EXPORT-IMPORT BANK OF INDIA

WORKING PAPER NO. 37

STUDY ON INDIAN PHARMACEUTICAL INDUSTRY

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EXECUTIVE SUMMARY

The Indian Pharmaceutical industry has been witnessing an impressive growth in the recent years, driven by rising consumption levels in the country and strong demand from export markets. The industry has seen significant progress in terms of infrastructure development, technology base and the wide range of products manufactured. Demand from the exports market has been growing steadily due to the capability of Indian pharmaceutical companies to produce cost-effective drugs.

Identifying new drug development targets, attaining regulatory approvals, and refining techniques in drug discovery and development are among the challenges that are being faced by the Indian pharmaceutical industry today. This Study provides an overview of the global and Indian pharmaceutical industry in terms of current scenario, performance, challenges and prospects, and the way forward.

Global Scenario

The global pharmaceutical market was estimated at US$ 962 billion in 2012[1] growing at a muted pace of 2.4 per cent y-o-y (on a constant currency basis) vis-a-vis 5.3 per cent in 2011. Regulated markets, such as the USA, Europe, and Japan, continued to grow at a slower pace (vis-a-vis the emerging markets) following the patent expiry of key drugs, saturation of markets and declining productivity of research and development activities. Additionally, the global economic slowdown has also contributed to a weaker pricing environment for branded drugs, which in turn led to higher substitution of generic drugs. Growth momentum in emerging markets continued in 2012.

The USA, Europe and Japan are the dominant markets in the global pharmaceutical industry. Sales of pharmaceutical products in the USA and Europe contracted by 1 per cent each, while sales in Japan remained stagnant. Sales of pharmaceutical products in Asia (excluding Japan), Africa and Australia accounted for 17 per cent of the total global pharmaceutical sales in 2012. With respect to therapy classes oncology retained the top spot with an 8 per cent share in the overall global pharmaceutical sales.

Global exports of pharmaceutical products (HS Code 30) registered a modest growth at a CAGR of 3.7 per cent between 2009 to 2013, from US$ 420 billion to US$ 486 billion. With a share of 15.4 per cent in the global exports of pharmaceutical products, Germany was the leading exporter of pharmaceutical products during the year 2013, followed by Switzerland (11.9 per cent), Belgium (10.4 per cent), and USA (8.2 per cent). As a region, Europe accounts for about 80 per cent (US$ 389 billion)[2] of the total exports of pharmaceutical products. With a share of 58 per cent (US$ 289 billion)[3] in the total global imports of pharmaceutical products, Europe was the largest importer of pharmaceutical products during the year 2013. Among the pharma-emerging markets[4], India registered a significant growth in exports accounting for 2.4 per cent share in the global pharmeceuticals exports in 2013. China has emerged as a significant importer of pharmaceutical products.

[1]IMS Health
[2]Trademap, ITC Geneva
[3]Trademap, ITC Geneva
[4]Brazil, China, India, Russia, South Africa

Key Developments in Regulatory Environment

Some of the recent developments and key trends in the regulatory environment that might significantly govern the global pharmaceutical sector are: shift in the position of US Food and Drug Administration (US FDA) on generic drug labeling, allowing generic companies to change their labelling, under appropriate circumstances, just like brand companies; The Supreme Court of the USA's ruling against reverse payment agreements (pay for delay); increased emphasis on Quality Risk Management (QRM) with risk management becoming a central component of any regulatory inspection and regulatory filing; stricter drug serialization regulations; anti-counterfeiting measures impacting generics negatively; tweaking of the products by innovator companies and filling of patent as new drug; innovator companies entering into licensing agreements with generic companies in the developing countries as creative business strategy of managing the competition, and by undermining the patent laws in the those countries; instituting new initiative by WHO called the Substandard/ Spurious/Falsely-labelled/Falsified/Counterfeit medical products (SSFFC) to check the spread of counterfeiting drugs; enhanced scrutiny of pharma-units by the USFDA for Current Good Manufacturing Practices (CGMP); increased incidences of import alerts and bans of pharma-units by the USFDA, especially in the Asian countries; and announcement of new fees structure by the USFDA under the GDUFA programme for the period, October, 2014 to September, 2015.

Key Trends in the Industry

Some of the key trends in the global pharmaceutical market that have been significantly defining the way forward in the sector are: mergers and acquisitions - with around 615 deals signed during 2013 valued at US$ 100 billion, translating into an increase by 34 per cent in value over the previous year; patent cliff – estimated at around US$ 38.7 billion in pharma revenue at risk due to patent expiration in 2014, and another US$ 47.5 billion in 2015; growth in generic industry - at 9 per cent CAGR from 2009 to 2014 and currently, estimated at US$ 129 billion; rise in the R&D expenditure - by the pharmaceutical industry from US$ 88 billion in 2004 to US$ 135 billion in 2013, and forecast to reach US$ 149 billion by 2018; increased outsourcing of R&D to Contract Research Organisations - growing at an annual rate of about 10 per cent between 2008 and 2013, and accounting for around 10 per cent of total global pharmaceutical R&D spend currently.

Indian Pharmaceutical Industry

Indian pharmaceutical industry can be broadly divided into two periods, the pre-patent regime (before 2005) and the post-patent regime. While the pre-patent or process patent regime helped the industry develop into a world-class generics industry, the post-patent or product patent regime is aimed at encouraging new drug discoveries over the long-term. However, the launch of patented products in India has been slow.

India gained a foothold in the global arena, with reverse-engineered generic drugs and active pharmaceutical ingredients (API) and now seeks to become a major player in outsourced clinical research and the contract research and manufacturing services (CRAMS) segments.

India has the highest number of manufacturing facilities (332 sites) approved by the US FDA. Indian pharmaceutical companies have manufacturing opportunities in two segments - formulations and bulk drugs. The industry is dominated by exports (in both bulk drugs and formulations), which contributed about 60 per cent to the industry's sales in 2013-14. Over 100,000

drugs, across various therapeutic categories, are being produced in India. The domestic formulations industry is highly fragmented, in terms of both the number of manufacturers and variety of products. There are 300-400 organised players and about 15,000 unorganised players. However, organised players dominate the formulations market, in terms of sales.

Industry Performance

The Indian pharmaceutical industry is ranked third largest in volume terms and 10th largest in value terms (2.5 per cent of global share). The size of Indian pharmaceuticals Industry is pegged at US$ 33.9 billion, growing at roughly 13 per cent CAGR over a 5-year period, up to 2013-14.

The industry has not been affected much by the global slowdown. Notwithstanding this, exports of pharmaceutical products increased by a mere 1.2 per cent in 2009-10 over the previous year to aggregate US$ 8.7 billion. Exports witnessed a complete turnaround, growing by a healthy 18.5 per cent from US$ 8.7 billion during 2009-10 to US$ 10.3 billion during 2010-11, and by 25.1 per cent to US$ 12.9 billion in 2012-13. However, in the recent years, though there has been an increase in exports in terms of absolute value, y-o-y, growth has shown a declining trend in USD terms mostly due to weakening of rupee.

USA (with a share of 30.9 per cent), Russia (4.8 per cent), South Africa (4.3 per cent), UK (3.6 per cent) and Nigeria (3 per cent) are the major export destinations for India's drug formulations and biological products during 2013-14. However, during 2013-14, the Netherlands, considered as gateway market for the EU, emerged as a major market for Indian formulations and biological products. USA (14.2 per cent), Germany (5.3 per cent), Brazil (4.5 per cent), UK (3.7 per cent), and Japan (3.5 per cent) were the major export destinations for India's bulk drugs and intermediates in 2013-14.

Share of formulations (75 per cent) in India's total export of pharmaceuticals is higher than that of bulk drugs (25 per cent).

Market Share in Select Regions

The EU (27) is the largest pharmaceutical market in the world. In the year 2013, the EU imported pharmaceutical products worth US$ 242 billion. During 2013, the EU accounted for 14.5 per cent share in India's total exports of drug formulations and biological products. In 2013, among EU (27) countries, UK, with a share of 26 per cent, was the largest market for Indian drug formulations and biological products. Germany is the leading destination for India's bulk drug exports.

USA is the second largest pharmaceutical market in the world. In the year 2013, USA imported pharmaceutical products worth US$ 63 billion. India is the fifth largest supplier of drug formulations and biological products to the USA. The USA made up to a share of 39.1 per cent in India's total exports of drug formulations and biological products in 2013. USA is also a significant market for bulk drugs exports from India accounting for 71 per cent of India's total bulk drug exports to North America.

Africa imported pharmaceutical products worth US$ 15.3 billion during 2013. Africa as a region accounted for a share of 21.2 per cent in India's total exports of pharmaceutical products during 2013. Bulk drug exports from India to Africa amounted to around US$ 371 million in the same year.

Asia imported drug formulations and biological products worth US$ 80.1 billion during 2013. During 2013, Asia's share in India's total exports of drug formulations and biological products

stood at 15.2 per cent. Asia is the second major export destination for India's bulk drugs exports accounting for 28.9 per cent of total bulk drugs exported from India in 2013-14.

Latin America imported pharmaceutical products worth US$ 27.3 billion during 2013. Latin America's share in India's total exports of drug formulations and biological stood at 6.8 per cent. Latin America accounts for 8 per cent of total bulk drugs exports from India. Brazil is the second major export destination for bulk drugs exports from India.

Key Industry Trends

India's formulations exports have grown at a CAGR of about 17 per cent (in dollar terms) over 5 years up to 2013-14. Growth in exports to the semi-regulated markets sustained at about 12 per cent y-o-y growth during 2013-14, while the exports to the regulated markets grew at a modest 10 per cent during the same period, compared to 18 per cent growth seen in the last year. The slowdown was mainly on account of import alerts on Indian companies by the USFDA. Growth in semi-regulated markets has been largely driven by Asia and Africa.

Bulk drugs exports are estimated to have grown at a CAGR of about 17 per cent between 2008-09 and 2013-14, mainly on account of India emerging as a preferred manufacturing hub for high quality APIs. Of the total drug master filings (DMFs) filed with the US FDA, India's share has risen sharply to about 53 per cent for the 6 months ending June 2014, from about 19 per cent in 2001.

M&A - During 2013, the Indian pharmaceutical industry witnessed a total of 30 M&A deals in the pharma and biotech sector (inbound, outbound and domestic). Total deal value increased from US$ 1.7 billion in 2012 to US$ 2.5 billion in 2013.

Patents - According to the Indian Patent Office, during 2012-13, a total of 43,674 patents were filed, of which only around 6.8 per cent were filed in the drugs and pharmaceutical sector; and of the total 4126 patents that were granted in the year, around 8.3 per cent share was for pharmaceuticals.

R&D - Indian pharmaceutical companies have significantly increased their R&D budgets. In 2013-14, leading Indian pharma players spent anywhere between ₹ 5 billion to ₹ 12 billion on R&D, which represented an increase both in absolute terms as well as in proportion to net revenues.

