and Innovation across various stakeholders and arms of the Government leading to evidence based decision making.

Some of the areas in which policy studies have been carried under ASPIRE include food price inflation, R&D in agriculture, pharmaceuticals, patents, steel related R&D and Innovation etc. Efforts are on to upscale the level of engagement of socio-economic ministries and public sector industries in ASPIRE for R&D management, Innovation and Policy including capacity building. During 2015-16, new studies apart from conducting a workshop on science technology and innovation ecosystem will be planned for evidence based policy interventions.

Acknowledgement

First and foremost, I would like to thank Dr. Ashutosh Sharma, Secretary, DST for reposing faith in us to conduct such a sensitive assignment.

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Abbreviations

ABLE	Association of Biotechnology Led Enterprises
ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredients
APIIC	Andhra Pradesh Industrial Infrastructure Corporation
BDMA	Bulk Drug Manufacturers Association
BLA	Biologic License Application
BP	Blood Pressure
BRICS	Brazil Russia India China South Africa
CCMB	Centre for Cellular and Molecular Biology
CDA	Confidential Disclosure Agreement
CEO	Chief Executive Officer
CFTRI	Central Food Technological Research Institute
CMIE	Centre for Monitoring Indian Economy
DNA	Deoxyribonucleic acid
FDA	Food and Drug Administration
GDP	Gross Domestic Product
GERD	Gross Domestic Expenditure on R&D
ICAR	Indian Council of Agricultural Research
ICMR	Indian Council of Medical Research
ICRISAT	International Crops Research Institute for the Semi-Arid Tropics
ICT	Information and communications technology
IICT	Indian Institute of Chemical Technology
IP	Intellectual Property
IPO	Indian Patent Office
JNPC	Jawaharlal Nehru Pharma City
MNC	Multi National Companies
MSME	Ministry of Micro, Small and Medium Enterprises
NDA	New Drug Application
NIC	National Industrial Classification
NME	New Molecular Entity
OECD	Organization for Economic Co-operation and Development
PATSTAT	Patent Statistical Database
PCT	Patent Cooperation Treaty
PPP	Public Private Partnership
R&D	Research & Development
SEZ	Special Economic Zone
SOPs	Standard Operating Procedures
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UN	United Nations
UPMA	Utkal Pharma Manufacturers Association
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

Executive Summary

Arun Jaitley in his Budget for this year announced a 10 per cent tax rebate on earnings from patent filings. This is seen as a welcome move for the pharmaceutical industry where many players have emerged on the global scene with patents indicating that the industry is seeing a widening base in research, from generics to new drugs. The pharmaceutical industry in India has not just strengthened its hold in generics but is beginning to see years of research that for so long perceived as fruitless. The pharmaceutical budgets may not match the global numbers but the RDI of the companies is slowly reaching the global scale. A stringent patent regime and reduced paperwork are bound to improve the innovation intensity in this sector. Academic and industry tie-up is seen as a win-win partnership and both sides are looking at each other expectantly. The government's role in facilitating this would go a long way in creating better output as has been observed globally. Successful PPP ventures like Pharma City have paved the way for more such ventures. The industry's interest in innovation and support of the government can act as a catalyst to boost the capabilities of the Indian industry. Interactions with industry experts, CEOs, contract research organizations, multinational company representatives, and advisors have helped corroborate these views.

Chapter 1: Introduction

Healthcare is amongst the primal needs of any nation. An industry that works to fulfill this need is thus bound to be vibrant, knowledge intensive and research driven. As our livelihoods evolve and as the average lifespan is showing a sure sign of improvement, it is imperative that the quality of life also keeps pace. In order to achieve this and to keep the cost of healthcare low, it is very important to have a vibrant pharmaceutical industry which is coming up with completely new molecules in a difficult and costly exercise, innovating with other parameters is possible for a country like ours to indulge in.

Novel Drug development is a specialized science. It is a long drawn process that requires a lot of patience as it requires resources and capital. The uncertainties and risk involved discourage many champions.

Compared to the rest of the world that started work on research and development almost a century ago, India took its maiden steps less than 50 years ago. The post independence era has seen the requirement of the Indian market and pharmaceutical segment evolve with changing focus. The Government, in its role, has ensured the industry receives the initial stimulus as well as requisite environment to grow, evolve and spread its reach to fulfill the needs of a growing population. Many of the initial pioneers in India may not be in the fray, but there are many new entrants who, by way continuous and fruitful results will encourage many more to follow suit.

Chapter 2: The Journey so far

As we trace the history of pharmaceuticals, whether in India or in the global scale, there are some common factors that seem to bind the rise and growth of the pharmaceutical industry. While wars and natural disasters urged hasty discoveries of medicines to cure the ailing and the wounded, it was only the vision of champions far and few which propelled New Drug Discovery. While traditional medicines have held their sway in countries like China and India, these countries have not failed to adopt the advent of modern day medicine. This is probably due to the fact that the efficacy of traditional medicine has never been documented in as structured a way, such as clinical trials, as modern day medicine. The years of peace in the social scenario have seen the rise of laws, treaties and mostly patents to ensure the original discovery continued to be rewarded. Process Patents made way to Product Patents in India following the signing of the TRIPS agreement, thereby creating a new wave of players who dominated the markets with expensive products. However, imposing compulsory licensing ensured that the market could not be dictated by a single unaffordable product. While, most diseases that are making an emergence worldwide, are included in the drug discovery programmes of leading pharmaceutical companies, there are region-specific diseases that are found mostly in the third world countries that find few takers for research like tuberculosis and malaria etc. These diseases are also called Orphan diseases. The growth and emergence of the pharmaceutical sector in the backdrop of all this can be best understood by tracing the history of the pharmaceutical sector as a whole with additional focus on India, as documented below.

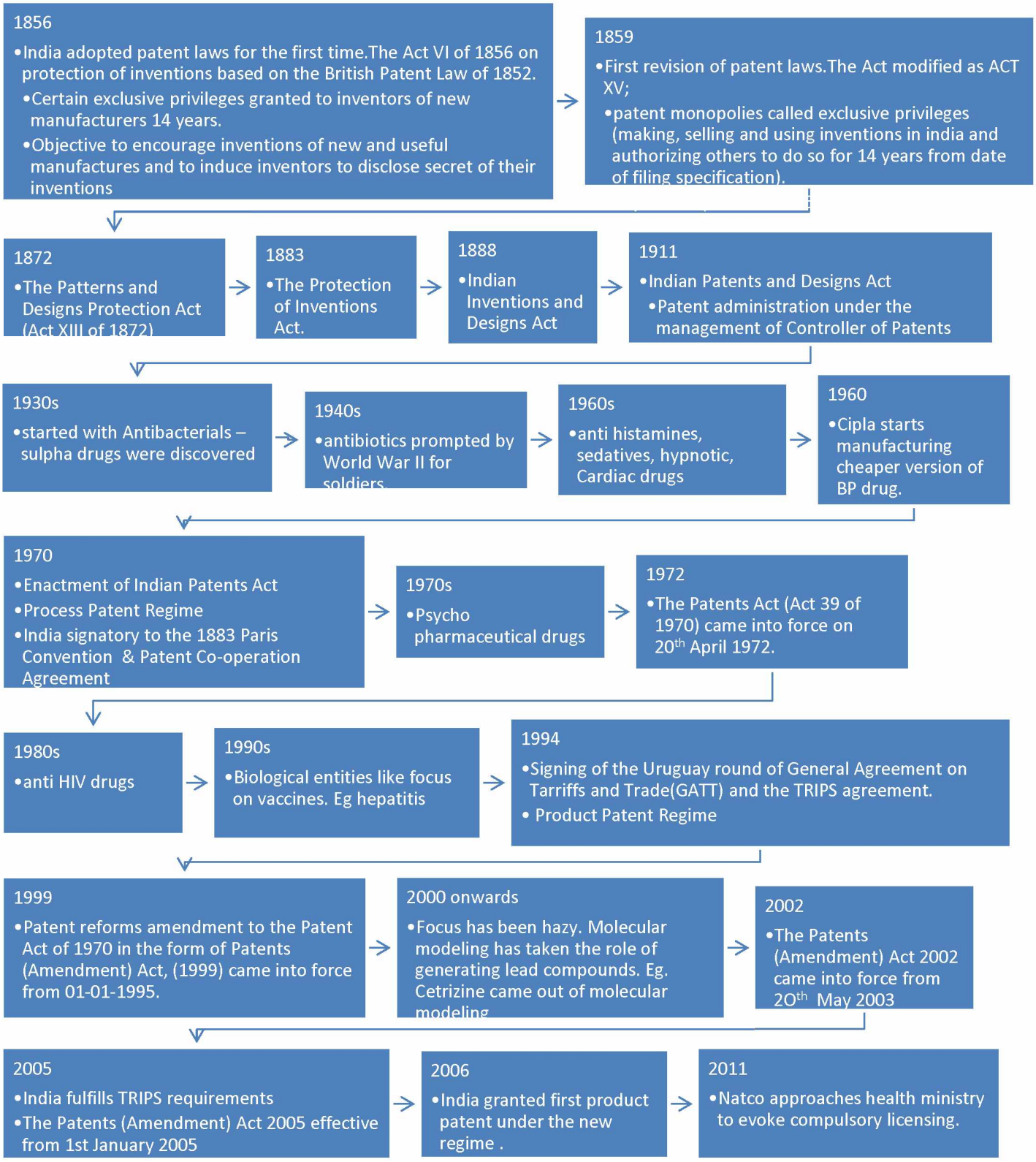


Figure 1: Indian Pharmaceutical industry growth

There are very few takers for orphan diseases like Tuberculosis, Filaria, etc. According to the Drugs for Neglected Diseases Initiative "Neglected tropical diseases continue to cause significant morbidity and mortality in the developing world. Yet, of the 1,556 new drugs approved between 1975 and 2004, **only 21 (1.3%) were specifically developed for tropical diseases and tuberculosis, even though these diseases account for 11.4% of the global disease burden**".

Disease	Number of cases in India(Percentage of Global Disease Burden)	Number of Cases in India and South Asia(Percentage of Global Disease Burden)
Ascariasis	140 million (17%)	237 million(29%)[a]
Trichuriasis	73 million (12%)	147 million(24%)[a]
Hookworm Infection	71 million (12%)	130 million(23%)[a]
Lymphatic filariasis	<6 million (5%) (based on 0.53% prevalence)	<60 million(50%)[b]
Trachoma	1 million (1%-2%)	2 million(2%-4%)[a]
Visceral Leishmaniasis	Not determined	200,000-300,000 cases (40%-60%)
Leprosy	87,190 registered cases (41%)	120,456 cases(57%)[b]
Rabies	20,000 cases/deaths (36%)	>=20,000 cases/deaths(57%) [b]
Japanese Encephalitis	1,500-4,000(incidence)	1,000-3,000(incidence,Nepal); 100-200(incidence, Sri Lanka)
Dengue	Not determined	Not Determined
Total		5.6-14.8 million

Table 1: Burden of Neglected Diseases

[a] **World Bank South Asia Region :Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka**

[b] **WHO South-East Asia Region: Bangladesh, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste**

(Source: The Neglected Tropical Diseases of India and South Asia: Review of Their Prevalence, Distribution, and Control or Elimination **Derek A. Lobo, Raman Velayudhan, Priya Chatterjee, Harajeshwar Kohli, Peter J. Hotez. • DOI: 10.1371/journal.pntd.0001222)**

As companies expand their global presence, there are companies that are working on research and development projects for finding cures to these neglected diseases that are more localized. As a part of their social responsibility, some companies do invest in research in these areas but the numbers are few. Leading

companies as a part of their social responsibility initiative have gone a step forward to setup centres to identify diseases as well as provide consultation and subsidized or free medicines.

2.1 The Industry at a glance

As a nascent nation that achieved Independence from British Rule in 1947, India had to ensure healthcare for a population that could not afford expensive medicines produced by the large pharmaceutical corporations. A look at some of the selected indicators of the pharmaceutical industry in 1952 shown below indicates the initial stages of the pharmaceutical industry.

				Employment	
Sector	**No. of units**	**Investments**	**Sales value (Rs Crores)**	**Technical**	**Non technical**
Public	11	1.48	1.16	181	1,492
Foreign	28	6.9	13.14	354	3,126
Large	54	9.26	13.38	1,076	15,896
Small	1,550	6	7	1,700	8,300
Total	1,643	23.64	34.68	3,311	28,814

Table 2: Indian Pharmaceutical sector in 1952 (Source: Narayana, 1984)

In a bid to provide affordable healthcare to all, the Government provided impetus to the generics industry. This helped spur the growth of companies with laboratories that worked on finding cost effective alternatives for manufacturing drugs thereby reducing the cost. The wave of affordable drugs supported by government policies helped support a developing economy as well as gradually managed to reach international shores. Evidence provided by the number of Abbreviated New Drug Application (ANDA)s filed by India suggests that India has established itself on the fore front of generic medicines with a steady growth rate in the last few years.

While medicines for common ailments came within the reach of the common man, there were not many companies that chose to foray into new drug discovery. In the nascent stage of the industry while the

scenario was not favourable, no change could be noted even as the industry continued to grow and mature. However, the industry is now more stable, mature and growing. To gain an accurate understanding of this growth would require quantification of measures that can reinforce the growth story. Conventional measures to measure R&D like R&D Expenditure of companies, Growth in R&D Expenditure, GERD and Patents were collected from various data sources including Prowess database, World Intellectual Property Organization, Indian Patent Office to understand the trends in research and development across organizations of various sizes in the pharmaceutical industry. The OECD Frascati Manual, Sixth Edition, defines GERD as the "Gross Domestic Expenditure on Research and Development is the total intramural expenditure on research and development performed on the national territory during a given period". The variations in the statistics pertaining to this would clearly define the quantitative investment to promote research in a particular sector, in this case the pharmaceutical sector. The data from the annual report of the Department of Pharmaceuticals shows a very encouraging scenario recording a slow yet sustained effort to increase the investment in R&D.

Year	Growth in R&D Expenditure(Rs. Crores)		R&D Expenditure as a % of Sales	
	Domestic Companies	Foreign Companies	Domestic Companies	Foreign Companies
Mar 1995	80.61	64.13	1.34	0.77
Mar 1996	142.50	83.37	1.71	0.91
Mar 1997	148.12	89.41	1.55	0.95
Mar 1998	154.15	90.65	1.43	0.88
Mar 1999	218.66	79.78	1.56	0.70
Mar 2000	256.80	90.17	1.56	0.66
Mar 2001	435.07	109.81	2.30	0.72
Mar 2002	597.91	110.04	2.64	0.65
Mar 2003	686.74	232.73	2.93	0.71
Mar 2004	1084.26	346.69	3.81	1.10
Mar 2005	1527.24	510.50	4.98	1.63
Mar 2006	1850.97	816.02	5.35	2.39
Mar 2007	2371.79	695.62	5.01	2.67
Mar 2008	2772.63	700.18	4.78	2.86
Mar 2009	3316.14	846.05	4.89	3.84
Mar 2010	3342.32	934.40	4.50	4.01

Table 3: Expenditure on R&D in Indian Pharmaceutical Sector (Source: Annual Report 2011-12, Department of Pharmaceuticals)

According to the 2016 Global R&D Funding Report of the R&D Magazine's Winter 2016 edition, "India's recent strong GDP growth and commitment to R&D currently rank it as the sixth largest R&D spender in the world". The report goes on to suggest that by 2018, India may supercede Germany and South Korea which are ranked 4th and 5th respectively.

Patents are a quantitative and rather direct indicator of invention (Griliches, 1984), so the number of patents filed at the Indian Patent Office and WIPO. Arun Jaitley in his Budget for this year announced a 10

per cent tax rebate on earnings from patent filings. According to the OECD Statistics database, there is also a growth in the number of PCT applications from India.

Year	Patent applications filed under the PCT based on country of inventor's residence
1999	70.2
2000	93.2
2001	133.2
2002	252.6
2003	309.4
2004	322.3
2005	346.4
2006	317.5
2007	332.0
2008	363.6
2009	392.5
2010	445.3
2011	402.2
2012	425.3331
2013	357.3413

Table 4: Year wise Patent applications filed under the PCT based on country of inventor's residence as India (Source: OECD Database data extracted on 21st June 2016)

Note: Fractional counts applied for patents with multiple inventors/applicants: When a patent was invented by several inventors from different countries, the respective contributions of each country is taken into account. This is done in order to eliminate multiple counting of such patents.

For example, a patent co-invented by 1French, 1 American and 2 German residents will be counted as:

- 1/4th of a patent for France,
- 1/4th for the USA
- and ½ patent for Germany.

However, the patents definition encompasses product as well as process patent. Thus, to arrive at a clearer picture of new drug discovery in India, New Drug Application (NDA)s filed at the United State Food and Drug Administration were used while ANDAs were considered as a proxy for the research into generics.

	Total NDAs filed at FDA	No. of NDAs by Indian companies at FDA
Jan-Mar 05	20	0
Apr-Jun 05	34	0
Jul-Sept 05	17	0
Oct-Dec 05	20	0
Jan-Mar 06	25	0
Apr-Jun 06	14	0
Jul-Sept 06	28	1
Oct-Dec 06	43	0
Jan-Mar 07	14	2
Apr-Jun 07	23	0
Jul-Sept 07	21	0
Oct-Dec 07	22	0
Jan-Mar 08	21	0
Apr-Jun 08	23	0

Jul-Sept 08	16	0
Oct-Dec 08	28	1
Jan-Mar 09	10	0
Apr-Jun 09	18	1
Jul-Sept 09	40	2
Oct-Dec 09	19	1
Jan-Mar 10	22	0
Apr-Jun 10	25	0
Jul-Sept 10	16	0
Oct-Dec 10	26	0
Jan-Mar 11	23	1
Apr-Jun 11	30	1
Jul-Sept 11	14	0
Oct-Dec 11	21	0
Jan-Mar 12	33	0
Apr-Jun 12	12	2
Jul-Sept 12	22	2
Oct-Dec 12	25	0
Jan-Mar 13	51	2
Apr-Jun 13	30	0
Jul-Sept 13	29	0
Oct-Dec 13	36	0
Jan-Mar 14	39	3

Apr-Jun 14	31	0
Jul-Sep 14	20	0
Oct-Dec 14	28	0
Jan-Mar 15	33	0
Apr-Jun 15	19	0
Jul-Sep 15	31	0
Oct-Dec 15	39	0
Jan-Mar 16	26	2

Table 5: Quarterly NDA Filing at US FDA (Source: US FDA http://www.fda.gov)

Years	ANDA filed by Indian Companies	Total ANDA filed
2001	10	135
2002	14	213
2003	17	174
2004	25	265
2005	28	243
2006	59	295
2007	113	405
2008	112	402
2009	118	395
2010	120	414
2011	136	433
2012	188	492

2013	155	393
2014	87	414
2015	179	556
2016(upto June)	91	299

Table 6: ANDA Filings at US FDA (Source: US FDA, Original Abbreviated New Drug Approvals (ANDAs) by Month, Generic Drug Approvals. Does not include tentative approvals)

2.2 Export & Import Scenario

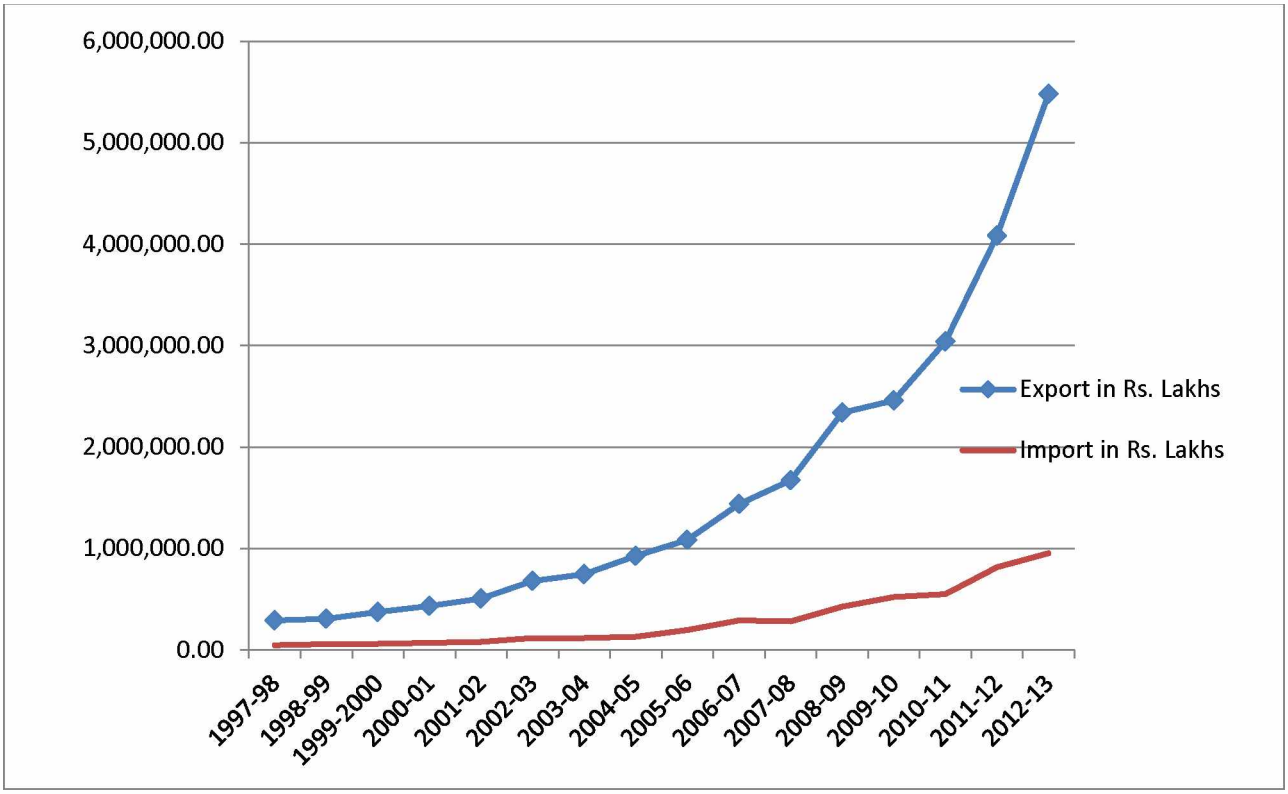


Figure 2: Exports & Imports of Pharmaceutical Sector(Source: Export Import Data, Ministry of Commerce, Government of India)

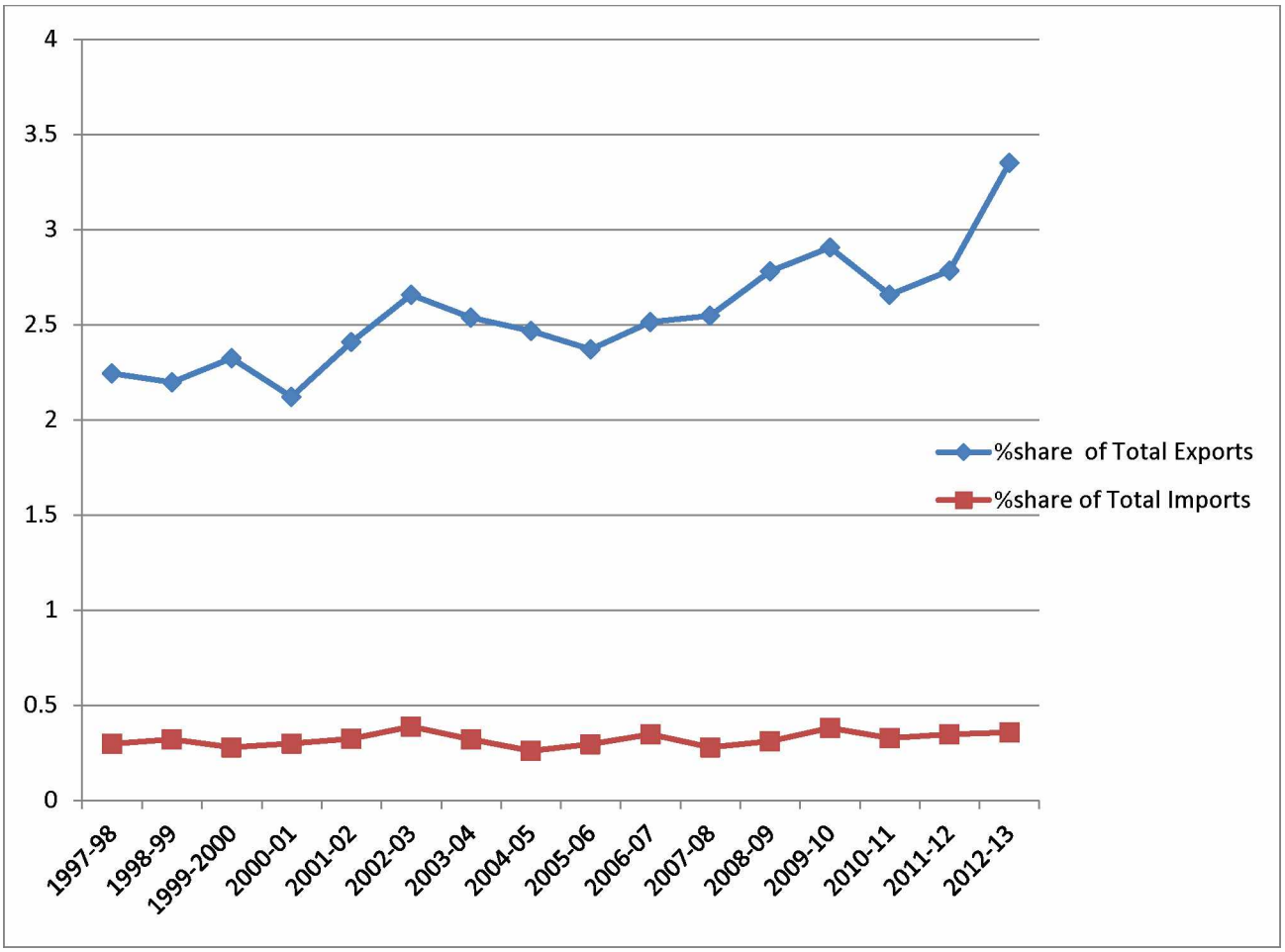


Figure 3: Pharmaceutical Exports & Imports as a %Share of total exports (Source: Export Import Data, Ministry of Commerce, Government of India)

2.3 Important measures

The Frascati Manual and relevant literature advocate the use of R&D Expenditure and R&D Intensity as a measure of interest to innovate in a scenario. Given this, a dataset of companies with NIC Code 21002, 21003, 21009 pertaining to Manufacture of allopathic pharmaceutical preparations, Manufacture of `ayurvedic' or `unani' pharmaceutical preparation, Manufacture of other pharmaceutical and botanical products respectively was drawn from the Prowess database. While the complete dataset of all companies irrespective of their NIC classification comprises of more than 28000 companies, the size of the dataset of companies relevant to the pharmaceutical sector mentioned earlier and with sufficient data available for analysis was 615.Using this dataset, the following measures were calculated.