Role of Exim Bank in Promoting Indian Pharmaceutical Sector

Exim Bank has been providing support to all segments in the pharmaceutical value chain. Exim Bank's exposure to pharmaceutical industry as on March 2014 has been 6.24 per cent in its total credit exposure. According to RBI's data on sectoral deployment of Gross Bank Credit, as of March 31, 2014, Indian banking sector's exposure on the drugs and pharmaceutical industry had been 0.8 per cent of the total non-food credit of the banking system, and 1.9 per cent of the total credit to the Industry Sector.

Exim Bank finances the pharmaceutical or biopharma companies to fund the research and development, new product development and other related costs for obtaining Intellectual Property Rights/regulatory approvals in regulated overseas markets. Financing by Exim Bank is in the form of either term loan/equity participation or a hybrid product.

The Bank supports the pharmaceutical companies in their strategic investments abroad for, inter alia, setting up manufacturing units and for acquiring overseas companies to get access to the foreign

market, technology, raw material, brand, and IPR.

Challenges and Prospects

Global pharmaceutical industry, in the recent years, is faced with four key challenges. These are as follows:

Global Health Care Reforms – Countries all over the world are steadily bringing about health care reforms transforming the health care sector from a volume-based to a value-based sector, significantly impacting the global pharmaceutical industry. Among the key developments, reducing costs, enhancing innovation and improving market access are the defining goals of the healthcare reform. Specific elements of reform vary by country, requiring pharmaceutical companies adopting national approaches. While many pharmaceutical companies are addressing these challenges arising out of health care reforms with a reactive approach, many others are considering health care reforms as prominent challenge in the next few years in terms of developing products that meet the goals of reformed systems.

Innovation and Value Addition - Product innovation and value addition has become one of the compelling challenges for the global pharmaceutical industry in view of the ensuing patent cliff and resultant revenue loss for the pharma companies. This has prompted them for increased R&D and new product development implying increased cost. Productivity in R&D is a constant challenge. Main challenges to productivity are managing risk without restricting innovation.

The ensuing patent cliff has also increased opportunity and competition in the generic industry; however, increased regulatory pressure on the generic industry introduced by the agencies is also envisaged to slow down the growth of the industry in the medium to long term.

Regulatory Compliance - Regulatory compliance has emerged as a critical challenge for the pharmaceutical industry, particularly in emerging markets, such as Southeast Asia, India, China and Latin America. Compliance issues facing the pharmaceutical industry include government policies, drug safety, counterfeiting, information security and privacy, intellectual property protection, corruption and adulteration, and M&A/joint venture (JV) and other third-party risks. Noncompliance is cost intensive, and may expose the companies to revenue losses, reputational risks, patient safety issues, criminal sanctions, and can jeopardize the future of the entire business unit.

Indian Pharmaceutical Industry – Key Challenges

Data Integrity – Data integrity practices followed in many USFDA approved units of Indian pharmaceutical companies have emerged as a major challenge for the industry in the recent times. Multiple data integrity issues reported by the investigators include failure to record activities contemporaneously; document back-dating; copying existing data as new information; re-running samples to obtain better results; and fabricating or discarding data. However, according to the industry sources, quality of finished drugs has not been under the US-FDA scanner. Nonetheless, such data integrity issues have resulted into import bans, which significantly impacted the performance of the companies, and also the pharmaceuticals in general.

Credibility of Clinical Trial Data - India has emerged as the ideal location to conduct clinical trials given its diverse pool of patients with diverse treatment needs, and access to a large, scientifically skilled,

workforce. However, capacity to regulate clinical trials has not kept pace with this growth leading to a number of reported unethical practices such as: limited patient compensation for adverse events; approval of drugs without clinical trials; and lapses in informed consent procedures. Government of India's recent efforts to bring in increased control on regulatory measures in clinical trial have resulted in delays in approvals and other complex procedural delays resulting in slowing down of the growth in clinical trial sector.

IPR - A major change in the patent laws in India was the enactment of the Patent (Amendment) Act, 2005, which made patent laws in India compliant with the TRIPS Agreement. Though there was an overall improvement in patent protection in India, recent issues such as granting of compulsory licenses (CLs) have been contentious. While CLs have been viewed as a necessary evil, in a developing country, like India, they have also caused grave concerns in the industry due to the revenue loss that CLs tend to cause.

Over Dependence on China for Bulk Drug and APIs - India is heavily dependent on China for bulk drug intermediates and APIs. Currently, China contributes 58 per cent of all such imports by value and almost 80 per cent by volume. Imports of APIs have grown at a CAGR of 18 per cent over the last decade. Over dependence situation on China for important bulk drugs and APIs is of significant concern for the Indian pharmaceutical industry as any shift in the Chinese policies or geo-political conditions between the two countries may result in a significant setback for the Indian formulation industry, which are heavily dependent on the API imports as raw materials.

R&D - The R&D profile of the Indian pharmaceutical industry includes development of generics, new drug delivery systems and new drug development. According to the Patent & Trademark Office (PTO) patents granted to Indian pharma companies constitute only 5 per cent for the new drug development and the rest has been on new processes, new dosage forms and drug delivery systems. Also the R&D activities of Indian firms are increasingly getting concentrated on life style diseases of global nature and little in addressing the drug delivery requirements of local diseases such as TB and malaria.

The trade liberalization measures though have attracted foreign investment in pharmaceutical R&D in India in the form of contract research, collaborative research projects, out-licensing and in-licensing partnerships, the scope for transfer of technology and joint ownership of technology has been very limited.

Further, the Indian pharmaceutical industry is also witnessing regulatory challenges with respect to uncertainties over the FDI policy, the new pharmaceutical pricing policy, a uniform code for sales and marketing practices, and compulsory licensing. These challenges have been slowing down the growth of the industry.

Way Forward

Manufacturing of Bulk Drugs and Intermediaries

Increased production of essential drug intermediaries and APIs at competitive prices should be the current focus of the Indian pharmaceutical industry to ensure adequate supply of essential raw materials and attain self-sufficiency, and reduce the dependence on imports.

Regulatory Compliance

In order to address GMP and data integrity issues, emphasis of Indian pharmaceutical companies should be on pursuing stronger compliance risk management capabilities, rather than to merely

satisfying the emerging legal requirements. Indian pharma companies are required to re-evaluate their organization's approach of managing compliance risks and adapt risk-based approach to compliance planning, execution, and monitoring and not depend overly on contract testing and production operations.

R&D - To promote novel research and development in the areas of neglected tropical diseases, there is a need for short/medium/long term policy to further incentivize the private sector for new drug development and bringing down the commercialization barrier in these areas. Public-Private Partnerships (PPPs) need to be more commercially oriented and proactive in bringing innovations to market. To commercialize new drugs developed for neglected tropical diseases, there is also a need to promote them by providing incentives to the private sector in the form of subsidies, or through drug assistance programmes, or by reviving public sector R&D for development of these drugs.

IPR - To promote IPR activity in the Indian pharmaceuticals industry, the pharmaceutical companies need to be encouraged to undertake new drug discoveries, innovate new dosage forms, and new uses of existing drugs. This may be done through subsidizing the cost of filing and maintenance of patents, and supporting the cost of litigations and other legal formalities. There is an urgent need for the SMEs to develop collaborative research culture with public and privately funded research organisations for their survival and increased participation in IPR activities.

Clinical Research & Trials - To address unethical practices in clinical research and encourage clinical trials in India, the approval mechanisms for protocols need to be more transparent and time efficient. In addition, a policy promoting clinical research and innovation needs to be supported by action at various levels, which may include rationalizing regulations; capacity building; accreditation of investigators, establishing sites and ethics committees; supporting infrastructure development; creating public education and awareness; and ensuring transparency and openness.

Pharma-SME Development – To help pharma-SMEs realize their transnationalisation potential there is an urgent need for provision of sufficient low cost finance, strengthening access to national research laboratories, promoting pharmaceutical SME clusters, and continuous training and skill development programmes for transnationalization.

Cluster Development - Setting up of pharma specific clusters in SEZ formats may help the industry in addressing the regulatory requirements and resultant costs. Common facilities, including common patent libraries, effluent treatment plants, and subsidized power may be some of the constituents of the clusters.

Skill Development and Training - There is a need to focus on skill development and training of personnel for the pharmaceutical and lifesciences industry at various levels, such as analytical, manufacturing and quality management, documentation, regulatory requirements and statistical techniques. Academic syllabus of pharmaceutical training institutions may include these areas.

Trade Issues - Trade barriers faced by the Indian pharmaceutical industry in overseas markets, such as delayed approvals, severe administrative requirements and sanctions, drop in approval rates, delay in consignment clearances, rejection of consignments, and higher fees and commissions may be addressed through diplomatic channels, in addition to negotiations between the trade players.

Pricing of Formulations – According to the industry, a stable pricing policy or market based price control may continue to encourage the formulation industry to invest in R&D in NDDS and dosage forms. They also suggest that the prices of the patented products may be regulated on Purchasing Power Parity basis.

Combination products (Fixed Dose Combinations-FDC) are India's indigenous contribution to the world, with considerable approvals by regulators in the overseas markets. Depending on efficacy testing and patient compliance, FDCs may be supported and encouraged in domestic markets.

Outlook

The global market for pharmaceuticals is forecast to register a steady growth. IMS Institute for Healthcare Informatics had forecast that global spending on medicines is expected to increase by 4 per cent to 7 per cent CAGR between 2014 and 2018. USA is expected to drive the growth, with its spending expected to increase between 5 per cent and 8 per cent. Emerging markets too are expected to register healthy growth, with projected growth rates in the range of 8 per cent to 11 per cent.

The Indian pharmaceutical industry is projected to grow steadily in the medium term. In terms of volume, the Indian pharmaceutical market is forecast to be a major market, second only to the USA by 2020 driven by rapid urbanisation and greater economic development. Rural markets are also projected to grow faster, driven by step-up from current poor levels of penetration.

A large number of patent expirations continue to offer strong growth prospects for the Indian generic players in the developed markets, steadily driven by the USA. Amongst new frontiers, Japanese generic market offers considerable potential for Indian generic companies, though with significant challenges. Emerging markets with some of them being for branded generics offer strong growth prospects for Indian players given the high out of pocket expenditure on healthcare in these markets, and relatively easier regulatory pathways.