Years	Sales in Rs. Crores	R&D Expenditure in Rs. Crores	Royalty in Rs. Crores	Technical know-how in Rs. Crores	Royalty, technical know-how etc in Rs. Crores	R&D Intensity	Royalty Intensity	Technical know-how Intensity	External-Internal R&D Ratio	Pure technical acquisition ratio
1990-91	4301.17	6.13	0	0.18	0.61	0.143	0.000	0.004	0.100	0.027
1991-92	5871.81	14.53	0	0.01	1.25	0.247	0.000	0.000	0.086	0.001
1992-93	7169.26	62.61	0	0	1.11	0.873	0.000	0.000	0.018	0.000
1993-94	8881.56	113.03	0	0	1.33	1.273	0.000	0.000	0.012	0.000
1994-95	10959.21	161.82	0.76	0.25	12.08	1.477	0.007	0.002	0.075	0.001
1995-96	13313.51	202.14	9.41	0	12.98	1.518	0.071	0.000	0.064	0.000

1996-97	14644.42	227.93	5.66	0	19.76	1.556	0.039	0.000	0.087	0.000
1997-98	16281.3	218.09	3.06	0.5	27.01	1.340	0.019	0.003	0.124	0.002
1998-99	19677.2	324.87	4.64	0	27.31	1.651	0.024	0.000	0.084	0.000
1999-00	22445.01	347.76	16.86	3.81	33.95	1.549	0.075	0.017	0.098	0.010
2000-01	23837.23	542.32	21.12	1.18	30.36	2.275	0.089	0.005	0.056	0.002
2001-02	26712.89	699.91	12.48	3.41	19.63	2.620	0.047	0.013	0.028	0.005
2002-03	31893.3	904.74	15.27	0.72	19.87	2.837	0.048	0.002	0.022	0.001
2003-04	37865.94	1459.18	13.69	1.65	18.48	3.854	0.036	0.004	0.013	0.001
2004-05	40481.9	2041.14	16.39	1.66	22.59	5.042	0.040	0.004	0.011	0.001
2005-06	48009.72	2711.07	27.29	0.22	33.51	5.647	0.057	0.000	0.012	0.000
2006-07	60237.28	3090.55	28.61	0.47	38.3	5.131	0.047	0.001	0.012	0.000
2007-08	70456.9	3475.69	34.74	0.2	41.62	4.933	0.049	0.000	0.012	0.000
2008-09	84068.36	4245.16	54.12	0.29	62.66	5.050	0.064	0.000	0.015	0.000
2009-10	94245.92	4396.35	54.37	6.31	67.07	4.665	0.058	0.007	0.015	0.001
2010-11	100666.3	4920.94	38.23	0.03	42.79	4.888	0.038	0.000	0.009	0.000
2011-12	104152.4	5444.97	25.88	0.21	29.64	5.228	0.025	0.000	0.005	0.000
2012-13	79252.91	4416.64	26.38	1.91	32.53	5.573	0.033	0.002	0.007	0.000

Table 7: Important Measures (Source: Prowess CMIE database)

- R&D Intensity = (R&D Expenditure/Sales) X 100

  This ratio illustrates the willingness of the industry to spend on R&D in comparison to its sales to gain advantage over competition. While a steady growth in this ratio indicates increasing interest in research and development, it also exhibits a maturing industry which is looking to improve its footprint not just in terms of sales but also in terms of better medicines and newer drugs. New drug discovery is a long process and continued and increasing R&D figures indicate sustained interest to establish a presence in this area which is slowly bearing fruit as the numbers of NDAs are signaling. For companies that rely

largely on generics, this ratio is still important because improved processes and lower cost of production are helping lower the cost of the drug thereby making it affordable for the masses. This translates into newer markets in time to cash in on the impending patent cliffs.

- Royalty Intensity = Royalty expenditure / Sales.

  This measure indicates the money that industry spends to acquire resources that it cannot produce in-house. While this is a good option for short term benefits, an increasing trend reflects that companies are willing to spend bigger sums of money on acquiring technology even in the face of improved turnover, rather than endeavour to reduce this burden by investing on in-house R&D. The said resource could be in the form of technology, intellectual property or tangible resource.

- Technical Know-How Intensity = Technical Know-How expenditure / Sales

  This ratio is an indicator of the money spent by companies on acquiring technical know-how as a percentage of their sales. While sales have seen an upward trend as shown in Figure 4, the table Important Measures shows a growing phase of technical know-how expenditure till 2001-02 and then a subsequent fall with the last few years showing a steady number. However, the ratio indicates that the contribution of this to the total expenditure of the company has slowly reduced implying that companies are improving sales are not leading to greater technical acquisitions. While, this does not necessarily mean that greater sums of money are being invested for in-house R&D on new technology, it indicates a stagnating phase of relying on externally acquired technology.

- External –Internal R&D Ratio = (Royalty+Technical Know-How Fees)/R&D Expenditure

  This ratio implicitly signifies the ratio of reliance of the industry on acquisition of intellectual property from external resources vis-à-vis spending on creating its own intellectual resources. The external sources cited earlier could also be foreign entities .This ratio displays a healthy falling trend implying companies are relying lesser on external sources and rather are investing on creating in-house resources.

- Pure Technical Acquisition Ratio = (Technical Know-How Fees)/R&D Expenditure +Royalty

  While buying a technology rather than making it in-house reflects a reliance on external sources for product creation, another perspective suggests that this ratio implies that companies are looking to reuse existing models and build better products from them, rather than begin from scratch.

2.4 Sales of the Drugs Sector

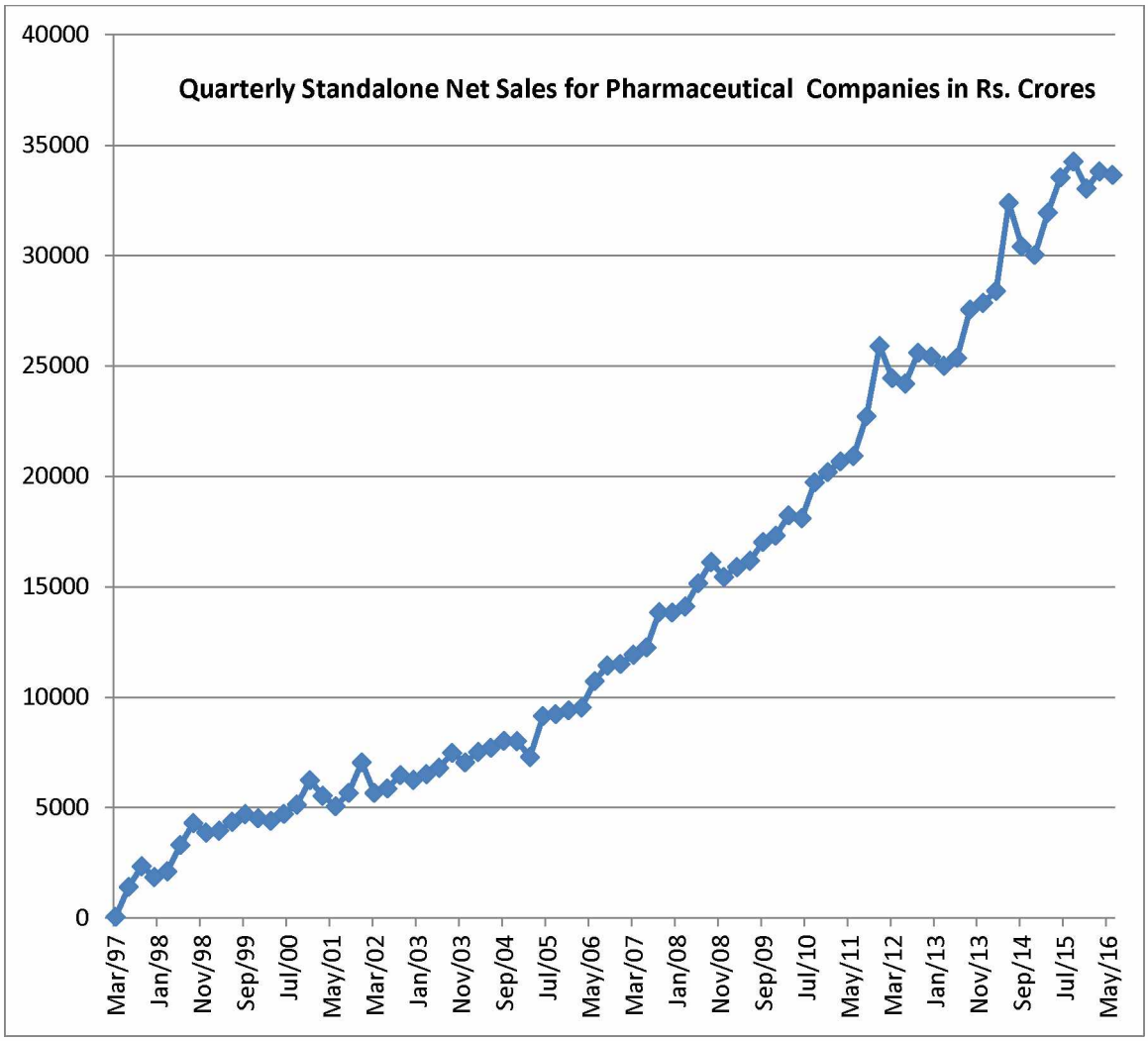


Figure 4: Standalone Net Sales of Pharmaceutical Companies in Rs. Crores (Source: Prowess CMIE)

Sales of the Pharmaceutical sector have seen a steady growth in the last decade or so. The main reason for this includes the increasing awareness about health and diseases. This awareness has spurred an increase in

the average longevity as well encouraged people to live a healthier life, albeit with the support of drugs to deal with a variety of chronic as well as lifestyle related ailments. The generics industry that has seen a phenomenal growth in India in the last many years has managed to bring medicines within the reach of the common man.

2.5 NDA, NME, BLAs, ANDA, Patent Data of top R&D spenders

Company	2012 Rx Sales(Rs. Crore)	2012 R&D spend(Rs. Crore)
Lupin Ltd.	7025.51	798.84
Dr. Reddy's Laboratories Ltd.	8244.5	690
Ranbaxy Laboratories Ltd.	6001.13	493.7
Cipla Ltd.	8180.52	425.14
Piramal Enterprises Ltd.	1284.39	257.67
Aurobindo Pharma Ltd.	5417.53	233.34
Wockhardt Ltd.	2466.99	219.47
Jubilant Life Sciences Ltd.	3135.77	143.75
Torrent Pharmaceuticals Ltd.	2718.65	132.73
Strides Arcolab Ltd.	709.03	122.38
Ipca Laboratories Ltd.	2782.5	111.71

Table 8: Top 10 Domestic R&D Spenders in 2012(Source: CMIE Prowess)

An updated view of the industry based on the year ended March 2015, compiled by BS Research Bureau shows a better trend. Interestingly, these 5 companies also feature in the list of the top 10 R&D spenders in the country according to the findings of Capitaline published in Business Standard in May 2016.

Company	R&D Spending(Rs. Crores)	Net Sales(Rs. Crores)	% of Turnover
Lupin	1118.60	12,770.00	8.9
Sun Pharma	1,955.00	27,981.00	6.99
Dr. Reddy's Labs	960.50	15,023.30	6.39
Aurobindo Pharma	346.55	12,121.00	2.86
Cipla	111.98	11,345.44	0.99

Table 9: Top R&D spenders in Pharma as of March 2015 (Source: http://www.business-standard.com/article/companies/lupin-tata-motors-lead-in-r-d-spending-116050600031_1.html)

Internationally, the spending trend has shown a slowdown in the pharmaceutical sector. Between 2013 and in 2015, the spending and sales have seen no growth or improvement. The top players in the pharmaceutical R&D have remained almost the same with a slight change in rankings of the companies.

Company	2012 Rx Sales(USD billions)	2012 R&D spend(USD million)
Pfizer	47.404	7,046
Novartis	45.418	8831
Merck	41.143	7,911
Sanofi	38.37	6117.8
Roche	37.542	8,032
GlaxoSmithKline	33.107	5255.7
AstraZeneca	27.064	4,452
Johnson & Johnson	23.491	5362
Abbott	23.119	2,900
Eli Lilly	18.509	5074.5

Table 10: Top 10 International Companies in 2012(Source: Pharma Exec 50)

Company	2015 Rx Sales(USD millions)	2015 R&D spend(USD million)
Pfizer	43,112	7,678.0
Novartis	42,467	8465.3
Roche	38,733	8,452.1

Merck & Co	35,244	6,613.0
Sanofi	34,896	5,638.2
Gilead Sciences	32,151	3,018.0
Johnson & Johnson	29,864	6,821.0
GlaxoSmithKline	27,051	4,731.1
AstraZeneca	23,264	5,603.0
AbbVie	22,724	3,617.0

Table 11: Top 10 International Companies in 2015(Source: Pharma Exec 50)

An interesting observation from the global top 50 based on the findings of Pharmaceutical Executive showed Ranbaxy making an appearance for the first time in 2013 and continuing on that rank in 2014. However, Sun Pharma that featured on the list in 2014 at rank 48 has advanced to 32 in the year 2015. Forbes list of World's Most Innovative Companies features Sun Pharma at rank 65 in 2014 and rank 71 in 2015. These facts highlight the fact that Indian companies are slowly emerging from the shadows of generics and making a noticeable foray into New Drug Discovery. This is further re-iterated by a profile of the NDAs filed by Indian companies at the US FDA office. The list features almost the same set of companies as those that invest the most in research and development in the pharmaceutical sector as highlighted in Table 8: Top 10 Domestic R&D Spenders in 2012 and Table 9: Top R&D spenders in Pharma as of March 2015.

The Table 12 below shows the NDA filings of companies whose headquarters/parent company/partner is located in India.

Company Name	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Lupin Ltd.				1									1			
Dr. Reddy's	1	1	1													2

Ranbaxy			1									2				
Alembic Pharmaceuticals													1			
Aurobindo						1		1	2							
Glaxosmithkline Cons		1					1		2					1		
Jubilant			2													
Matrix Labs[1]											1					
Piramal Imaging														1		
Strides Acrolab							1									
Sun Pharma									1		1			2		1

Table 12: NDA Statistics (Source: US FDA) (The numbers have been calculated using the headquarters or/of the parent company)

Another common metric used to measure the performance of a sector is the number of employees employed by the sector. The data collected from Bulk Drug Manufacturers Association shows a steady growth in the number of employees in the sector, indicating the increasing foothold of the pharmaceutical industry.