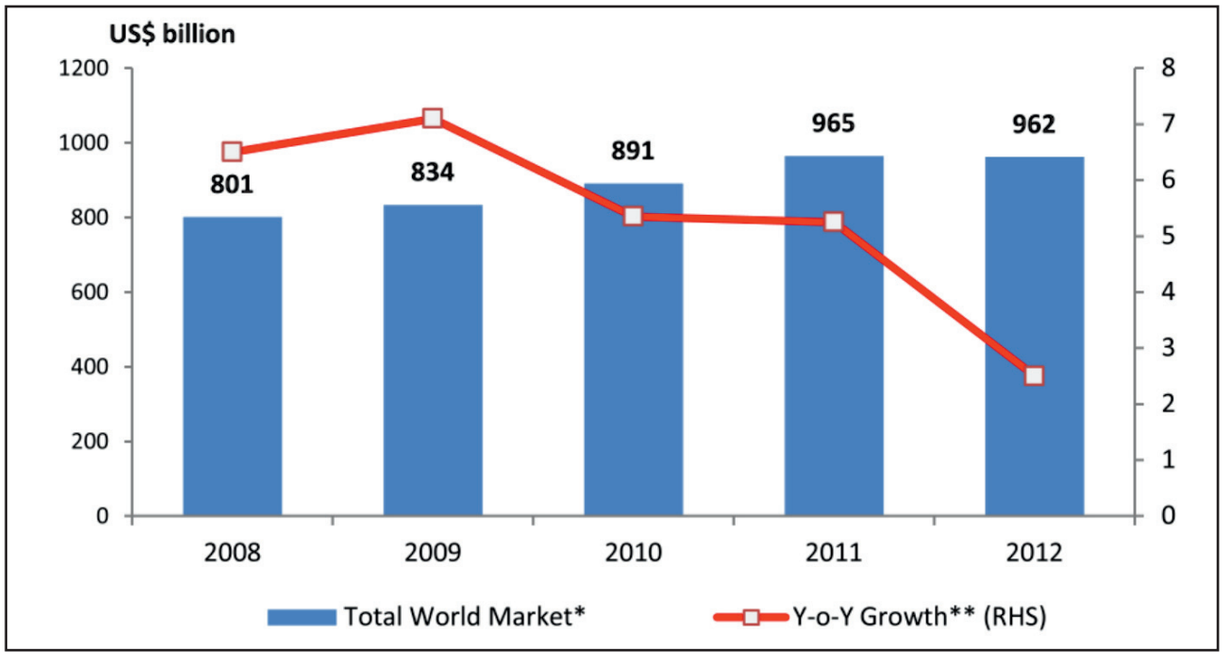
Besides new markets, Indian pharmaceutical companies are also tapping new areas, such as biologics/biosimilars for long-term growth avenue. Despite challenges, leading Indian pharmaceutical companies is envisaged to continue to exhibit strong profitability indicators and credit metrics. Outlook for the Indian pharmaceutical companies remains favourable as companies are forecast to continue to benefit from the recovery in the domestic market, strong growth potential for generics in the developed markets, and potential outsourcing opportunities.

1. GLOBAL SCENARIO

The global pharmaceutical market was estimated at US$ 962 billion in 2012[5]. In 2012, the global pharmaceutical industry (including audited and unaudited markets) grew at a muted pace of 2.4 per cent y-o-y (on a constant currency basis), vis-a-vis a growth of 5.3 per cent in 2011. Regulated markets such as the US, Europe, and Japan, continued to grow at a slower pace (vis-a-vis the emerging markets) following the patent expiry of key drugs, saturation of markets and declining productivity of research and development activities. Additionally, the global economic slowdown has also contributed to a weaker pricing environment for branded drugs, which in turn led to higher substitution of generic drugs. Growth momentum in emerging markets continued in 2012.

North America (mainly the US), Europe and Japan are the dominant markets in the global pharmaceutical industry. Despite shrinking by 1 per cent y-o-y in 2012, the North American market remained the single-largest market and accounted for more than a third of the total pharmaceutical sales for the year. Sales contracted, as many leading branded drugs went off-patent during the year. The rate of discovery and production has not been able to match pace with the rate of erosion (loss of patent exclusivity).

Exhibit 1.1: Global Sales in Pharmaceuticals



* Actual quarterly exchange rates have been used to compute global sales.
** Growth in constant dollar terms
Source: IMS Health

[5]IMS Health

Table 1.1: Region-wise Sales in Pharmaceuticals (2012)

World Market*	Global Sales		% Constant US$ Growth	
	US$ billion	Market Share (%)	y-o-y	CAGR (2007-12)
North America	349	36.2	-1.0	2.2
Europe	222	23.1	-0.8	1.1
Japan	112	11.7	0.0	3.2
Asia, Africa, Australia	168	17.5	12.8	12.9
Latin America	73	7.5	10.9	11.5
Total	**962**	**100.0**	**2.4**	**5.3**

* - Includes both audited and unaudited markets.
Note : Sales cover direct and indirect pharmaceutical channel purchases in US dollars from pharmaceutical wholesalers and manufacturers. The figures above include prescription and certain over-the-counter data and represent manufacturer prices. Asia excluding Japan.Total may not add due to rounding off.
Source: IMS Health

Sales of pharmaceuticals in Europe declined by about 1 per cent y-o-y, while sales in Japan remained stagnant. Pharmaceutical sales in other regions, such as Asia (excluding Japan), Africa and Australia, grew by 13 per cent y-o-y and accounted for about 17 per cent of total global pharmaceutical sales in 2012. Latin America registered a healthy growth of 11 per cent y-o-y, contributing US$ 72.8 billion of global sales during the year. Increasing prevalence of diseases, rising penetration of healthcare and increasing affordability have aided the growth in these markets.

With respect to therapy classes, oncology retained the top spot with a 8 per cent share in overall global pharmaceutical sales. Growth moderated to 8.5 per cent, as a few major drugs have lost patent

Table 1.2: Therapy-wise Sales in Pharmaceuticals

Rank	Therapy Class	Global Sales (2013)	Market Share	Growth y-o-y
		US$ billion	(%)	(%)
1	Oncologics	67.1	7.7	8.5
2	Pain relievers	57.3	6.6	4.7
3	Anti-diabetics	54.4	6.2	10.2
4	Anti-hypertensives	49.6	5.7	-1.7
5	Anti-bacterials	40.2	4.6	2.6
6	Mental health	39.5	4.5	-2.6
7	Respiratory Ailments	38.1	4.4	-1.8
8	Autoimmune Diseases	31.1	3.6	14.4
9	Lipid regulators	28.9	3.3	-10.8
10	Dermatologics	26.8	3.1	11.3
	Total leading therapy classes	**324.4**	**49.5**	

Note: 1) Sales cover direct and indirect pharmaceutical channel purchases in dollar from pharmaceutical wholesalers and manufacturers. The above figures include prescription and certain over-the-counter data and represent manufacturer prices. Totals may not add due to rounding off. 2) Growth is calculated at constant US$ to normalise for exchange rate fluctuations.
Source: IMS Health

exclusivities over the past few years. The market for anti-diabetics and auto-immune diseases grew by 10 per cent and 14 per cent, respectively. The auto-immune category includes leading drugs, such as Remicade, Enbrel and Humira, which treat a wide variety of immunological diseases and contribute to nearly US$ 20 billion in global pharmaceutical sales. The anti-diabetics segment grew with the growing prevalence of the disease.

Global exports of pharmaceutical products (HS Code 30) registered a modest growth at a CAGR of 3.7 per cent between 2009 to 2013, from US$ 420 billion to US$ 486 billion. With a share of 15.4 per cent in total global exports of pharmaceutical products, Germany was the leading exporter of pharmaceutical products during the year 2013, followed by Switzerland (11.9 per cent), Belgium (10.4 per cent), and USA (8.2 per cent). As an aggregate, Europe accounts for about 80 per cent (US$ 389 billion)[6] of total exports of pharmaceutical products. In terms of growth, exports from India registered the highest growth at a CAGR of 23.7 per cent during the period 2009 to 2013, followed by Italy at a CAGR of 12.2 per cent, and Switzerland at a CAGR of 8.9 per cent.

With a share of 58 per cent (US$ 289 billion)[7] in total global imports of pharmaceutical products,

Table 1.3: Major Exporters and Importers of Pharmaceutical Products (HS Code 30) in the World

Exporters	2013	Share in global exports	CAGR	Importers	2013	Share in global exports	CAGR
	US$ billion	(%)	(%)		US$ billion	(%)	(%)
Germany	74.9	15.4	4.7	USA	63.4	12.7	3.2
Switzerland	57.6	11.9	8.9	Germany	45.2	9.1	0.3
Belgium	50.4	10.4	0.1	Belgium	41.0	8.2	0.7
USA	39.7	8.2	-0.6	UK	27.7	5.6	7.8
France	37.0	7.6	2.6	France	26.1	5.2	1.5
UK	32.1	6.6	1.3	Switzerland	22.1	4.4	7.7
Ireland	26.1	5.4	-2.4	Italy	21.0	4.2	3.1
Italy	23.6	4.9	12.2	Japan	20.9	4.2	12.4
Netherlands	22.5	4.6	-4.0	Netherlands	16.9	3.4	-9.3
Spain	13.0	2.7	6.0	China	15.1	3.0	25.9
India	11.7	2.4	23.7	Russian Federation	14.6	2.9	14.4
World	**485.5**	**100.0**	**3.7**	**World**	**498.3**	**100.0**	**4.3**

Source: Trademap, ITC Geneva; Exim Bank Analysis

[6] Trademap, ITC Geneva
[7] Trademap, ITC Geneva

Box - 1:

Pharma emerging Growth Requirements

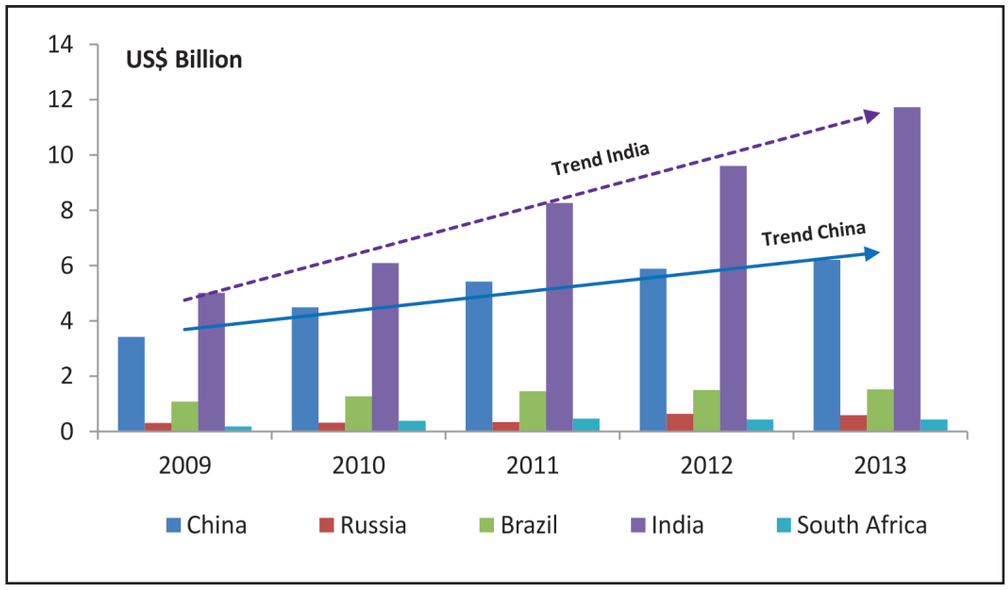
Tier 1	**+US$71 bn Growth**	• China
Tier 2	**+US$12-22bn Growth**	• India • Russia • Brazil
Tier 3	**+US$ 1-7bn Growth**	• Turkey • Indonesia • Poland • Argentina • Thailand • S Africa • Mexico • Pakistan • Egypt • Venezuela • Ukraine • Romania • Vietnam

Source: IMS Heath 2013

Europe was the largest importer of pharmaceutical products during the year 2013. USA as a country was the second largest importer of pharmaceutical products accounting for 12.7 per cent (US$ 63 billion)[8] of total imports during the same period.