Year	No of Employees
Mar 1995	1,81,497
Mar 1996	2,04,609
Mar 1997	2,11,614
Mar 1998	1,89,295
Mar 1999	2,13,999
Mar 2000	2,43,410
Mar 2001	2,33,704
Mar 2002	2,26,416

[1] Matrix was acquired by Mylan in 2006 and renamed to Mylan in 2011

Mar 2003	2,23,556
Mar 2004	2,40,791
Mar 2005	2,65,396
Mar 2006	2,90,021
Mar 2007	3,36,211
Mar 2008	3,53,692

Table 13: Employees in Pharmaceutical Sector (Source: BDMA Hyderabad Statistics)

ANDA Statistics

India's strong presence in generics has time and again been reiterated by various studies. A profile of the ANDA filings by Indian companies at the US FDA re-enforces the fact while giving an insight into the continued interest of companies that invest in R&D in generics to continue with the same. The following table shows the ANDA filings of companies whose headquarters/parent company/partner from India.

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Agila Specialities	0	0	0	0	0	0	0	2	0	0	1	0	0	0	0	0
Ajanta Pharma	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Ajanta Pharma Ltd	0	0	0	0	0	0	0	0	0	0	1	0	0	0	5	3
Alembic Ltd	0	0	0	0	0	0	0	0	2	4	0	2	1	0	0	0
Alembic Pharms Ltd	0	0	0	0	0	0	0	0	4	3	3	3	3	5	10	1

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Alkem	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
Alkem Labs Ltd.	0	0	0	0	0	0	0	0	0	1	1	1	3	1	3	2
Aurobindo	0	0	0	2	5	4	0	0	0	0	1	4	1	0	0	0
Aurobindo Pharm	0	0	0	0	0	0	0	1	3	2	0	0	0	0	0	0
Aurobindo Pharma	0	0	0	0	0	3	25	12	15	12	0	0	0	0	0	0
Aurobindo Pharma Ltd.	0	0	0	0	2	3	2	0	0	0	13	25	19	6	32	28
Aurobindo Pharma USA	0	0	0	0	0	0	0	0	0	0	2	0	0	0	1	0
Biocon Ltd	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Cipla	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	0
Cipla Ltd	0	0	0	1	0	3	9	6	2	1	3	3	3	1	1	0
Cadila	0	0	0	0	0	0	0	0	0	0	0	0	1	4	0	1
Claris	0	0	0	0	0	0	0	0	0	0	0	0	5	1	0	0
Claris Life Sciences	0	0	0	0	0	0	0	3	0	3	0	1	0	0	0	0
Dr. Reddys LA	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dr. Reddys Labs Inc	1	2	1	1	1	5	2	4	1	1	2	1	0	1	0	0

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Dr. Reddys Lab Intl	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Dr. Reddys Labs Ltd	3	1	0	1	2	3	7	8	10	9	12	15	16	8	2	1
Dr. Reddys Labs SA	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Emcure Pharms	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Emcure Pharms India	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Emcure Pharms Ltd	0	0	0	0	0	0	0	0	0	0	0	6	11	7	0	0
Emcure Pharms USA	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0
Emcure USA	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Famy Care Ltd	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
FDC	0	0	0	0	0	0	0	2	1	0	0	0	0	0	0	1
Gland Pharma	0	0	0	2	1	1	1	0	2	0	0	4	0	1	0	4
Glenmark Generics	0	0	0	0	0	4	9	5	7	14	11	10	8	4	3	0
Glenmark	0	0	0	0	0	0	0	0	1	2	1	0	0	0	3	1

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Pharms																
Glenmark Pharms Ltd	0	0	0	0	0	0	0	1	0	0	0	0	0	4	0	9
Granules India	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
Hetero Labs Ltd III	0	0	0	0	0	0	0	4	3	2	1	4	3	1	2	0
Hetero Labs Ltd V	0	0	0	0	0	0	0	0	0	0	0	0	1	7	8	3
Inventia	0	0	0	0	0	0	0	0	0	0	0	1	0	0	2	0
Ipca Labs	0	0	0	0	0	2	2	3	3	0	1	1	3	3	0	0
Jai Pharma	0	0	0	0	0	0	0	0	0	0	0	0	7	4	14	5
Jubilant Cadista	0	0	0	1	2	1	1	1	0	1	4	3	3	1	12	2
Jubilant Generics	0	0	0	0	0	0	0	0	0	0	0	0	3	2	12	0
Jubilant Hollistrstr	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Jubilant Life	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	1
Jubilant Organosys	0	0	0	0	0	0	0	0	0	0	2	3	0	0	0	0
Lupin	0	0	3	0	5	5	6	3	3	0	2	0	1	0	1	0
Lupin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Atlantis																
Lupin Ltd	0	0	0	0	0	0	0	0	0	10	11	9	18	12	29	4
Lupin Pharms	0	0	0	2	0	1	1	1	0	1	4	2	1	0	0	0
Macleods Pharms Ltd	0	0	0	0	0	0	0	0	0	0	0	12	2	7	12	5
Marksans Pharma	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	1
Matrix[1]	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0
Micro	0	0	0	0	0	0	0	0	0	1	1	4	2	0	0	0
MSN Labs	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Natco Pharma Ltd	0	0	0	0	0	0	1	0	0	2	3	2	1	1	1	2
Natco Pharma	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Onco Therapies	0	0	0	0	0	0	0	0	0	0	10	16	0	0	0	0
Orchid Healthcare	0	0	0	0	3	3	4	3	4	2	1	5	0	2	4	1
Panacea Biotec	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Piramal Critical	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Ranbaxy	3	6	8	9	3	2	7	2	6	3	1	0	0	0	0	0
Ranbaxy Labs Ltd	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0
Strides Arcolab	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Strides Arcolab Ltd	0	0	0	0	0	0	0	0	1	3	2	1	0	1	1	0
Strides Pharma	0	0	0	0	0	0	0	0	0	0	0	0	1	5	4	0
Sun Pharma Inds	0	0	0	0	0	0	6	7	2	1	3	5	1	0	1	2
Sun Pharma Inds(IN)	0	0	0	0	0	4	2	0	0	0	0	0	0	0	0	0
Sun Pharma Inds Inc	0	0	0	0	1	0	1	0	2	2	0	0	6	5	0	0
Sun Pharm Inds Ltd	0	0	0	0	0	3	0	0	2	2	3	0	8	4	3	2
Sun Pharma Global	0	0	0	0	0	0	1	7	7	5	9	7	11	6	5	1
Suven	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Torrent Pharms	1	0	0	0	1	0	3	2	3	4	7	0	0	0	0	0
Torrent	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Pharms LLC																
Torrent Pharms Ltd	0	0	0	0	0	0	0	0	0	0	1	8	6	6	8	0
Unichem	0	0	0	0	0	1	0	2	2	2	0	0	0	0	0	0
Unichem Labs Ltd	0	0	0	0	0	0	0	0	1	0	2	1	1	1	4	3
Unichem Pharms(USA)	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Unique Pharm Labs	0	0	0	1	1	1	1	0	0	1	0	0	1	0	1	0
Wockhardt	1	5	5	4	2	6	12	14	12	5	4	1	0	0	0	0
Wockhardt Bio AG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Wockhardt EU Operatn	0	0	0	0	0	0	00	0	0	0	0	0	1	0	0	0
Wockhardt Ltd	0	0	0	0	0	0	0	0	0	0	0	9	1	0	1	0
Wockhardt USA	0	0	0	0	0	0	0	4	0	1	2	1	0	0	0	0
Zenotech Labs	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Zydus Hltcare	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0

Company	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016(upto
Zydus Pharms USA	0	0	0	0	8	4	6	4	2	0	0	0	0	0	0	0
Zydus Pharms USA Inc	0	0	0	0	0	0	2	6	11	6	7	8	3	10	2	6

Table 14: ANDA Statistics (Source: US FDA) (The numbers have been calculated using the headquarters or/of the parent company)

2.8 WIPO Facts

Applicant	Publication	*Rank*
COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH	117	*194*
RANBAXY LABORATORIES LIMITED	37	*624*
RELIANCE INDUSTRIES LIMITED	34	*679*
WOCKHARDT LIMITED	31	*753*
HETERO RESEARCH FOUNDATION	27	*868*
INDIAN INSTITUTE OF TECHNOLOGY	25	*931*
TATA CONSULTANCY SERVICES LTD.	24	*964*
LUPIN LIMITED	21	*1087*
PIRAMAL ENTERPRISES LIMITED	20	*1145*
CADILA HEALTHCARE LIMITED	18	*1241*

Table 15: PCT Top Applicants (Publication Year 2014)(Source: WIPO Statistics Database Last Updated: 12/2015)

These figures from World (WIPO) show that pharmaceutical companies dominate the list of companies that have filed the maximum number of applications for patents. It is no wonder then, that, pharmaceuticals as a sector, contribute to around 19.91% of the patent applications in a single field of technology between 2000 to 2014.

• The statistics are based on data collected from IP offices or extracted from the PATSTAT database (for statistics by field of technology). Data might be missing for some years and offices or may be incomplete for

some origins. The data relating to population and gross domestic product (GDP) are from the UN Statistics Division and the World Bank.

• A resident filing refers to an application filed in the country by its own resident; whereas a non-resident filing refers to the one filed by a foreign applicant. An abroad filing refers to an application filed by this country's resident at a foreign office.

• Where an office provides total filings without breaking them down into resident and non-resident filings, WIPO divides the total count using the historical share of resident filings at that office.

• IP filings and Economy lists patent, trademark and industrial design filings worldwide by applicants from this country (resident + abroad).

Chapter 3: Patent Facts

The patent cliff is nearing. The patent cliff is likely to bring a loss to the tune of almost 7.1 billion$ to major pharmaceutical companies.

IPO patent data trend and % change that shows India is doing better

WIPO patent data trend and % change that shows India is doing better.

Years	Patents granted at Indian office for drugs	Total patents granted
2006-07	798	7539
2007-08	905	15261
2008-09	1207	16061
2009-10	530	6168
2010-11	596	7509
2011-12	282	4381
2012-13	344	4126
2013-14	256	4226
2014-15	389	5978

Table 16: Patents at IPO(Source: Indian Patent Office, Annual Reports)

4: Import and Export Scenario

Top 10 exporters and importers of pharmaceuticals, 2015

(Billion dollars and percentage)

	Value	Share in world exports/imports		Annual percentage change			
	2015	2010	2015	2010-15	2013	2014	2015
Exporters							
European Union (28)	340	66.1	63.9	2	3	5	-5
extra-EU (28) exports	159	26.7	29.8	5	4	5	1
Switzerland	65	10.6	12.2	6	6	8	-3
United States	52	9.6	9.8	3	-1	10	8
India	14	1.5	2.6	14	13	6	6
China a	14	2.3	2.5	5	3	9	1
Canada	8	1.2	1.4	6	7	29	7
Singapore	8	1.3	1.4	5	-14	4	-7
Israel	7	1.4	1.2	0	-8	2	6
Japan	4	0.9	0.7	-2	-8	-9	15
Panama b	4	0.6	0.7	6	-3	-16	-15
Above 10	**514**	**95.7**	**96.6**	-	-	-	-
Importers							
European Union (28)	260	52.1	47.5	1	2	6	-8
extra-EU (28) imports	80	13.5	14.6	2	2	9	-4
United States	90	13.9	16.4	3	-2	14	17

Japan	24			3.7	4.4			3	-10	-4	15
Switzerland	23			4.0	4.2			2	10	6	-9
China a	20			1.7	3.7			9	17	18	7
Canada c	13			2.6	2.3			0	-1	4	-6
Russian Federation c	9			2.4	1.7			-2	10	-12	-31
Australia c	8			1.8	1.4			-1	-9	-9	-13
Brazil c	7			1.4	1.3			0	8	0	-12
Mexico a, c	5			1.0	1.0			1	1	-1	-3
Above 10	**460**			**84.6**	**83.8**			**-**	**-**	**-**	**-**
a Includes significant shipments through processing zones											
b Includes Secretariat estimates.											
c Imports are valued f.o.b.											

Table 17: Top 10 exporters and importers of pharmaceuticals, 2015 (Source: World Trade Organization Statistics)

Chapter 5: Analysis of Pharmaceutical clusters

Cluster Development Programme for Pharma Sector (CDP-PS) was launched by the Minister of Chemicals and Fertilizers, Shri Ananth Kumar on June 17, 2015 to enable the pharmaceutical industry in India to become more productive, capable and competitive. This programme is designed to enable the development of clusters in a PPP mode in a structured and scientific manner. Existing clusters are also expected to benefit from this programme by means of upgradation and 6 new Greenfield clusters are expected to emerge. This scheme is proposed as a Central Sector Scheme and Rs.125 crores has been allocated for the same under the 12th Plan. As of January, 2016, the Government is keen on proceeding with implementation of the recommendations of the Katoch Committee Report on Active Pharmaceutical Ingredients (API)s.

The pharmaceutical clusters in India can be classified as manufacturing clusters and R&D clusters. A brief description of both types of clusters is as follows.

Biotechnology Cluster	Karnataka-Bangalore
Bulk Drugs	Gujarat - Ahmedabad, Ankleshwar, Vapi, Vadodara Maharashtra-Mumbai, Tarapur, Aurangabad, Pune Telangana-Hyderabad, Medak Tamil Nadu- Chennai Pondicherry Karnataka-Mysore, Bengaluru Andhra Pradesh-Vizag

	Goa
Formulations	Goa Maharashtra - Mumbai, Pune Telangana-Hyderabad Himachal Pradesh-Baddi Uttaranchal-Pantnagar

Bangalore, in Karnataka is the Biotech capital for India. India houses 380 biotech companies of which a majority of 198 are in Karnataka and 191 in Bangalore alone. Bangalore and Karnataka jointly contribute 27% to the revenue of the sector. The other key clusters include Mumbai and Ahmedabad in the West (Maharashtra and Gujarat respectively), Hyderabad (Telangana) in the South and the area in and around New Delhi in the North. The Western belt houses companies that are large pharmaceuticals with a prominent manufacturing and R&D base, who have active interest in pursuing the manufacture of biogenerics.

Hyderabad has several vaccine manufacturers and other large biotech companies involved in research. The regions in and around New Delhi house several key research centres and univerisites that are involved in research.

Karnataka –Bangalore

Biotechnology, post the ICT success, has emerged as a recent rapidly expanding sector in Bangalore. The city accounts for over 50% of the 380 biotech companies in India. The city has revenue of over $550 for 2008-2009 which is over 20% of the total biotech revenue for the country. Bangalore is the country's largest cluster, the city boasts of 198 biotech firms. Biocon, the nation's leading biotech company is headquartered in Bangalore. Some of the key life science companies to look out for in Bangalore include: Advinus Therapeutics, Astra Zeneca, Aurigene Discovery services, Biocon India, Jubilant Biosys, Metahelix Life Sciences, Strand Life Sciences, Strides Arcolab and Xcyton Diagnostics Government of Karnataka is investing

Rs. 5,500 crore in Bangalore Helix Biotech park which is spread over 106 acres at the Electronics City, off Hosur Road in Bangalore. Bangalore can boast of good Universities like the Indian Institute of Science, JNCASR, NCBS, University of Agricultural Sciences. ABLE the Trade association for Biotech Industry is headquartered at Bangalore. Bangalore has opportunities in Contract Research Space and lot of potential in the Stem Cell area.

Telangana - Hyderabad

Biotechnology is an important industry in Telangana. There is a high concentration of biotech companies producing recombinant therapeutics for human consumption. It also has the second largest recombinant DNA therapeutic production facility in the world, which is also being used by multi-national companies to produce their own recombinant products. Hyderabad is called “Bulk drug Capital of India”. Telangana has a dominant position in the bulk drugs and pharmaceutical sector with Hyderabad accounting for nearly one third of India's total bulk drug production. Hyderabad has witnessed infrastructural development in the biotech domain wherein the Knowledge Park, the Biotech Park, Genome Valley and other projects have come up giving the city an advantage over others. Hyderabad is also a house for research and development Centres like Centre for Cellular and Molecular Biology (CCMB), Indian Institute of Chemical Technology (IICT), International Crop Research Institute for Semi-arid Tropics (ICRISAT),Central Food Technology Research Institute (CFTRI) and Institute for Life sciences centre is based out of Hyderabad having 32 laboratories and 12 research centres. (ILSC) The Government of Telangana offers opportunities in Therapeutics, Diagnostics, Industrial Biotechnology, Inputs to the industry (hardware suppliers - Instrumentation and Chemicals), and Agricultural Biotechnology in the biotech space.

Andhra Pradesh-Vizag

The Andhra Pradesh government is planning to setup two pharma clusters in Andhra Pradesh, one in Vizag and the other in Nellore. The existing Jawaharlal Nehru Pharma City(JNPC) is spread over 2200 acres at

Parawada in Vizag housing over 63 corporate industries including multinationals like Eisai(Japan), Pharma Zell(Germany), Hospira(USA) and SNF(France). The mix of industries includes bulk drugs, active pharmaceutical ingredients and intermediates. It was launched as a Special Purpose Vehicle by Ramky Group and Andhra Pradesh Industrial Infrastructure Corporation (APIIC).

Tamil Nadu - Chennai

According to the Tamil Nadu Global Investors Meet magazine, the state is the fifth largest pharmaceutical producing state in the country, accounting for nearly 10% of the national production of pharmaceutical products in the country. The manufacturing units in the state are involved in production of capsules, tablets, dry syrups, external preparations, cycotoxic drugs, APIs, vaccines and bio-pharmaceutical products. Tamil Nadu was the first state in India to introduce a Biotech Policy in the year 2000. The key areas in bio-technology that are slated to get special thrust include healthcare, industrial enzymes, contract-research, marine and environmental biotechnology and agricultural biotechnology. TICEL Bio Park, Chennai, established in Nov 2004, is a unit of Tamilnadu Industrial Development Corporation (TIDCO) is promoted by TIDEL Park Ltd, Indian Bank, Karur Vysya Bank and Indian Overseas Bank. It currently provides space and training and a bio-resource centre is proposed here. Technical parameters for this park were provided by the Cornell University, USA and the Government of Tamil Nadu conferred the status of Research and Development Organization on TICEL. The park is spread over 5 acres of land in Chennai at a capital outlay of Rs.625 million (US$ 12.5 million) and is completely occupied with national and international clients. Another bio-tech park at Coimbatore, a marine bio-tech park near Mahabalipuram, , Integrated Vaccine Complex at Chengalpattuand, Medipark slated to be India's first infrastructure initiative for promotion of medical equipment and a bio-pharmaceutical SEZ are expected to start soon. The proposed SEZ is expected to be of 365 hectares at Denkannikotta and Hosur Taluk, Krishnagiri District with USFDA compliant Bio-Pharmaceuticals facility, Clinical Research Organization (CRO), Joint Commission on

Accreditation of Healthcare Organizations (JCAHO) certified Hospital, Poison Control Centre, Centre for Regenerative Medicine among other facilities.

Maharashtra

The state accounts for 40 per cent of the country' pharmaceuticals output. It has strong research capabilities and accounts for over 30 per cent of country's patents (Source: Public Private Partnerships in India, Ministry of Finance, Government of India). It has a presence of reputed companies focusing on the biotech sector including Wockhardt, Nicholas Piramal, Cipla and Lupin, among others and state is setting up biotech parks at Hinjewadi, near Pune. Major opportunities have emerged in the pharmaceutical sector, primarily in the areas of contract research, contract manufacturing and clinical trials. The state boasts of low costs, strong manufacturing base, well developed laboratory and R&D infrastructure and a strong resource pool. The backward linkages with the well-developed chemicals and petrochemicals sector are an added advantage. Maharashtra Industrial Development Corporation(MIDC) is developing a pharma cluster at the industrial estate at Dindori, near Nashik

Gujarat

Gujarat accounts for 28 per cent of national pharmaceutical production (2006-2007). First state to manufacture APIs and finished dosage forms. It is a home to 902 allopathic manufacturing units and 2,122 contract manufacturing units. Gujarat accounts for exports worth US$ 1.4 billion (2006-2007). It has number of clinical research organizations in India and over 100 companies with WHO-compliant manufacturing units, academic and research institutions providing over 4,600 technically-skilled manpower per annum. India's largest biotech park of 700 acres being developed at Savli, Vadodara. Key players are Zydus Cadila, Torrent Pharma, Sun Pharma, Intas Pharma, Alembic, Dishman Pharma. Mumbai is home to the two major pharmaceutical associations including Indian Drug Manufacturers Association (IDMA) and organisation of Pharmaceutical Producers of India (OPPI).

Odisha

Cuttack and Bhubhaneshwar form the cluster zone for the pharmaceutical cluster in this region, as per the Government of Odisha. The two cities are strategic in terms of their development as well as the fact that they form the business centre of Odisha. Manufacturing units in this region are involved in the manufacture of proprietary drugs, formulations and generics. The Utkal Pharmaceutical Manufacturers' Association (UPMA) was created in 1985 to further the pharmaceutical industry in this region. It claims to be the only sector-specific association in Odisha. The Drug Controller, Odisha and leading pharmaceutical industries from the region conceived this association. The 75 members of this association are involved in a variety of manufacturing including Liquids,Tablets, Capsules Ointments, surgical dressings, disinfectants. A Common Facility Centre at Mancheswar Industrial Estate Bhubaneswar provides common testing laboratory, training for documentation and technical operations of machinery for staff, seminars for knowledge upgradation, assistance with marketing of drugs produced in this cluster, a knowledge bank for information exchange and availability of consortium and sub contract exchange facility for members of the cluster.

Indore BDS Cluster

Indore pharmaceutical cluster is one of the oldest clusters in the country, nearly 100 years old. This segment mainly comprises of the formulation segment, almost 95%. There are very few industries in the bulk drugs category or the research and development category. According to a report by SIDBI, the Indore pharmaceutical cluster comprises of 0.79% of the total MSME registered in India. It is a relatively small cluster with around 45 companies in the small category. Most of the companies are private limited or partnership type of firms.

The R&D Clusters are as follows.

Key R&D Clusters

Captive R&D Units	National Capital Region Ahmedabad Mumbai Aurangabad Hyderabad Bengaluru Chennai
Contract R&D Units	Mumbai Hyderabad Bengaluru Chennai Ahmedabad

Source: E&Y Analysis

Examples of Initiatives to Build Regional Biopharmaceutical Industry Clusters

In **France**, the national government has provided funding to support the development of eight regional innovation clusters focused on biopharmaceuticals. Such efforts seek to integrate regional universities, large companies, and small and medium enterprises (SMEs) in directed joint R&D, education and training, and infrastructure development. Two (in Paris and Lyons) are designated for global leadership, and one (in Alsace) represents a tri-national cluster also involving academic and industrial participants in Germany and Switzerland. Each cluster has a 3-year performance contract and roadmap.

In **Germany** starting in the early 1990s, the federal government ran a series of competitions (BioRegio and BioProfile) to encourage the development of regional bio-clusters. They have been succeeded by several programs that provide funding for R&D projects (funded at least half by industry), business incubators, joint marketing, and other networking/linkages. For example, the Heidelberg cluster focuses on personalized medicine, and the Munich cluster on clinical trials. Public funds up to €40 million ($53.4 million) each are matched by private industry, with about a third of the total going to research and education institutions and 40 percent reserved for projects of SMEs.

In **Italy**, many regional governments, with support from the national government, have created nonprofit foundations to support cluster formation, often giving these foundations responsibility for research and science park development.

Chapter 6: Industry Experts Speak

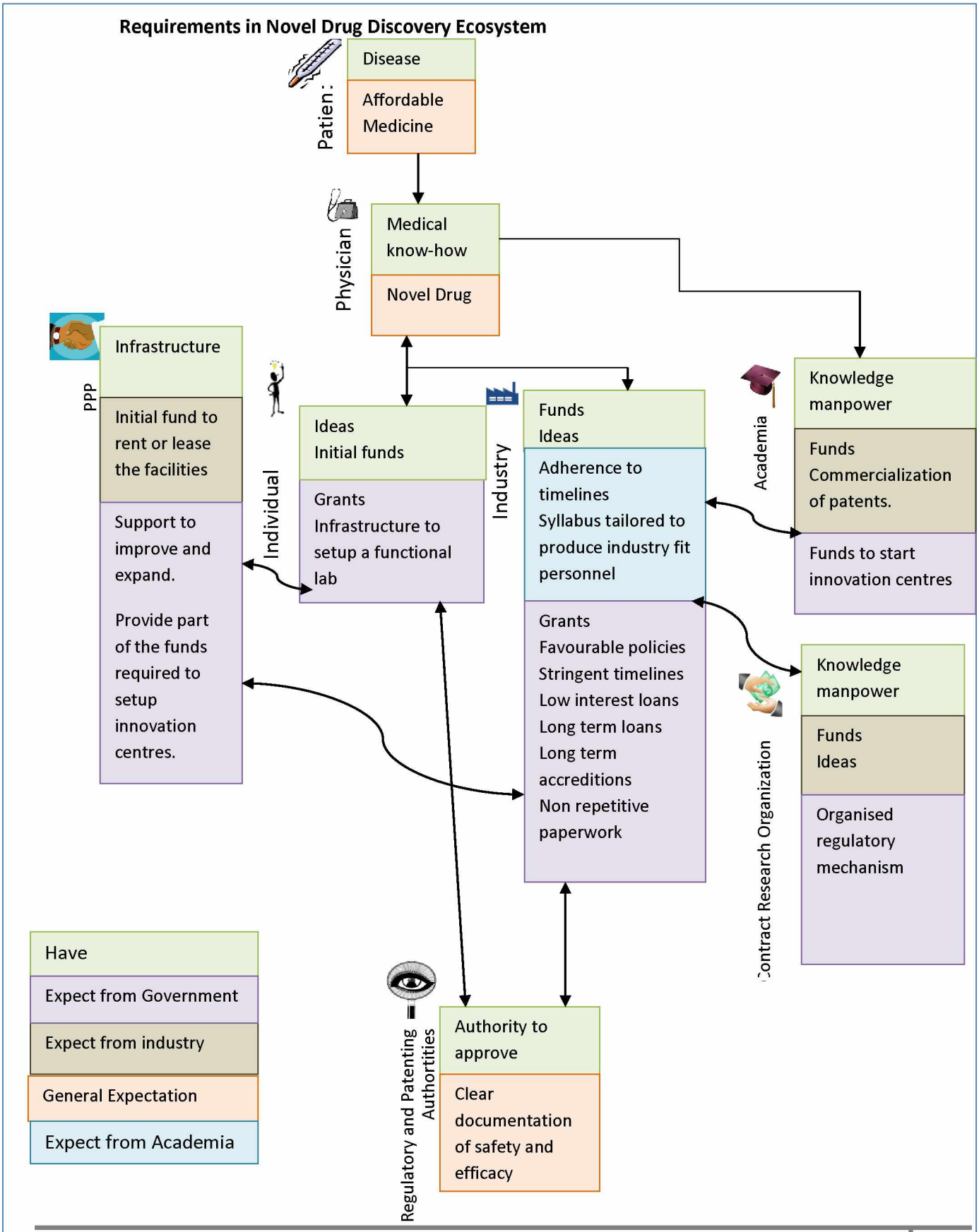
An important part of the preparation of this paper involved meeting almost 11 experts from the industry who have been closely associated or participated in the growth of the pharmaceutical industry in India. The key people among them involved CEO of an upcoming pharmaceutical companies, industry advisers, key management of a reputed contract research firm, founders of a nutraceutical firms, legal and drug discovery experts from a multinational firm and key personnel from PPP initiatives. The interviews lasted varying times from 1 hour to 3 hours and were recorded verbatim. Due to reasons of confidentiality as agreed to at the time of the interview, only the key points of the interview are published here. To understand the growth of the Vizag cluster, a visit was conducted to the Jawaharlal Nehru Pharma City at Parawada, Vizag and a similar exercise was conducted by visit to the Bulk Drugs Manufacturers Association at Hyderabad, Telangana.