Among the pharma-emerging markets, India's exports of pharmaceuticals have registered a significant growth at a CAGR of 23.7 per cent during the period 2009 to 2013 accounting for 2.4 per cent share in global exports of pharmaceuticals in 2013. China has emerged as a significant importer of pharmaceutical products growing at a CAGR of 25.9 per cent during the same period. In 2013, Brazil, Russia, India and China (BRIC) as an aggregate accounted for 4.1 per cent of global exports and 7.8 per cent of global imports of pharmaceutical product.

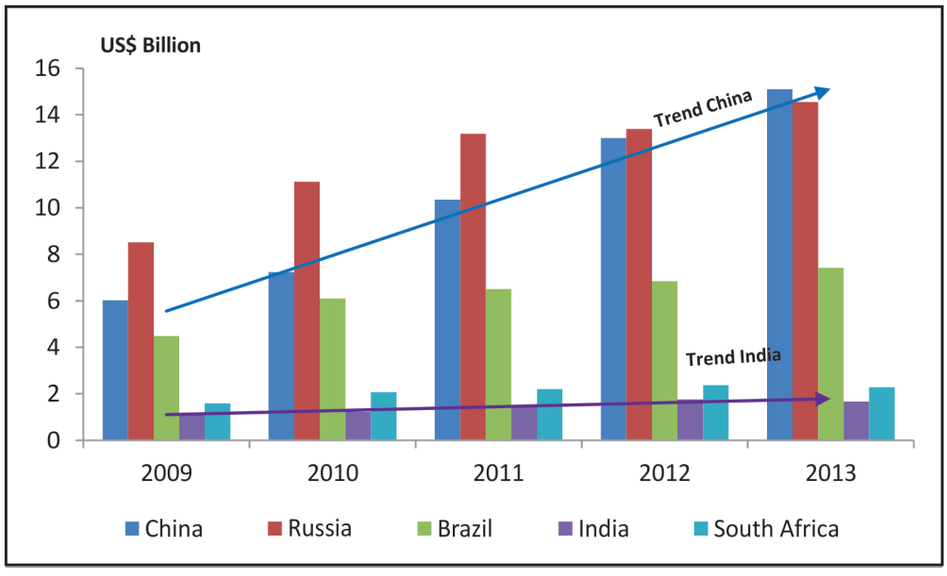
Exhibit 1.2: Export of Pharmaceutical Products from BRICS



Source: Data derived from Trademap, ITC Geneva; Exim Bank Analysis

[8] Trademap, ITC Geneva

Exhibit 1.3: Import of Pharmaceutical Products from BRICS



Source: Data derived from Trademap, ITC Geneva; Exim Bank Analysis

2. KEY DEVELOPMENTS IN REGULATORY ENVIRONMENT

The pharmaceutical industry is influenced by a host of practices, which may primarily relate to price regulations, patent laws, safety policies, promotion regulation, insurance, procurement regulation, etc. Hence, the regulatory mechanism plays a crucial role in the trade and development of the pharmaceutical industry. Some of the recent developments and key trends in the regulatory environment that might significantly govern the global pharmaceutical sector are briefly discussed in the current chapter.

Impact of FDA and Court Rulings - Several decisions made by the Supreme Court of the USA in 2013 are anticipated to have a profound impact on the US as well as global pharmaceutical industry. For generic pharmaceuticals, the Court confronted the law governing a controversial pharmaceutical marketing practice known as reverse payment agreements (pay for delay) in which branded drug companies pay generic companies to delay the commercialization of their products. The verdict is anticipated to bring about increased competition in the branded drug segment earlier in its commercial lifecycle. Though this is envisaged to be good for consumers, but disadvantageous for innovator companies.

In another key decision the Court ruled that generics manufacturers are substantially immune from civil claims regarding injuries caused by their products. This decision basically eliminates the primary incentive for evaluating safety and design defects before marketing a generic product. This ruling is threatened by a proposed shift in FDA position on generic drug labeling. The FDA has submitted a proposed rule that would allow generic companies to change their labelling under appropriate circumstances, just like brand companies. FDA's Proposed Rule would allow generic manufacturers to independently update product labeling through the "changes being effected" (CBE-0) supplement process currently only available to branded drug manufacturers for product safety labeling. Under the Proposed Rule, generic manufacturers could unilaterally change their safety-related product labeling, and those changes could take effect simultaneously with the companies' notification to the FDA and of the branded drug manufacturer. No prior approval would be required; if this rule is adopted, the regulatory and liability landscape for the generic drug industry is envisaged to be completely transformed.

Quality Risk Management (QRM) - The International Committee of Harmonization (ICH) issued its ICH Q8, Q9 and Q10 guidances between 2005 and 2009. Validation guidance in 2011 formally began the agency's push to instill the concepts of scientific understanding and risk management as a basis for product design and quality. Despite these frameworks the industry has been slow to adopt these principles as part of its core drug development philosophy as the list of companies under warning letters or consent decrees continues to lengthen. However, several factors are driving the change at seemingly slow pace. First is the growing realization that the industry must get better at identifying and developing new drug therapies to remain competitive. This has prompted the industry to start looking at formalized decision-making tools as part of their risk management process. Second, in Asia, risk management is becoming a central component of any regulatory inspection and regulatory filing. While in the USA,

the focus has been on clinical risk management via its REMS program, Asia is focusing on risk management tools for tactical components like facility design qualification, equipment selection, and commissioning and qualification. This is driving the integration of risk management tools as part of the overall project planning exercise rather than a checkbox activity. In the USA, many large multinationals are transforming their development programs to leverage knowledge management and utilized formal risk management tools. This trend is envisaged to help move the industry towards a more scientifically-based development philosophy.

Drug serialization - Anti-counterfeiting activities are rapidly becoming the central focus of many countries' regulatory landscape. Global pharmaceutical industry faces counterfeiting challenges as well as theft, diversion and false returns to manufacturers. The World Health Organization (WHO) estimates counterfeit drugs to constitute approximately 1 per cent of the supply in developed countries and 30 per cent to 40 per cent in developing countries. In November 2013, the U.S. passed the Drug Quality and Security Act (H.R. 3204), which would preempt all state laws relating to drug pedigrees and track-and-trace systems, to assure the security and safety of drug supply chain. The rollout is anticipated to take place over the next decade with the goal of acheiving unit level traceability for all drugs manufactured in the USA. Serialization regulations are also in place currently in Turkey, India, China, Brazil, Argentina and South Korea. At the latest Global Track and Trace Roundtable, held in October 2013, almost every major pharmaceutical market stated plans to formalize serialization by 2017.

Anti-Counterfeit Measures - On October 1, 2011, Anti-Counterfeiting Trade Agreement (ACTA) has been signed as a multilateral treaty by thirty-one countries (Australia, Canada, Japan, Morocco, New Zealand, Singapore, South Korea, USA, EU, and its 22 member states), for the purpose of establishing international standards for intellectual property rights enforcement. The Agreement aims to establish an international legal framework for targeting counterfeit goods, generic medicines and copyright infringement, and propose to create a new governing body outside the existing regulatory framework, such as WTO, WIPO, and the United Nations. The move has been largely detrimental for Indian generic pharmaceutical industry. Though the World Health Organisation (WHO) has dropped its plan to include generic drugs in its definition of counterfeit goods, still generic manufacturers are facing the challenge of seizure by EU Custom Officials, even if the consignment is in trans-shipment stage. EU Regulation 1383/2003 allows for seizure or delay at Customs if the goods are suspected to be of patent infringement. Such challenges are reported even though the origin and destination does not have such anti-counterfeit measures in force.

Licensing Agreements - The ensuing patent expiration of blockbuster drugs and apprehensions of resultant revenue loss have been prompting the large innovator companies, mostly multinationals, to reduce their focus on new drug discoveries. Instead, these companies tweak the existing compounds, and calling them new. This practice, increasingly followed by drug manufacturers in the developed countries, is being opposed by the national patent organizations in the developing countries, such as India and Egypt. The tweaked products are perceived as a threat to the generic drug industry, and viewed this practice hindering the achievement of affordable healthcare. Another approach adopted by the innovators is to sign licensing agreements with generic companies in the developing countries. While such moves are seen as favourable for the generic drug industry,

they are perceived as creative business strategy of managing the competition by undermining the patent laws in the developing countries. This in turn threatens to reduce the competition needed to keep the medicine prices low and may ultimately shrink the global supply of affordable medicines.

SSFFC – WHO has come up with another initiative, called Substandard/Spurious/Falsely-labelled/Falsified/Counterfeit medical products (SSFFC), which has excluded the originally inclusive IP Issues, such as patent infringement from its ambit. SSFFC has been making slow but steady progress through meetings in 2012, 2013 and the latest on October, 2014. The goal of the SSFFC Mechanism is to promote international collaboration on strategies to address the falsification of medicines from the standpoint of public health, excluding trade and intellectual property considerations. A major focus is on getting products registered and maintaining a two-way flow of information once the product is in use; e.g. WHO will inform the national authority of any withdrawals, suspensions or delisting of prequalified medicines and they, in turn, will keep WHO informed of any national deregistration or issues about the medicine's safety or efficacy. Through such mechanism, WHO also envisages strengthening of national and regional capacity by developing strategies to prevent SSFFC medical products reaching patients.

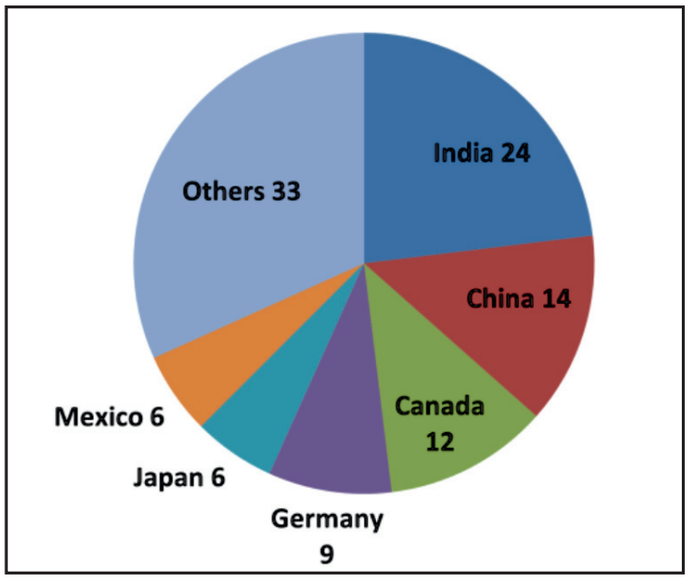
Current Good Manufacturing Practices (CGMP) - The US FDA inspects manufacturing sites in order to check adherence to current good manufacturing practices. The manufacturing operations must comply with current good manufacturing practices (CGMP) in order to have a site clearance. In case of deviations from ideal manufacturing practices, the FDA lists down deviations in Form 483, and share the observations with the manufacturers, who then are expected to reply to the FDA with their corrective and preventive actions that will provide assurance of their adherence to the CGMP requirement. In case of further non-compliance or inadequacy of corrective and preventive actions, the FDA may issue a warning letter or an import alert. As a consequence of the increased focus of the US FDA on generic drug manufacturers, the number of warning letters issued to drug manufacturing sites has increased. On account of this, countries with a large manufacturing base have shown a rise in drug manufacturing warning letters and import alerts.

The warning letters are intended to enable defaulting firms to increase their compliance before further regulatory actions, such as import alerts and consent decrees, which altogether prohibits these firms from supplying to the US market. Consequently, during the period between 2005 to March 2014, close to 103 warning letters were issued by the US FDA to drug manufacturers.

Country-wise, India had a larger share of warning letters compared to other countries. However, on a per site basis, India's 332 approved sites accounted for just about 24 drug manufacturing warning letters as compared to Canada's 25 sites which accounted for 12 warning letters. Thus, on a per site basis, India accounted for a lower number of warning letters as opposed to countries, such as Canada and Germany. This indicates that the FDA's focus has been more on company-specific actions as opposed to any country-specific actions.

As of March 2014, import alerts were issued against 100 drug manufacturing firms. Import alerts are publicly available documents that enable the physical impounding of any drug substance produced at the affected plant site. The

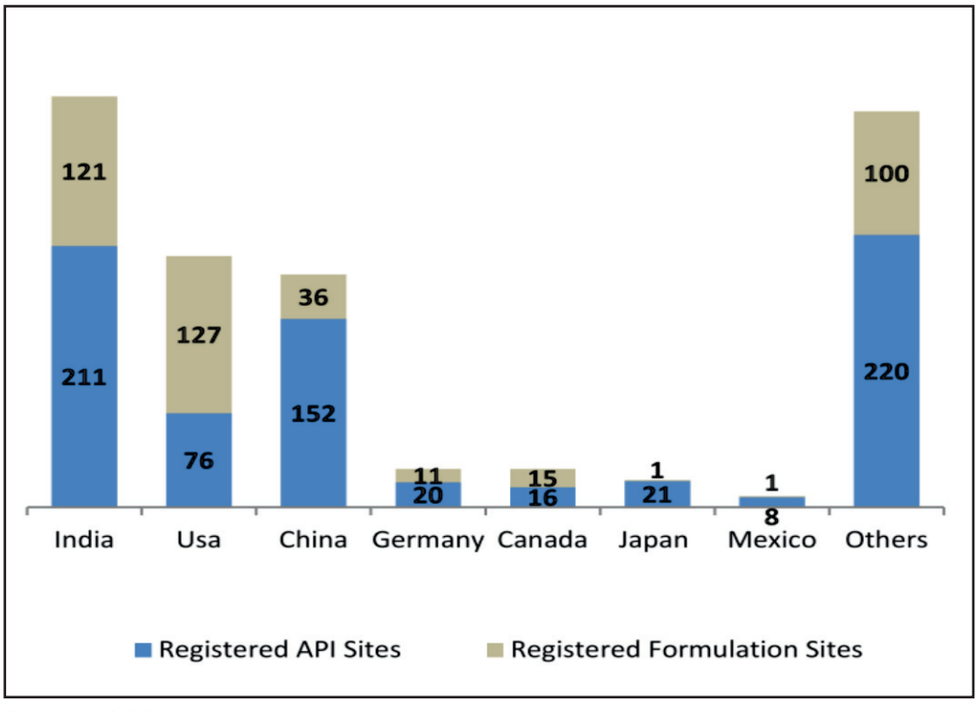
Exhibit 2.1: No. of Warning Letters Issued



Source: US FDA

manufacturer has to stop all production from the factory site, until resolution of the issues. The FDA generally imposes an import alert against a drug manufacturing site in cases where the FDA deems that sufficient response to a warning letter is missing. Most import alerts have thus been issued against firms which failed to comply even after receiving the warning letters. However, in certain instances, where the FDA deems serious nature of violations during a site inspection, they issue direct import alerts. Overall, country-wise, China, with its much smaller manufacturing base, has a higher number of firms under import alerts as compared to India and other countries.

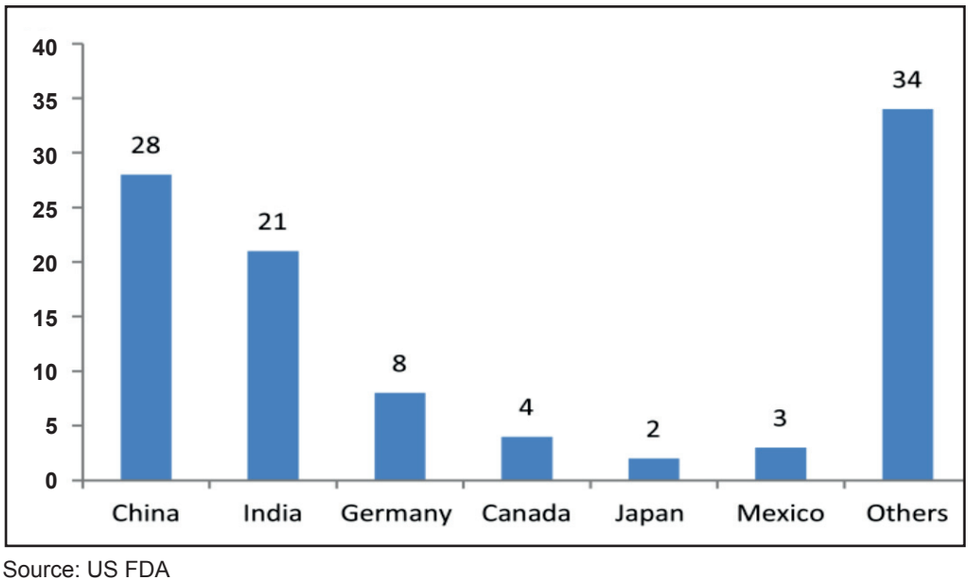
Exhibit 2.2: Approved Manufacturing Base



Source: US FDA

Import alerts - Import alerts issued against Indian manufacturing plants[9] in 2013 accounted for 49 per cent of the total 43 such imports alerts issued by US FDA worldwide. The import alerts have been issued on account of several violations by the Indian companies in areas of quality control issues, hygiene, lack of reliability and accuracy of data and adulteration. An import alert effectively bans all exports of pharmaceutical products from such manufacturing plants into the USA, and renders all the stocks of the impacted production batches unsalable in the USA market. This has dented the prospective revenue streams of banned Indian manufacturers. Similarly, the R&D effort that went into the development of new molecules, for which approvals were planned to be obtained for manufacture in the banned facilities, cannot be commercialised/monetised for the duration of the import alert. However, the import alerts have so far not reduced the Indian pharmaceuticals exports to the US by a substantial amount. Most of the manufacturing sites which came under the FDA import alert in 2013 and 2014 were small API manufacturers. Sun Pharma's Gujarat-based API unit that came under FDA import alert in March 2014 accounts for less than 1 per cent of the company's revenue. A substantial revenue impact is anticipated for Wockhardt (above 25 per cent top-line erosion likely) and Smruthi Organics Limited (above 50 per cent). Significant revenue erosion is also not anticipated for Ranbaxy Laboratories and RPG Life Sciences Limited. However, they may face a substantial opportunity loss on account of postponed product introductions and expenditure on corrective actions along with the time and effort required to regain FDA approval (usually one to two years).

Exhibit 2.3: Country-wise Number of Firms under Import Alert



Source: US FDA

[9]Wockardt; Ranbaxy Laboratories Ltd., Sun Pharmaceuticals, Dr. Reddy's, Lupin, Cadilla Pharmaceuticals

Generic Drug User Fee Amendment (GDUFA) - The US FDA has announced a new fee structure under the GDUFA programme for the period, October, 2014 to September, 2015. The latest order has reduced the dossier filing fees by about 8-15 per cent, and hiked the site registration fees by about 15-22 per cent. FDA expects close to 1,276 ANDA (Abbreviated New Drug Applications) filings and 701 DMF (Drug Master Files) filings during 2015.

Table 2.1: New GDUFA fee structure

Application fees US$	**2015**	**2014**	**2013**
ANDA Fee	58,730	63,860	51,520
PAS Fee	29,370	31,930	25,769
DMF Fee	26,720	31,460	21,340
Facility Fees US$	**2015**	**2014**	**2013**
API Domestic	41,926	34,515	26,458
API Foreign	56,926	49,515	41,458
FDF Domestic	247,717	220,152	175,389
FDF Foreign	262,717	235,152	190,389

ANDA: Abbreviated new drug application
API: Active pharmaceutical ingredient
PAS: Prior approval supplement
Source: US FDA

3. KEY TRENDS IN PHARMACEUTICAL MARKET

Reducing cost of production, enhancing innovation and improving market access are the defining goals of the pharmaceutical sector, in the recent years. Some of the key trends in the global pharmaceutical market that have been significantly defining the way forward in the sector are discussed this chapter.

Mergers and Acquisitions (M&A)

Mergers and Acquisitions have been dominating the global pharmaceutical industry after the global financial crisis. During 2013, the global pharma industry saw 615 deals valued at US$ 100 billion, which was higher than the deals signed in 2012 (valued US$ 67 billion). This translates to an increase of 34 per cent in 2013, in the value of mergers and acquisitions deals compared to the previous year. Among the total transactions that underwent in 2013, 37 transactions had published values in excess of US$ 500 million, up from 33 in 2012. As in the previous years, most of the deals were located in the USA and Western Europe. The main deal drivers during 2013 were access to new products, tax savings and economies of scale.