Most people interviewed agree that government has ensured a lot of proactive participation in the growth of the pharmaceutical industry in India from a complete import oriented to an emerging generics giant. There was unanimous consent to the fact that the government's policies and incentives have ensured that the common man's need and government's prerogative of providing affordable healthcare to all sections of society is being largely met. History shows that the path so far has been far from easy but we have made rapid progress considering the age of the industry in India vis-à-vis globally. The industry and the government are looking at the next milestone, which is novel drug discovery. It is a cumbersome and expensive process with no assured returns. But it is a stage that the industry needs to mature to. Concerted efforts in this direction are hardly 3 decades old and also the healthcare needs have been evolving. When India gained independence and was yet to be self sufficient, generics were the call of the day and the efforts in the direction have borne ample fruit. Now with an economy that is looking to evolve to the next stage, it is no surprise that new drug discovery has to become the **mantra** for any company looking for longer stay in the market. The impending patent cliff and the trend of outsourcing some part of the drug development

cycle will give a huge impetus, if we can setup the right bait. Fluent English speaking scientists, large population for trials, increasing life expectancy, emerging awareness about health and quality life even beyond the prime years along with a market where many diseases treated as orphans continue to plague large sections of the population are slowly shifting the spotlight to India. Companies headed by evangelists that invested in R&D despite lot of pressures and stuck to it, are beginning to bear the fruits of the work as the patent figures indicate. It may take some years but the optimism is unanimous. For its part, the industry and experts largely felt that one blockbuster drug will lead the way to many more and this may happen soon enough. The successful public private partnerships like Jawaharlal Nehru Pharma City in Vizag are indicative of how a good equation will infuse confidence in MNCs to setup shop in India as well as encourage scientists with small capital and innovative ideas to start shop.

Reduction of repetitive paperwork for grants, low interest long term loans, extended periods to show results as innovation is a time consuming process as also the short duration of grants were some of the hurdles that some of the companies had faced but they all agreed that these are teething problems that may soon go away. IP Protection, compulsory licensing only on a pure merit basis of the disease and the drug as also a more conducive environment to conduct clinical trials were seen as catalysts that can help spur growth in the industry. Tax Exemption for R&D expenditure incurred abroad as in the case of clinical trials would be a welcome step. Science Promotion and talent recognition procedure that avoids same beneficiaries for grants and focuses entirely on merit of current project rather than past laurels would also see some new innovators emerge was one of the views expressed. Punitive action for infringement of patent as also a confidentiality agreement with government would infuse more confidence in conjunction with a speedier system for approvals.

To foster industry academia tie-up there was a feeling that there is a lack of proper communication channels leading to mismatch in expectations, which is resolved would provide more fruitful tie ups as has been seen worldwide.


Requirements in Novel Drug Discovery Ecosystem
Patient:
Disease
Affordable Medicine
Physician
Medical know-how
Novel Drug
PPP
Infrastructure
Initial fund to rent or lease the facilities
Support to improve and expand.
Provide part of the funds required to setup innovation centres.
Individual
Ideas
Initial funds
Grants
Infrastructure to setup a functional lab
Industry
Funds
Ideas
Adherence to timelines
Syllabus tailored to produce industry fit personnel
Grants
Favourable policies
Stringent timelines
Low interest loans
Long term loans
Long term accreditions
Non repetitive paperwork
Academia
Knowledge manpower
Funds
Commercialization of patents.
Funds to start innovation centres
Contract Research Organization
Knowledge manpower
Funds
Ideas
Organised regulatory mechanism
Regulatory and Patenting Authorities
Authority to approve
Clear documentation of safety and efficacy
Have
Expect from Government
Expect from industry
General Expectation
Expect from Academia

Excerpts of Interviews

Advisor to a prominent Pharma company

- Drug discovery is a very big and exciting opportunity for anyone to be a part of, but it can be very expensive, time-consuming, fruitless at times. The most important aspect for a compound to become a drug is balancing between safety and efficacy. Every drug has to be safe. An unsafe drug even if efficacious will not be accepted. No drug is 100% safe. Every drug carries a risk. If the safety is better while the efficacy is same, it is a prospective new drug.
- Players in drug discovery: Organic Chemist, Pharmacist, Pharmacologist, Toxicologist, Physicians, Statisticians, Molecular Biologists. All need capacity building from time to time to ensure quality of research.
- An average lead time of 10-12 years is required for a molecule to enter the market as a drug or therapeutic drug after rigorous testing. Anti cancer drugs have the fastest process timeline. Cancer kills in 6-12 months, so the pipeline is fastest, as there are no drugs available. So it is becoming a popular area of research.
- Global consumption in 2008: total market 738 billion
    - NA – 48%
    - EU – 11%
    - Japan – 8%
    - Africa, Asia and Eastern countries – 8%
    - Latin America -4%
- China is emerging as fastest with 28% growth. Our growth is about 12 billion dollar industry
- Alzheimer's drug takes the longest time for approval because they act on CNS. As extensive testing is required, it takes longest time to pass through regulatory mechanisms. Increasing senior citizen

population has their own requirements, mostly CNS. Companies are afraid to invest in this segment as market may not be able to support. How to balance product mix to suit requirements of diverse population

- According to McKinsey report, market will cross 1300 billion dollars – 2015 from 738 in 2008.
- Because of amount of money spent to bring a new drug and the cost of future money to be spent on R&D, the cost of drugs is more. If patents expire, drugs cost falls by 80-90%. The approaching patent cliff is one such phenomena. That is why big pharmaceutical companies are setting up so many R&D centres.
- Discovery research requires money, scientific pool of people, people with expertise, people who are prepared to think out of the box, knowledge pool, abreast with latest developments in the market place. Because of time, money and effort involved, , even by the biggest companies, can't have more than 1 molecule come in the market in a year
- Ever since genome structure was unveiled, bio pharmaceuticals are becoming popular.
- First 3 years of its life, the drug's survival is difficult.
- Big pharmaceutical companies are buying off bio pharmaceuticals, to survive. Big pharmaceuticals have the money while the bio pharmaceuticals have the talent. Talent and money being mutually exchanged is a good mix.
- Growing Stringent regulatory controls-Regulatory controls are becoming more liable. Manufacturers and users are suing if there are any adverse affects. Over a period time, more regulatory concerns are increasing.
- When a drug is tested and used by the market after its release, the drug is modified if the body is no longer responding. 3-5 years after introduction a drug builds up its own market. Adverse reactions come into the open only after increased usage.

- In fact Phase 4 trial comes after release of drug into the market. It is like a watchdog and it is mandatory. Reporting of all the adverse events in the first 4-5 years of release into the market is a regulatory mechanism. Companies are liable to report and the drug can be withdrawn. Based on the phase 4 feedback, there is a black box warning put on the box of the drug. If the adverse effects are still not controlled, it may be withdrawn.
- Rofecoxib was a very good analgesic, because it was causing cardiac ailments. They had to withdraw the drug when the market was almost 2 million or more. Then cases are filed claiming damages, the litigations go on and this becomes a big expense. When drugs are withdrawn from the market, cessation of the market and the focus comes on the adverse affects and litigations take up big amounts of money.
- Declining productivity of R&D.
- Expiry of patents leads to cutting down of margins by emergence of generics which makes it unviable to manufacture the drug anymore.
- Emergence of e-pharmaceuticals.
- Europe has been the centre of global pharmaceutical industry. Germany has been a forerunner. The market dates back to 300 -400 yrs. Most of the initial companies established as pharmacists first and then grew into mfg companies. Their grip on the industry is very old. They knew the drugs and market, knew importance R&D and focused 14-16% of revenues were pumped into R&D right from the beginning, especially 50 years. Earlier the expenses were not so much. After emergence of antibiotics the focus has shifted. Earlier hit and miss, now there are cures to cure the infection. Now antibiotics are curing infections, so they are venturing full blast. Infection can lead to lot of things but now control is possible.
- Each decade has given it own significant therapeutic segments
- Indian pharma industry started with tincture 1935
- Real growth post independence.

- All medicines were imported and they were sold at the same rate as global prices. So affordability was low.
- Government of India established IDPL with each center having its own focus
- Hyderabad for bulk drugs
- Hrishikesh for anti biotics
- Chennai for surgical instruments.
- Produced world class products at cheap rates and IDPL survived very well.
- Private companies taking cue from IDPL setup their own pharmaceutical units.
- Cadila, Lupin started in 70s and 80s and branched into various therapeutic segments.
- IDPL slowly phased out.
- Industry focused more on cheap drugs.
- 1970s patent regime changed from product to process. This gave a big impetus as we did not have to wait for global pharmaceutical companies to bring drugs to market in India. We could make cheaper drugs in India.
- More people joined the band wagon. So very less money was available for R&D as margins had to be cut.
- Glenmark, Lupin, Cadila, realized the imp. Of R&D and started centres in 90s.
- Natco does oncology. Glenmark psycho pharmaceutical and asthma. Suven works on CNS.
- Each company is focusing on 2-3 areas
- Biocon has introduced a new drug / molecule in the market.
- Research is happening but it not for public so as to guard interests.
- A first timer may happen from India very soon. This will provide a boost to the market.
- Top co. s say they spend about 5% of revenues on their R&D.
- Reasons for India lagging behind in R&D:

- Not early starters
- Our strong history is only 50 years
- Real discovery focus started in mid 90s.

- Government has given a lot of incentives.
  - Allowed companies to take advantage of patents
  - Developed Pharma City in Vizag. State Govt have taken lead to declare some districts as backward, maybe as an incentive for capital investment.
- About 25-30% consumer generics consumed in the world are from India. From total importer, India has evolved into an exporter is a big growth.
- It has met the needs of the public.
- IPR is not weak as many MNCs are filing patents here.
- Data safety is an issue for MNC. Also loss of patent related cases and compulsory licensing may be dissuading companies to invest in India.
- It takes time to settle down and India is a big market and BRICS is the focus of the global industry.
- The reason why traditional medicines are not as accepted as allopathy :
  - Mercury and arsenic drug levels are concern.
  - Efficacy not documented.
  - Lack of control.
  - Matter of belief.
  - Lack of clinical trials.
  - It is still not established chemical structure.
  - There are some GMP units like those of Himalaya etc but controls cannot be enforced.
  - But Regulatory Authority is looking at herbal supplements for levels of mercury, arsenic and lead. No control on the levels.

- Success of new molecules is the true measure of R&D. If R&D cannot contribute to bring better or safer drugs, the market is not reached then there is no use. If society is benefitted, that would be a true indicator of R&D success.

CEO of an upcoming pharmaceutical company

- Low Cost Bank Interest Loan with low interest rate will encourage more people to avail the funds. For established pharmaceutical companies to get money is not too difficult, but it is challenging for new players. Sometimes the effort and expenditure far outweigh the fund. Low cost funding is the main incentive that should be given.
- R&D itself is a tricky situation. There is no guarantee. For process R&D ,it is ok...but innovation R&D cannot be always expected to give a result. If it's a loan, whether or not results come, the loan will be repaid. Failure is a norm for innovation R&D. Even in process R&D when the product is finally ready, it may become obsolete.
- The timelines and accountability are not upto the mark. Process R&D in India is good but in innovative R&D we are yet to prove.
- It's the mindset of the management. Even if they want to spend, markets don't allow them to spend.
- Greater awareness about drug discovery, R&D and innovation at the top level will encourage speedy processing of funds and loans.
- A co. spends 45-50 crores per year. 1000-1500 crores is spent in Hyderabad alone on pharmaceuticals. Allocations for innovation are very less.
- Dr. Reddy's started innovative R&D operations, but had to close down. Glenmark is doing because they have had some success. A blockbuster drug may happen but there are no guarantees. Malarial drug is not a global drug.

- There is a possibility that a global drug will happen from India but not sure when. Success will bring more players into the market.
- The regulatory regime and dedicated teams are an expected outcome from industry.
- Maintaining data secrecy - Currently there are no signing of CDAs. There should be a CDA. There should be accountability and punishment.
- The benefits that are given have to be long term for innovation to sustain. The timespans should be something like 20 years. It should be extendable 5 years before expiry. Real players don't take advantage.
- Industry academia is where the innovation happens all over the world. The academic stream in India has people who give precedence to publishing papers. The sense of timelines and deliverables is not so stringent leading to about 20 years from concept to market.
- In industry sponsored collaborations-the money goes to buy equipment for the University which could lead to incremental innovation, but does not always happen. Industry's perspective and academia's perspective to innovation suffer from disconnect.
- Appropriate informed Leadership is required to scrutinize applications to discern genuine ones.
- Average of 18% of revenues is spent globally for R&D in pharma industry. This is possible because of the age of the industry and products that are sold globally at that price. In India there is no global product, so there is no money to invest back. But foreign players are there since 100 years, the money is therefore recovered by the products.
- In India there is price control on even the innovative drugs. It may good for the people but no new innovative drug is coming out. In process formulation we are good. But when it comes to innovation, we cannot gauge the success as there is no output. There are many people putting efforts but not much of concerted effort on drug discovery.