Table 3.2: Top Locations of Global M&A in the Pharma Industry (2013)

	Acquiror Location		
Target Location	**North America**	**Western Europe**	**Japan**
China	2	2	
LatAm	4	5	
India	3	2	
CEE	5	5	
Other	9	6	1
Total	**23**	**20**	**1**

Source: IMAP's Pharma & Biotech Industry Global Report — 2014

Table 3.1: Summary of Mergers and Acquisitions in the Pharma Industry

	Location of Target									
Range	**North America**	**Western Europe**	**China**	**CEE**	**India**	**Japan**	**LatAm**	**Other**	**Total 2013**	**Total 2012**
More than US$ 1 bn	9	6						2	17	14
US$ 100 mn - US$ 1 bn	33	25	16	4	2		2	6	88	75
US$ 10 mn - US$ 100 mn	31	32	47	4	7	2	4	12	139	102
Less than US$ 10 mn	20	21	26	1	4	10	1	14	97	62
Unknown	111	87	8	26	8	9	11	14	274	203
Total	**204**	**171**	**97**	**35**	**21**	**21**	**18**	**48**	**615**	**456**

Source: IMAP's Pharma & Biotech Industry Global Report — 2014

Patent Cliff

Over the past century, Loss of Exclusivity (LOE) or patent cliff has emerged as a major concern for the pharmaceutical industry. In 2014, about US$38.7 billion in pharma revenue has been estimated to be "at risk" due to the LOE. By 2015, the figure is expected to reach US$ 47.5 billion (nearly matching the loss level of US$ 54.7 billion during the 2012 patent cliff). Some of the large blockbluster drugs, such as Copaxone (Teva), Nexium (AZ), and Namenda (Forest Laboratories) is projected to be significantly impacted by the patent cliff. As the next patent cliff will be in 2015, pharma companies have been following unconventional means, such as legal protection, acquisition, corporate transformation, and regulatory shields to write-off patent cliff-related revenue losses. For instance, Forest Laboratories' acquisition of Actavis is projected to offset the losses from Namenda, the branded version of which was withdrawn from the market in August 2014. It is reported that Novartis has drawn upon substantial benefits from the US ban on Ranbaxy. The latter holds the first-to-file status for Diovan, a drug from the house of Novartis. However, due to the ongoing ban, Ranbaxy has been unable to launch its generic version in the USA. Therefore, the entry of other US generics is also barricaded. Novartis continues to generate revenue from Diovan, despite the patent loss in 2012. Similarly, other companies, such as Novo Nordisk (Drug: NovoRapid; LOE: September 2013) and Allergen (Drug: Restasis; LOE: May 2014) continue to reap the benefits, even after the patent expiry. Further, Symbicort (LOE: October 2014) and Advair (LOE: August 2014) will continue to enjoy exclusivity (after patent expiry) due to the difficulties faced by generic manufacturers to prove bioequivalence for their generic alternatives. Going ahead in 2015, Pfizer and Novartis are expected to recover from the revenue loss from LOE on their small molecules (Celebrex and Gleevac) through corporate transformation (Pfizer's three-way business split) and new molecule-discovery-based risk sharing (for Novartis). Biologics, such as Lantus (expected 2015 revenue of US$ 6.5 billion) and Neulasta (expected 2015 revenue of US$ 3.4 billion) will continue to enjoy their biologic status (even after patent expiry), with Lantus facing a delayed threat from biosimilars being developed by Eli Lilly and Boehringer Ingelheim, and Merck and Samsung. Key drugs and companies facing patent cliff is presented in Annexure -1.

Growing Generic Industry

Due to several patent expirations, the generic drug industry has experienced significant growth during the recent years. The global market for generic drugs was worth US$ 84 billion in 2009, and has been projected to reach US$ 129 billion by 2014, growing at a 9 per cent CAGR. Rising cost pressure on health care has resulted in an increase in generic pharmaceutical usage as generic drugs cost 30 to 80 per cent less than their patented equivalents. Although there is still room for growth in generics, delivering is becoming more complex as: commoditization, combined with extensive reforms in both regulated and unregulated markets, are increasing the pressure on prices; product portfolio becoming increasingly complex; managing business while maintaining lean structure and striving for cost leadership has become more intricate; quality control in manufacturing is becoming a challenge; and new players intensifying competition. As a result of these challenges the global generic market is projected to grow slow at 6 to 7 per cent per year until 2018.

R&D activities and Contract Research Organisations

Pharmaceutical industry is knowledge intensive and R&D investment plays a crucial role in the growth of the industry. R&D spending by the pharmaceutical industry continues to rise in the recent years. Between 2004 and 2013 the total industry expenditure on R&D rose from US$ 88 billion to US$ 135 billion, and is forecast to reach US$ 149 billion by 2018[10]. At the same time, the estimated cost of bringing a new chemical or biological product to market has more than trebled from US$ 451 million to US$ 1.5 billion[11]. Meanwhile, the average number of annual US Food and Drug Administration (FDA) approvals for new molecular entities (NMEs) that fell from 31.5 in 1990 to an average of 22.9 during the period 2001-2010[12] has been showing an upturn with the average annual NME figures for the years 2011-2013 rising to 32. One notable trend observed in R&D strategy in pharmaceutical industry, in the recent years, have been to forge stronger alliances with universities, with some companies moving their R&D bases closer to university sites to promote collaboration and enhance the scientific dialogue. In addition to partnerships, other prominent trend include asset swaps, carve outs, and transaction collaborations across the industry in an effort to spread risk and reduce R&D investment. There is also a rise in R&D licensing, as well as outsourcing to Contract Research Organizations (CROs). Although preclinical and clinical trial activity has been outsourced for some time, pharma companies are now starting to contract drug research and registration work. The global drug discovery outsourcing market (including early stage R&D) has been growing at an annual rate of about 10 per cent between 2008 and 2013. Currently, outsourcing accounts for around US$ 13 billion per year, close to 10 per cent of total global pharmaceutical R&D spend. This figure is forecast to double to US$ 25 billion by 2018[13]. Close to 40 per cent of the estimated US$ 51 billion spent on clinical development in 2013 was outsourced[14].

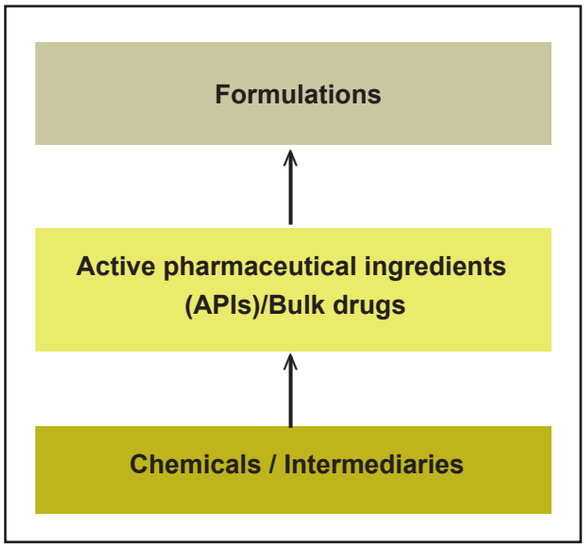
[10] World Preview 2013 Outlook to 2018, EvaluatePharma, June 2013
[11]The R&D cost of a new medicine, J. Mestre-Ferrandiz, J. Sussex and A. Towse, Office of Health Economics, December 2012 (Hansen, 1979; Wiggins, 1987; DiMasi et al, 1991; OTA, 1993; DiMasi et al, 2003; Mestre-Ferrandiz et al, 2012)
[12]FDA official figures, March 2014
[13]The New Trends of Global Drug Discovery Outsourcing 2013, Research and Markets report, September 2013
[14]Quintiles talks R&D spend and outsourcing trend in Second Public Offering, Outsourcing – pharma.com, 10 March 2014

4. INDIAN PHARMACEUTICAL INDUSTRY

Industry Characteristics

The evolution of the Indian pharmaceutical industry can be broadly divided into two periods, the pre-patent regime and the post-patent regime. In the pre-patent regime (before 2005), India recognised only process patents, which helped in building the basis of a strong and competitive domestic industry. In 2005, India entered the product patent regime which marked the end of a protected era, and signaled a new phase in the integration of Indian players into the global market. While the earlier process patent regime helped the Indian pharmaceutical industry develop into a world-class generics industry, the product patent regime is aimed at encouraging new drug discoveries over the long-term. However, the launch of patented products in India has been slow.

Exhibit 4.1: Indian Pharmaceutical Industry Value Chain

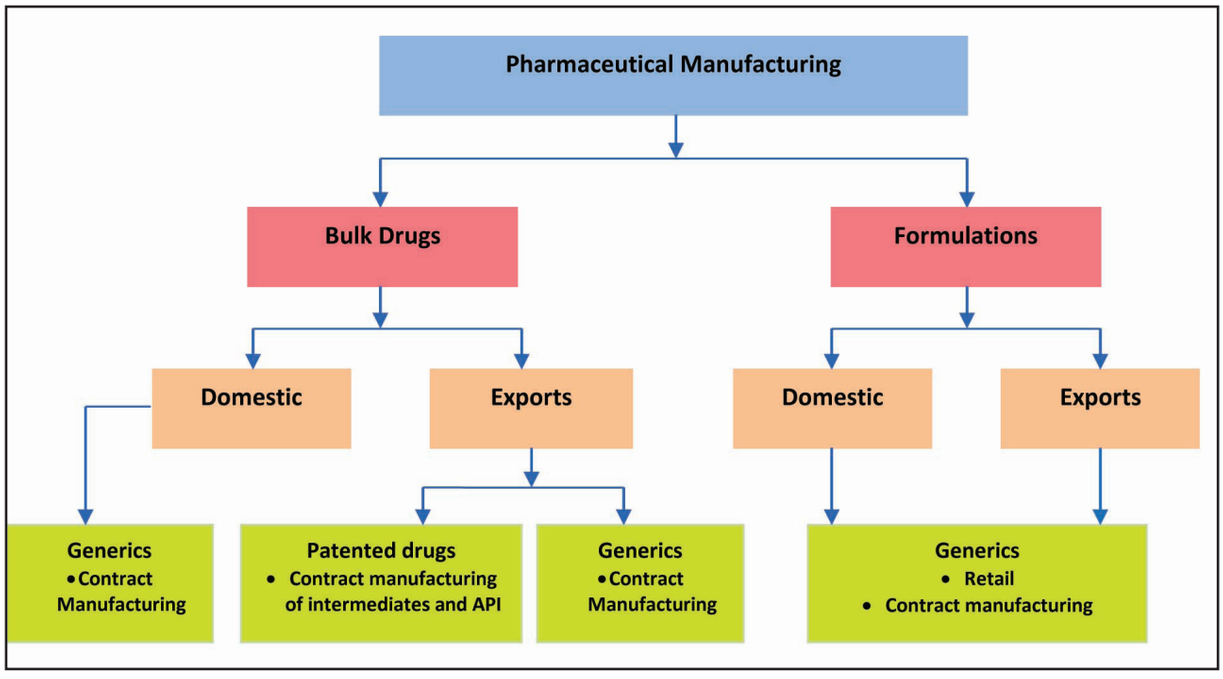


Source: CRISIL Research

India gained a foothold in the global arena, with reverse-engineered generic drugs and active pharmaceutical ingredients (API). India now seeks to become a major player in outsourced clinical research and the contract research and manufacturing services (CRAMS) segments. India has the highest number of manufacturing facilities (332 sites) approved by the US Food and Drug Administration (US FDA). Further, in 2011, one-third of all Abbreviated New Drug Applications (ANDA) approved by the US FDA, belonged to Indian companies.

Indian pharmaceutical companies have manufacturing opportunities in two segments - formulations and bulk drugs. The formulations segment can be further categorised into domestic consumption and exports. Traditionally, the domestic segment accounts for 40-50 per cent of the total formulations production, with exports accounting for a larger share. In contrast, in the case of bulk drugs, domestic consumption accounts for only 10-20 per cent of the total production. Hence, the Indian pharmaceuticals industry is dominated by exports (in both, bulk drugs and formulations), which contributed about 60 per cent to the industry's sales in 2013-14. Formulations are exported either through contracts (supply) or directly sold (retail) in the market. Similarly, bulk drugs are either supplied under a contract, in case of patented drugs, or are sold outright, in the case of off-patent drugs. In the coming years, Indian pharmaceutical manufacturers are poised to extend their presence in on-patent regulated markets, while maintaining a strong foothold in the generics (off-patent drugs) market as well.

Exhibit 4.2: Manufacturing by Indian Pharmaceutical Players



Over 100,000 drugs, across various therapeutic categories, are being produced in India. The domestic formulations industry is highly frag-mented, in terms of both the number of manufacturers and variety of products. There are 300-400 organised players and about 15,000 unorganised players in the manufacturing of pharmaceuticals. However, organised players dominate the formulations market, in terms of sales. In 2013-14, the top 10 formulations companies accounted for 42.2 per cent of total formulation sales. Share of top 10 MNC pharmaceutical companies has reached close to 20 per cent as on March 2014.

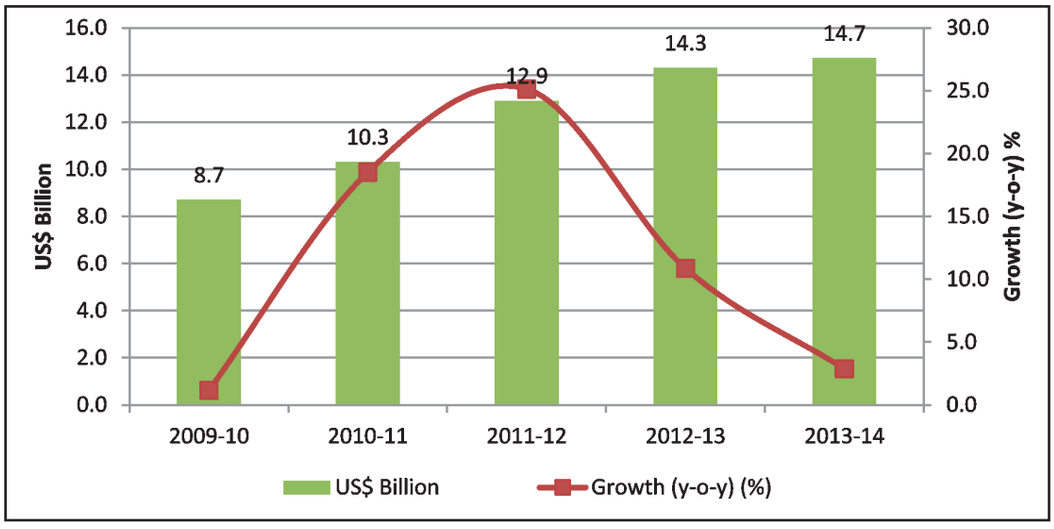
Industry Performance

Globally, the Indian pharmaceutical industry is ranked third largest in volume terms and 10th largest in value terms (2.5 per cent of global share). The size of Indian pharmaceuticals Industry is pegged at US$ 33.9 billion, having grown at roughly 13 per cent CAGR over a 5-year period up to 2013-14. One of the reasons for the lower rank in terms of value, and higher rank in terms of volume is the low cost drugs manufacturing in India; the price differential is estimated to be ranging from 5 per cent to 50 per cent lower as compared to developed countries. The industry has attained self-reliance in the production of formulations, and produces almost 70 per cent of bulk drug requirements of the country. India is also one of the major producers of generic drugs in the world.

Export

Indian pharmaceutical companies have not been affected much by the global slowdown, largely because of cost advantages in production. Notwithstanding this, performance on the export front has been rather modest; exports of pharmaceutical products increased by a mere 1.2 per cent in 2009-10 over the previous year

Exhibit 4.3: Export of Pharmaceuticals Products from India



Analysis based on classification of HS Code by DGCIS as bulk drug and drug intermediates, and drug formulations and biologicals
Source: DGCIS (Data Source); Exim Bank Analysis

Table 4.1: India's Major Export Destinations for Pharmaceutical products (Formulations & Biological)

2009-10			2013-14		
Importers	**US $ million**	**% Share**	**Importers**	**US $ million**	**% Share**
U S A	1248.9	24.1	U S A	3445.8	30.9
U K	269.4	5.2	Russia	535.9	4.8
Russia	259.0	5.0	South Africa	474.0	4.3
South Africa	203.3	3.9	U K	400.8	3.6
Nigeria	167.0	3.2	Nigeria	337.8	3.0
Germany	116.9	2.3	Germany	222.2	2.0
Ukraine	116.2	2.2	Kenya	215.7	1.9
Vietnam	102.6	2.0	Netherlands	185.5	1.7
Sri Lanka	100.2	1.9	Australia	173.6	1.6
Kenya	99.5	1.9	Brazil	161.4	1.4
Total	**5190.7**		**Total**	**11139.9**	

Source: Ministry of Commerce & Industry, GOI; Exim Bank Analysis

to aggregate US$ 8.7 billion. However, exports witnessed a complete turnaround, growing by a healthy 18.5 per cent from US$ 8.7 billion during 2009-10 to US$ 10.3 billion during 2010-11, and in the following year by 25.1 per cent to US$ 12.9 billion. However, in the recent years, though there has been an increase in exports in terms of absolute value, y-o-y growth has shown a declining trend in USD terms mostly due to weakening of rupee. Share of pharmaceuticals in India's total exports has increased from 2.1 per cent in 2000-01 to 4.7 per cent in 2013-14.

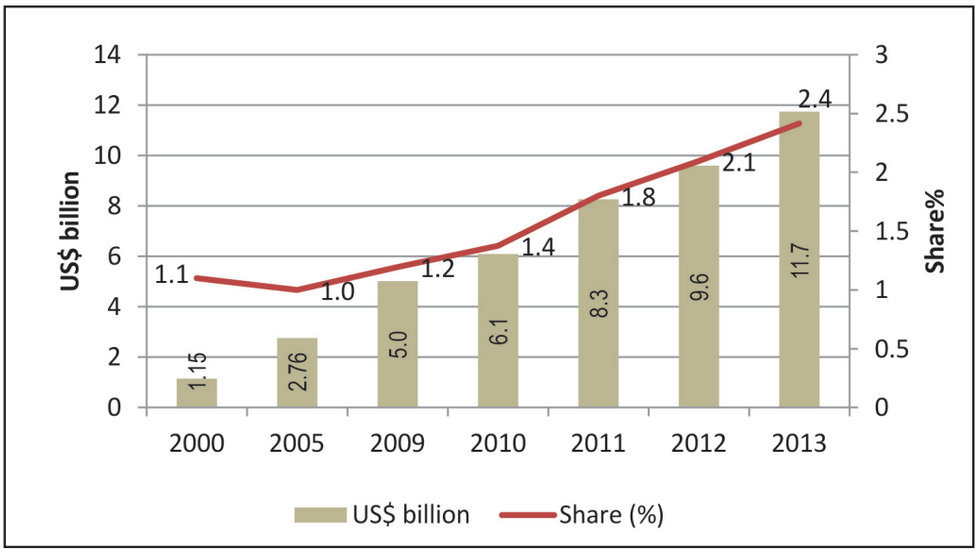
The major export destinations for India's drug formulations and biological products during 2013-14 were: USA (with a share of 30.9 per cent) followed by Russia (4.8 per cent), South Africa (4.3 per cent), UK (3.6 per cent) and Nigeria (3 per cent). As can be seen from the Table 4.1, USA and Russia have retained their positions as major destinations for Indian pharmaceuticals since 2009-10. However, during 2013-14, the Netherlands, which is considered as gateway market for the EU emerged as a major market for Indian formulations and biological products. Other markets that have emerged as major markets during the year are Australia and Brazil. These countries have replaced Asian countries, such as Sri Lanka and Vietnam.

On the other hand, major export destinations for India's bulk drugs and intermediates during 2013-14 were USA (14.2 per cent), followed by Germany (5.3 per cent), Brazil (4.5 per cent), UK (3.7 per cent), and Japan (3.5 per cent).

India's Market Share in Select Regions

India exports both bulk drugs and intermediates, and formulations and biological products. However, share of formulations (75 per cent) in total export of pharmaceuticals is higher than that of bulk drugs (25 per cent).

Exhibit 4.4: India's Exports of formulations and biological (HS Code 30) to the World and % Share in World Exports



Source: Trademap, ITC Geneva, Exim Bank Analysis

India's exports of formulations and biological products (HS Code 30) have been increasing over the years from US$ 1.15 billion in 2000 to US$ 11.7 billion in 2013 showing a CAGR of 21%. From being the fifteenth largest exporter in 2009, India has risen to the rank of being the eleventh largest exporter in the world during 2013. The share of India's export of formulations and biological products in the world exports has increased considerably from 1 per cent in 2005 to 2.4 per cent in 2013.

Table 4.2: Region-wise Bulk Drug Exports from India

Region	Exported Value (US$ million)
EU	**941.3**
America	**859.6**
North America	*613.9*
Latin America	*245.7*
Asia	**884.3**
East Asia	*17.7*
West Asia GCC	*107.0*
West Asia Others	*249.3*
North East Asia	*336.0*
South Asia	*174.3*
Africa	**371.0**
West Africa	*64.5*
Southern Africa	*0.0*
Central Africa	*15.9*
East Africa	*50.5*
North Africa	*124.4*
Total	**3056.3**

Source: DGCIS, Exim Bank Analysis

EU (27)

EU (27) is the largest pharmaceutical market in the world. In the year 2013, EU imported pharmaceutical products worth US$ 242 billion. Germany with a share of 15.6 per cent in total imports was the largest importer, in the EU, followed by Belgium (14.2 per cent), UK (9.6 per cent), and France (9.0 per cent). The region has large volume (78 per cent of total imports) of intra-regional trade; other source countries include: USA (13.7 per cent), Switzerland (8.4 per cent), and Singapore (2.0 per cent). India accounts for a share of 0.7 per cent in EU's total imports of pharmaceutical products mainly drug formulations and biological products. During 2013, EU accounted for 14.5 per cent share in India's total exports of drug formulations and biological products. In 2013, among EU (27) countries, UK, with a share of 26 per cent, was the largest market for Indian drug formulations and biological products, followed by Germany 15.5 per cent, the Netherlands (12.5 per cent) and France (8.4 per cent).

The EU is also the largest market for India's bulk drugs exports. In 2013-14, bulk drugs exports from India to the EU amounted to US$ 941.3 million. With 17.1 per cent share in total bulk drugs imported from India by the EU, Germany is the leading destination, followed by the UK (12 per cent).

North America

USA is the second largest pharmaceutical market in the world. In the year 2013, USA imported pharmaceutical products worth US$ 63 billion. Major source countries for USA include Germany (17.6 per cent), Switzerland (13.2 per cent), Ireland (11.9 per cent), Israel (8.5 per cent) and India (7.2 per cent). India is the fifth largest supplier of drug formulations and biological products to the

USA. USA made up to a share of 39.1 per cent in India's total exports of drug formulations and biological products in the year 2013. USA is also a significant market for bulk drugs exports from India. In 2013-14, bulk drugs export from India to the USA amounted to around US$ 433.9 million which is around 71 per cent of total bulk drugs exported to North America.