- CNS drugs - Timeline for CNS drugs is long, success rate dismal and requirement is very huge. Previously average Indian's lifespan was 60 , now it is 80. Post retirement, the diseases are more from CNS as there is no active life, unlike in the west. What we call old age is senility is also a part of this segment. Quality of life needs to be maintained. We need medications to deal with these kind of ailments Dementia, Obesity, Parkinsons, they cannot be quantitatively measured unlike BP, Sugar., even cancer. But for memory, it cannot be measured. These have qualitative measures. There are only specialists who can do it and there are scales to measure it. Interpreting those rating scales is very difficult and trials take longer unlike BP whose effect can be seen in 1 week. Lot of trials fail because they were done only for 6 months. Now it is 9 months. High attrition. Failure rate is high. Ageing population is growing, so the risk population is fast growing. Cognition problems are starting early due to lifestyle of IT sector. There is a theory that they want to do this very early. Mild cognitive impairment is the early signs of Alzheimer's. At around 45 you start losing your memory a little bit. As you are growing older, the number of people living becomes more. These diseases come naturally with age... Other things can be controlled with exercise, diet etc...but not these. Age related problems are problems are chronic rather than acute.
- Creating a dedicated regulatory infrastructure in a time bound manner with accountability, secrecy and proper incentives for innovation would help improve R&D in the country. If work is done outside it should still be counted as innovation and global trials should also be given benefit.
- Patenting is not given benefit. It should be encouraged
- Attitude to timelines, IP and confidentiality are issues for industry academia tie –up. The apprehensions are holding back the industry.
- Perceptions of the universities about businesses should also change. It may be a long drawn process.
- It all comes down to accountability, IP and secrecy. Number of papers should not be a key item in promotions.

- Globally R&D is being cut down, especially early stage R&D. They rather outsource it. It makes it cheaper.
- Everywhere 60-70% comes from universities and smaller companies that tie up with each other, especially in pharmaceutical industry.
- Cutting down fixed expenses is the prime concern globally.
- Vaccines are bio generics. Bio pharmaceuticals require target identifying and target validation requiring innovation - be it one or many molecules involving biology. Biologics and Biogenerics have much potential, because globally everybody is looking at their direction to get developed drugs to the market at the same time to develop them in a generic fashion is going to be a challenge. The time it takes is very heavy compared to others and cost is high.

A leading figure in the pharmaceutical industry who worked with initial drug discovery efforts

- The government should give some money or seed money and provide pilot plant for upcoming innovators to launch their ideas. This will encourage people who have ideas but no seed capital. This will spur development. These can be built at all the major hubs.
- Leadership is lacking. The most important aspect of spurring innovations is to have leaders with that kind of vision who can lead the projects. But today this is not commonly seen. There is missing link between translation of bench ideas to pilot plant. This gap can be filled by government setting up such sample pilot plants that can help incubate ideas. Pilot plant complete with analytical facilities.
- Large institutional leadership is lacking.
- Harnessing of talent is required. There is a lack of clarity on what national institutions should do. Should they do research to advance national interest? Should they do path breaking to win international recognition? Should they do any teaching/academic research at all? There should be clear answers to these questions.

- Infrastructure – It is not enough to create infrastructure but to see that the infrastructure functions. For example : Corporate funding is often used to buy expensive equipment at institutes, but if the equipment breaks down, it takes a long time to fix as the spares may not be easily available or the fix may not be easily available.
- Innovation requires intellectual freedom. Innovation can't happen in highly structured, bureaucratic setup. India should be proud to have a chain of CSIR institutes (43), ICMR, ICAR institutes and our national research labs.
- India has the critical mass to make an impact in science and innovation and to compete with advanced nations. In my opinion, if the excellent and extensive infrastructure in science and technology is managed properly, India can be a super power in research and innovation. India has amongst the largest number of labs for every conceivable resource. Dr.Reddy's once quoted that post Independence India has not produced a Nobel laureate in any field. All the few Indians who got Nobel Prizes were born in British era. The key lies in harnessing talent. If we manage our resources and harness our talent, Indian science will emerge as world class in Research and Innovation.
- Indian Pharmaceutical Industry and Drug Discovery 15-20 years ago. In the 90s and the early part of this century, there were 8-10 Indian pharmaceutical companies present in drug discovery research (new molecule discovery research). Some of these endeavours have had initial success and showed great promise for the future. However in the past few years we have witnessed that these groups have failed with the closure of some of the research centers. Present day pharmaceutical industry is more occupied with generics than patentable New Chemical Entity (New molecule research).
- Science management is very important. Space and atomic energy are two spheres where we have made massive progress. When better management is lacking, there is no impact. In case of space and atomic energy, the mission oriented programmes have created great impact. Right from their inception, there have been mission and deadlines in these two sectors, leading to rapid progress.

Even the new molecule discovery programme in India should be given a mission oriented approach to make it more successful and rapid. . If made into a mission, give it a commitment of 20 years, then it will be a success.

- Drug discovery research is highly interdisciplinary. Productive interaction amongst chemists, biologists, medical professionals and technologists is required for successful pursuit of discovery programmes right from the inception of the idea. It's not necessary to have large budgets or super automation. It is good ideas that matter or how good ideas are. Automation has increased but patents have not enhanced. Lots of innovative research and development is growing. Research and development productivity is diminishing. Size and money are not important. Management is important. Evaluating the feasibility of the idea is important. Excellent laboratories exist in the West with large teams, yet there are failures. A lot of companies have vanished with mergers and acquisitions coming into the picture.
- The Intellectual Property law provision is in place but is there stamina to do R&D?
- Empowering companies to continue concerted sustained approach to research is lacking.
- The number of companies doing new molecule research is probably single digit.
- Merck's drug Januvia is 1st in class drug, not produced locally. A strip of 7 costs Rs.299. If it is produced locally it would be Rs. 10. In the interest of the public health and health security this law can be invoked, so it should be given to 2-3 players. Compulsory licensing should be given only in the following circumstances. When the drug is very expensive. When the drug is not produced locally, it is imported.
- Disease or ailment is a threat to national health security. When a virtual monopoly can be simulated, compulsory licensing should be like an ordinance, used to benefit people but should not be freely used.

- Cultivating the scientific spirit and temper is very crucial. Belief in scientists is most crucial. Rewarding successful innovators with equity in excess of 10% can be done as an incentive.
- Some rules like the following may help:
    - Companies with Rs.2000 crores should pump Rs. 100 crore into discovery research.
- Filing returns should be mandatory and there should be Punishment for malpractice. Government should trust the companies in their governance. Government should do what industry cannot do.
- IICT can act as a referral centre. Expertise to provide advice when industry is in trouble.
- Revocation of license should be done if the company is not conforming.
- There should be a champion in the house for drug discovery to happen. Government should have workshop for CEOs of drug manufacturing companies where they can interact with people from the government, who in turn can reinforce their faith while the company leaders can express their concerns to the government. India can be a hub of clinical research because of the vast number of untreated sick people. In India it will take 2 weeks to complete the trials that take 2 -3 months to complete in the US.
- The regulatory environment needs to be looked at.
- In Clinical Trials - Phase 1 comprises of healthy people, informed people. Phase 2 comprises of informed people who have given consent to trials to alleviate their hardship. Insurance has to be provided in case of contingencies.
- IND Application processing expertise must be made available. IN the US, 4 weeks after sending the application if there is no response from the government, it means a go ahead. In India no such assumption can be made.
- Even Germany has drug price control.
- Even though the patent law was passed in 1971, it was enacted only by 31st March 2005. The government must assure protection of intellectual property as well as set a global market goal like

- if Net sales are between 1000 crores and 2000 crores then R&D investment should be 3%,
- if Net sales between 2000 crores and 3000 crores, then R&D investment should be 5%,
- if Net sales between 8000 crores and 10000 crores, then R&D investment should be 7.5%,
- if Net sales more than 10,000 crores then R&D investment should be 15%.

- Giving them a benefit of 120 or 150% benefit will make it a mission. We should encourage indigenous discoveries and treat sick people all over the world. Protecting health should be a mission. Tata and Mahindra have put us on the world map in the automobile industry. There is hope. Each CEO who champions innovation will change the mindset of many people and thereby make more champions. Giving benefits like those for export will spur innovation.
- If company has patents then the government should allow the drug price control order to be relaxed. Further SOPs for companies that come out with the first molecule like free land, power etc. will encourage innovation. There may be around 15-20 companies in Hyderabad, 20-30 in Mumbai, 6 in Ahmedabad and 5-6 in Delhi with a potential for innovation. Inviting them for a meeting with the prime minister, drugs controller, ICMR and Finance Minister to discuss the various issues relating to drug discovery may provide useful impetus.
- Prepare the ground for migrated talent to come back to India. China sends its post doctoral students to the US with a scholarship backed by the Government of China to study and come back and implement their learnings.

Key people from a leading multinational firm

- Law and order problem are an important concern especially during communal problems and political volatility.
- Some companies, last year, spent 37% of total revenue on R&D.
- Indian government should take firm political decisions to give stability.

- Local people being displaced when the unit is setup often demand jobs even without the requisite skill sets. Administration is very supportive.
- Alzheimer's on the rise even in younger population. So setting up free clinics could help. The medicines and doctor are the choice of the patient.
- The company is very strong on compliance and ethics. Tele conference timings are very difficult to maintain because of the political instability.
- There is an excellent mix of people from different pharma related backgrounds.
- Employee Engagement is very high.
- Being innovator organizations, the year on year output expected cannot happen. It is a long term process. There should be a bifurcation for generic and innovator drug companies. Going for NDA filing and product approval is longer as compared to ANDAs. Drug discovery is long term project that may take 3-5 years. In innovative R&D it is difficult to show fixed outcomes every year.
- Development planned by the companies is for 5 years so approvals also should be in the range of more than 3 years.
- Global R&D team works on drug discovery research, formulation research, clinical research, process research. Big in-house strength of skilled manpower is available. Scientific advisory board are in-house comprising of leading universities and institutes. Based on these scientific advisors, the discovery is planned.
- One of the molecules for breast cancer had 83 synthetic steps and is now launched in 30 countries taking 15-16 years to launch this product.
- Tie-up with academic, educational institutes can be helpful.
- Open and reverse innovation are both in place.

- In MNCs, for local manpower, trainees are taken from universities with tie-up and trained. After evaluation if they are good, they are recruited.
- India has the capability to carry out basic research from molecule to filing. The basic question is of industry academia collaboration. If the system were more transparent, it would be helpful. Cost efficiency and freedom to pursue R&D will help produce a new molecule every year. Tie up with institutes are taking a lot of time as they are not sure and firm. Collaborations are not working because the internal processes are not helping. If institutes do research they can do so in a conservative way, but if it is for MNC the commercial terms are very high. Some flexibility should be given. India can be a hub of scientific expertise.
- Companies should follows GMP.
- There are companies that are not sure about starting clinical trials in India. Clinical research org are not seemingly very compliant.
- CNS as an area is gaining popularity. Most of the companies there are not willing to take a risk where market is big; patients are many but no medicine. KAN (Knowledge Action Network) has expertise in CNS.
- A High rating can be given to Indian R&D potential. When it comes to formulation research, India is very high. R&D for active ingredients India is very high. Discovery research, monoclonal antibodies and biotechnology the R&D is low.
- Health awareness is very important as it protects innovator drugs. In Japan, people prefer buying original innovator drug. From where should the medicine be bought is also an awareness. The digitalized medical practitioner can explain to the doctor how the drug will exactly work and important points. In Japan, US and Europe this is happening but in India there is very less awareness. Patent protection has improved in the last 3-5 years. But lot more needs to happen. The companies that spend billions of dollars in innovation and launching product, the company's vision also should

be to help people. For ex: Awareness about dementia is very low in Indians. In Japan they have a call center for dementia patients for advice. In Japan about 3 million patients for dementia of which only. 1 million go for treatment. Patient awareness about the disease has improved. General public has awareness on health and fitness and they are working closely with doctors, companies and institutes to improve health at the beginning itself. Our role is to provide safety quality and efficacy of a medicine. We don't go to to the market based only on clinical trials. The family members of the patients give the feedback which supports in improving the efficacy of the drug.

- Getting the right product pricing is important to prevent generic drugs from taking over the drugs.
- Lot of institutes and industry are looking for collaborations for a new innovator drug. The pharmaceutical drug market will advance more because of the upcoming mergers and acquisitions.

Head of a nutraceutical firm

- Pharma is an experience oriented industry.
- Drug discovery has no guaranteed results and time consuming which is why usually private entrepreneurs are not encouraged to take up innovation.
- Research and Development in institutions is happening but it is not according to industry needs. Indian R&D institutions are working on academic research, rather than technological development.
- Technological development is the key for industry. If talent is there, government should be supportive and provide encouragement. The mechanism for identifying talent is missing. There is a lot of talent in and around people, however the mechanism to identify it is missing.
- In case of grants or funds - if the number of beneficiaries are too high then fund amount becomes too less. The funding mechanism should be such that if only one project is to be funded it should be purely on merit basis. Otherwise the meager amount becomes a deterrent and really interested people may not be encouraged to take it up. Another major deterrent is the number of visits that need to be paid before procuring a grant.

- The accounting that needs to be shown after the grant should be looked at. The grant is given in March then by April they want the list of all the expenses by end of April. Giving the grant 1-2 years in advance and then asking for a plan and being made accountable for the rest of the period is a better idea.
- The government should realize the importance of innovative R&D and provide support them in a broader way. Repeated grants to the same person do not help. The nature of the grant should be such that it should help as seed or incubation capital and not as a continuing support for the project. After 3 or 5 years, the project should be able to run without a government grant. This would help make projects more efficient as also provide chance to newer players to get a chance to get funded. Grant should be supportive and not repetitive.
- Identifying talent, providing encouragement are the primary factors. Disbursal of money is often followed by expected return. But when the pressure of the expected return is reduced or taken away, the project may yield better results and even the quality of projects will improve. There are a number of centralized labs. If a small or medium enterprise is provisionally provided with centralized, general facilities, there is a possibility to come up with new ideas.
- Government should not fund organizations based on the lack of funds alone. It should fund purely based on merit. Innovation should be encouraged from a very early. Incorporating in primary education itself would definitely help. Innovation and practices for innovation can be taught without an experience right from the elementary level.
- Centres for Excellence should be created, not just in metropolitan cities but also in other areas, so as to make access available to inaccessible places. Nurturing talent from all areas repeatedly is a foremost priority. This nurturing of talent can be done the way it is done is music talent shows. If scientist is to be encouraged, go to every nook and corner to give people exposure. There are people who really want to be in science but don't know how to get rewards.

- Providing instrumentation labs in pharma city parks where industries can be serviced probably on a charitable basis would be a very welcome move.
- People in the new area are also to be supported like nutraceuticals. This is a business worth 1000 billion dollars. There are nutraceutical forums in Mumbai. Every area is open to innovation. Companies can be started by individuals.
- Patenting should be given as education as a part of curriculum. Fourth standard students in US have education of patents. Protecting thoughts is an important task.
- Government funds should be given to people who can account for it properly, by outcomes and not by balance sheets because every rupee is hard earned money.
- Regular NCEs cannot be developed by small and medium companies and bigger companies have already started working on this. Science talent should be there.
- Even single highly motivated people can motivate an entire generation as is evident from the music talent shows. This motivation should happen not only in science but all areas of development. Similarly money can also assist in encouraging innovation. A right idea at the right time in the right brain is innovation.
- Role models, scientific winners and developers in the field of research and development should be given recognition and publicity similar to what is given to film stars and sports persons.
- The media focus is important. Tuning the mind will orient right attitudes towards research and development. If science is given that focus, people would be discovery oriented and rewarded. Just Indian Badminton League changed the mindset of people towards badminton, so too will a similar idea in R&D bring about a change in the mindset of people towards R&D. It should be seen with such a spirit.
- The pioneers in R&D in pharma like Sun Pharma, Lupin are far and in between. In case of most other companies, they are starved of funding so no immediate R&D.

- Science propagation at all levels. Competition drives innovation and development. Getting the first molecule may the most difficult challenge. But once one molecule is out, many more companies will be vying with each other to put their molecule in the market. Clearly put, competition will bring about innovation.

Dr. P P Lal Krishna, CEO, Jawaharlal Nehru Pharma City, Vizag

The Jawaharlal Nehru Pharma City is a PPP that now houses over 90 companies and can accommodate another 30 more. The Pharma city provides the basic infrastructure like roads, power, water, effluent treatment facilities, labs, water so that a company can just walk in with their chemicals and start working in the labs. It is a 971.66 Ha Industrial park. They have plans to come up with an Innovation Centre, which will be a refinement on the Pharma city park. The Centre would be such that an innovator would be able to walk in with an idea and initial capital and would be able to start his venture. The innovation centre would provide labs, initial setup infrastructure. Once the commercial manufacturing would commence, the innovator would repay as a percentage of royalty or repay in installments. It would help the innovators to start with smaller initial sums and focus only on developing their ideas. If such PPPs like JNPC are flourishing, then an innovation centre will definitely flourish. If government gives loans to setup such parks, it will be useful as they would be able to provide a bench for innovators to work on. They would not have to worry about the infrastructure maintenance and costs and would merely be bringing their idea to the work bench. Once the idea is ready for commercialization they would be able to focus on expanding their work areas and repayment of loans etc. For developing parks like this, the Government plays a crucial role in getting approvals, providing seed capital, providing some benefit like first 3 years interest free or waiver of loan EMIs or EMI free period. This would encourage companies interested in PPP to setup such parks which in turn would spur innovation. But without government participant, mere investments by companies would

not yield any result. Once one scientist show a success story, the government may be convinced and it will encourage others. There has been considerable interest in developing such parks as Pharma City in different states and different areas of the country and even from abroad.

Chapter 7: OLS model

The first pull from the Prowess database yielded 615 companies. From this set, the companies that had at least 1 NDA or 1 ANDA filing between the years 2001 and 2015 were filtered. Amongst these companies, those which had relevant data in R&D Expenditure (Capital and Current) and Net Sales for more than 10 years were selected. The new subset had 28 companies. The years, for which no ANDA or NDA filing was done, the missing values were replaced by 0. Both Net Sales figure and R&D Expenditure figures are in Rupees Millions. The NDA and ANDA values of the previous year are taken as the NDA and ANDA data are for the year ending in December while the Net Sales and R&D data are for the year ending in March. That is the reason why R&D Expenditure of the previous year is being considered to develop the model.

Summary Statistics, using the observations 1:01 - 38:13

(missing values were skipped)

Variable	Mean
NetSalesinMillions	1.3638e+010
RD_Capital_Current_Exp	9.3467e+008

For the model, a panel data regression model (Pooled OLS) was used with NetSales as the dependent variable. The following equation estimates the NetSales of the pharmaceutical industry

NetSales = constant + α * R&D Capital and Current Investment of Previous Year

+ β * NDA filings of Previous Year + γ ANDA filings of previous year

Pooled OLS, using 392 observations

Included 28 cross-sectional units

Time-series length = 14

Dependent variable: NetSalesinMillions

	Coefficient	*Std. Error*	*t-ratio*	*p-value*	
Const	4.70306e+09	5.50616e+08	8.5415	<0.00001	***
RD_Capital_Current_Exp_1	9.16909	0.409672	22.3815	<0.00001	***
NDA_1	4.97103e+09	1.85867e+09	2.6745	0.00780	***
ANDA_1	1.26066e+09	1.91248e+08	6.5917	<0.00001	***

Mean dependent var	1.44e+10		S.D. dependent var	1.89e+10
Sum squared resid	3.41e+22		S.E. of regression	9.38e+09
R-squared	0.755207		Adjusted R-squared	0.753315
F(3, 388)	399.0050		P-value(F)	3.7e-118
Log-likelihood	-9555.190		Akaike criterion	19118.38
Schwarz criterion	19134.27		Hannan-Quinn	19124.68
Rho	0.839080		Durbin-Watson	0.545541

***, ** and * indicates statistical significance at 1, 5 and 10%, respectively

The Proposed Model:

NetSales=(4.70306e+09)+ 9.16909*(R&D Capital and Current Investment of Previous Year) + 4.97103e+09* (NDA of previous year ending December) + (1.26066e+09)* (ANDA of previous year ending December)

F-test confirms the explanatory power of the equation is statistically significant. Adjusted R^2 is good and observed at 75%. The role of different variables as determinants of Net Sales is given below.

It is observed that the coefficient of R&D investment of previous years is positive and statistically significant at 1% level. This suggests that R&D investment of previous years and the Net Sales has a positive relationship for the given sample of pharmaceutical firms.

It is observed that the coefficient of ANDA filings is positive and statistically significant at 1% level. This suggests that ANDA filings and the Net Sales have a positive relationship for the given sample of pharmaceutical firms.

It is observed that the coefficient of NDA filings is positive and statistically significant at 1% level. This suggests that NDA filings and the Net Sales have a positive relationship for the given sample of pharmaceutical firms.

Chapter 8: Conclusion and Recommendations

While the pharmaceutical sector has seen a phenomenal growth in the last few decades, new drug discovery remains elusive. Most experts believe that a one first-timer from India will prompt others to follow suit. While several attempts have been made in the past and there are companies that continue their efforts, the results are still in the pipeline. It is claimed by the department that India is the only country with largest number of US-FDA compliant plants (more than 262 including APIs) outside of USA, almost 1400 WHO-GMP approved pharmaceutical plants and 253 European Directorate of Quality Medicines (EDQM) approved plants with modern state of the art technology.

The government, on its part has made the pharmaceutical sector, very lucrative and provided impetus to the industry by implementing recommendations of the Planning Commissions, encouraging clusters. The Department of Pharmaceuticals that is currently under the Ministry of Chemicals and Fertilizers is slated to become a ministry by itself.

"Make in India" and the STI Policy have all paved the way for innovation in this sector. It remains to be seen if the future brings forth a first-timer from India as some industry experts claimed may happen. Reduced paperwork and ease of grant procurement by new entrants might hold the key as also by increasing the performance review period to 5 years. Loans with fewer guarantees and better patent protection regime are bound to positively impact the industry. Increased partnerships between industry and academic institutions can go a long way in tapping the talent in the Indian universities and other academic institutions. Successful PPPs like Pharma City in Vizag have made the environment more conducive to more such ventures. Some industry experts expressed views that pilot plants would also help early stage innovators to undertake research.

The proposed model shows how an investment in research and development can only positively influence the sales of a company, as can an ANDA or NDA.

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Appendix

Data Tables

Standalone Net Sales for Drugs Sector in Rs. Crore

Mar-97	54.55
Jun-97	1411.81
Sep-97	2349.23
Dec-97	1852.79
Mar-98	2119.23
Jun-98	3309.6
Sep-98	4302.31
Dec-98	3867.33
Mar-99	3959.11
Jun-99	4352.36
Sep-99	4697.42
Dec-99	4522.41
Mar-00	4397.05
Jun-00	4719.11
Sep-00	5137.99
Dec-00	6241.01
Mar-01	5537.75
Jun-01	5066.61
Sep-01	5661.9

Dec-01	7052.89
Mar-02	5662.93
Jun-02	5862.91
Sep-02	6468.34
Dec-02	6263.03
Mar-03	6523.12
Jun-03	6800.03
Sep-03	7478.71
Dec-03	7047.47
Mar-04	7527.43
Jun-04	7708.68
Sep-04	8030.24
Dec-04	8010.12
Mar-05	7286.9
Jun-05	9145.62
Sep-05	9234.1
Dec-05	9402.56
Mar-06	9536.33
Jun-06	10724.11
Sep-06	11441.45
Dec-06	11510.39
Mar-07	11919.32
Jun-07	12257.39

Sep-07	13844.24
Dec-07	13837.06
Mar-08	14112.86
Jun-08	15160.87
Sep-08	16119.04
Dec-08	15450.81
Mar-09	15897.91
Jun-09	16175.86
Sep-09	17036.34
Dec-09	17319.76
Mar-10	18244.34
Jun-10	18115.23
Sep-10	19736.66
Dec-10	20195.04
Mar-11	20685.89
Jun-11	20930.69
Sep-11	22726.94
Dec-11	25908.67
Mar-12	24454.54
Jun-12	24202.29
Sep-12	25595.92
Dec-12	25423.89
Mar-13	25009.57

Jun-13	25366.94
Sep-13	27564.69
Dec-13	27858.89
Mar-14	28409.79
Jun-14	32397.29
Sep-14	30425.96
Dec-14	30025.68
Mar-15	31949.63
Jun-15	33542.75
Sep-15	34259.35
Dec-15	33043.5
Mar-16	33811.1
Jun-16	33657.43

(Source: CMIE Prowess Database , Drugs and Pharmaceutical Sector)

Top 10 Pharmaceutical Companies

based on sales and spend in 2015

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top-selling Drugs [USD in mln]
1	**Pfizer** New York, New York [pfizer.com]	$43,112	$7,678.0	Prevnar 13 [5,940] Lyrica [4,839] Enbrel [3,333]
2	**Novartis** Basel, Switzerland [novartis.com]	$42,467	$8,465.3	Gleevec [4,658] Gilenya [2,776] Lucentis [2,060]
3	**Roche** Basel, Switzerland [roche.com]	$38,733	$8,452.1	Rituxan [7,321] Avastin [6,945] Herceptin [6,794]
4	**Merck & Co.** Kenilworth, New Jersey [merck.com]	$35,244	$6,613.0	Januvia [3,863] Zetia [2,526] Janumet [2,151]
5	**Sanofi** Paris, France [sanofi.com]	$34,896	$5,638.2	Lantus [7,089] Plavix [2,140] Lovenox [1,907]
6	**Gilead Sciences** Foster City, California [gilead.com]	$32,151	$3,018.0	Harvoni [13,864] Sovaldi [5,276] Truvada [3,459]
7	**Johnson & Johnson** New Brunswick, New Jersey [jnj.com]	$29,864	$6,821.0	Remicade [5,779] Stelara [2,474] Zytiga [2,231]
8	**GlaxoSmithKline** Brentford, England [gsk.com]	$27,051	$4,731.1	Seretide/Advair [5,625] Pediarix [1,120] Triumeq [1,116]
9	**AstraZeneca** London, England [astrazeneca.com]	$23,264	$5,603.0	Crestor [5,017] Symbicort [3,394] Nexium [2,496]
10	**AbbVie** North Chicago, Illinois [abbvie.com]	$22,724	$3,617.0	Humira [14,012] Viekira Pak [1,639] Lupron [826]

Table 18: Top 25 pharma companies globally based on revenues (Source : Pharm Exec's Top 50 which used data from EvaluatePharma)

Number of pharmaceutical manufacturing units in 2011-12 in India

Sl. No	State	No. of manufacturing units		Total
		Formulation	Bulk Drugs	
1	Maharashtra	1928	1211	3139
2	Gujarat	1129	397	1526
3	West Bengal	694	62	756

4	Andhra Pradesh	528	199	727
5	Tamil Nadu	472	98	570
6	Others	3423	422	3845
	Total	8174	2389	10563

Source: Annual Report 2011-12, Department of Pharmaceuticals

Number of pharmaceutical educational institutions and students in 2011-12

Sl	Item	Total numbers
1	No of Universities	409
2	No of colleges	25990
3	No of science colleges	4696
4	Annual student output at degree level in science	2000374
5	Annual student output at degree level in engineering	1663619
6	Total no of pharmacy colleges	1162
7	Number of B Pharm colleges	848
8	Number of Masters in pharmaceuticals area and PhD offering colleges	191
9	No of B Pharm students in pharma	51716
10	No of Masters and Phd students output in pharma	5648

Source: Annual Report 2011-12, Department of Pharmaceuticals

Distribution of pharmaceutical companies based on turnover in 2011-12

Turnover	% Distribution
0-10 Cr.	70
10-50 Cr.	20
50-100 Cr.	5
100-500 Cr.	3
500 + Cr.	2

Source: Annual Report 2011-12, Department of Pharmaceuticals

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