Africa

Africa imported pharmaceutical products worth US$ 15.3 billion during 2013. Among the African countries, Algeria with a share of 15.0 per cent in total imports was the largest importer followed by South Africa (14.9 per cent), Egypt (11.9 per cent), Nigeria (7.1 per cent), Tunisia (3.9 per cent) and Morocco (3.7 per cent). India was the second largest source country for drug formulations and biological for Africa with a share of 16.3 per cent. The major source countries for Africa include France with a share of 20.5 per cent, Germany (11.1 per cent) and Switzerland (6.5 per cent). Africa as a region accounted for a share of 21.2 per cent in India's total exports of pharmaceutical products during 2013. In 2013-14, bulk drug exports from India to Africa amounted to around US$ 371 million.

Asia

Asia imported drug formulations and biological worth US$ 80.1 billion during 2013. Among Asian countries, Japan with a share of 26 per cent in total imports was the largest importer followed by China (18.8 per cent), Saudi Arabia (6.4 per cent), South Korea (5.3 per cent) and Turkey (5.2 per cent). The main source countries for Asia include: Germany (15.9 per cent) USA (14.8 per cent), Switzerland (9.7 per cent), and France (9.2 per cent). India's share in Asia's total imports of drug formulations and biological was 2.2 per cent during 2013. During 2013, Asia's share in India's total exports of drug formulations and biological stood at 15.2 per cent. Asia is the second major export destination for India's bulk drugs exports. During 2013-14, bulk drugs exports from India to Asian region amounted to around US$ 884.3 million, which is around 28.9 per cent of total bulk drugs exported from India.

Latin America

Latin America imported pharmaceutical products worth US$ 27.3 billion during 2013. Among Latin American countries, Brazil with a share of 27.2 per cent in total imports was the largest importer followed by Mexico (18.4 per cent), Venezuela (11.8 per cent) and Colombia (8.5 per cent). The main source countries for Latin American imports include: USA (19.1 per cent), Germany (14.9 per cent) Switzerland (7.2 per cent), and France (6.9 per cent). India's share in total imports of drug formulations and biological products by Latin America stood at 2.9 per cent, during 2013. In 2013, Latin America's share in India's total exports of drug formulations and biological stood at 6.8 per cent. Latin America accounts for 8 per cent (US$ 245.7 million) of total bulk drugs exports from India. Brazil is the second major export destination for bulk drugs exports from India.

Key Industry Trends

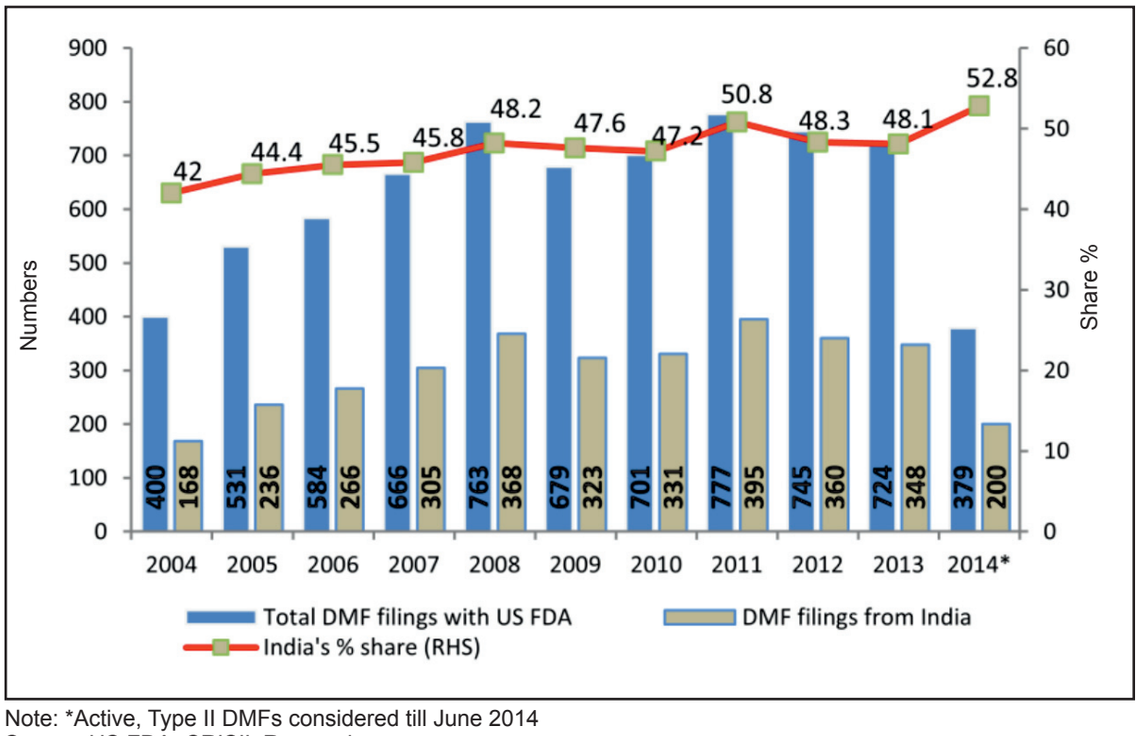
India's formulations exports have grown at a CAGR of about 17 per cent (in dollar terms) over 5 years up to 2013-14. The growing need for generic medication in developed countries looking at cutting healthcare costs is a key driver for Indian exports of formulations. Moreover, India's ability to offer cost-effective generic drugs through a highly evolved manufacturing base has helped the country to increase its exports to semi-regulated markets as well. Growth in exports to the semi-regulated markets sustained at about 12 per cent y-o-y growth during 2013-14, while the exports to

the regulated markets grew at a modest 10 per cent during the same period, compared to 18 per cent growth seen in the last year. The slowdown was mainly on account of import alerts on Indian companies, slowdown of growth in Europe and increased competition during the year. Growth in semi-regulated markets has been largely driven by Asia and Africa. The Eastern African countries such as Kenya, Tanzania, Uganda, Ethiopia, Zambia, Malawi, Zimbabwe and Mozambique represent an important export cluster for Indian pharmaceuticals. A major driving factor for Indian exports to Africa has been India's strong presence in the anti-retroviral, anti-malarial and anti-tubercular segment which forms major items of imports of pharmaceuticals in Africa. Moreover, many large Indian companies such as Ranbaxy are directly supplying to large institutional buyers, such as the United Nations Children's Fund (UNICEF), PEPFAR, the United Nations Development Programme (UNDP) and the International Development Association (IDA). These factors are estimated to have helped in increasing the exports to these markets.

Key Segments

Bulk drugs exports are estimated to have grown at a CAGR of about 17 per cent between 2008-09 and 2013-14, mainly on account of India emerging as a preferred manufacturing hub for high quality APIs. The demand growth has been led by both innovator companies - looking at cutting down costs - as well as a large number of generic formulators, who have steadily targeted regulated markets, such as the USA and the Europe, and looking for steady supplies of quality API. Consequently, the Indian API market has seen

Exhibit 4.5: DMF filings (Global vs India)



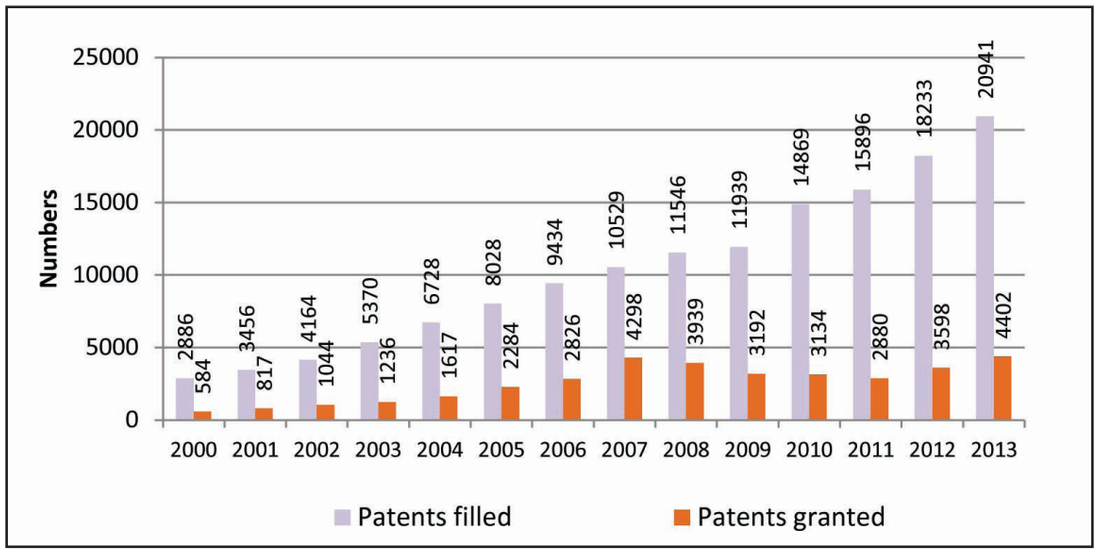
Note: *Active, Type II DMFs considered till June 2014
Source: US FDA, CRISIL Research

many tie-ups between large global companies and Indian API manufacturers. Also, many Indian API makers have considerably increased their manufacturing capabilities as evident from the rising share in total DMF filings in the US markets. Consequently, exports to regulated markets, which had a 48 per cent share in total bulk drug exports, have grown at 20 per cent CAGR in the last 5 years. Of the total drug master filings (DMFs) filed with the US FDA, India's share has risen sharply to about 53 per cent for the 6 months ending June 2014, from about 19 per cent in 2001, indicating Indian players' capability to maintain the required quality standards to export to the regulated markets. A DMF provides an indication of the bulk drug manufacturing capabilities of players (in terms of the quality standards at their facilities for processing, packaging, and storage of drugs), which is used by global pharmaceutical companies that are outsourcing production activities (innovator). India is considerably ahead of its competitors in terms filing of the total number of DMFs. While India has filed 3200 DMFs from January 2004 to June 2014, its closest competitor, China had filed about 1,000.

M&A

During 2013, the Indian pharmaceutical industry witnessed a total of 30 M&A deals in the pharma and biotech sector (inbound, outbound and domestic). While maintaining the same number of deals as in the year 2012, total deal value increased from US$ 1.7 billion in 2012 to US$ 2.5 billion in 2013. On the private equity side, a total of 14 deals were consummated in 2013, aggregating US$ 427 million of investment, as opposed to 14 deals with US$ 180 million of investment last year. This implies a more than doubling of average deal size.

Exhibit 4.6: Patents Filed by India outside India (2000-2013)



Note: This data is not restricted to pharmaceuticals; major share (20.4 per cent) of patent application for 2013 were for pharmaceuticals
Source: World Intellectual Property Organization (WIPO); Exim Bank Analysis

Table 4.3: Patents Filed and Granted in the Pharmaceuticals Sector by the Indian Patent Office

Year	Patents in Pharmaceuticals			Total Patents	
	Filed	Granted	Share of patent granted to filed (%)	Filed	Granted
2008-09	3672	1207	32.9	36812	16061
2009-10	3070	530	17.3	34287	6168
2010-11	3526	596	16.9	39400	7509
2011-12	2762	282	10.2	43197	4381
2012-13	2954	344	11.6	43674	4126

Source: Office of the Controller General of Patents, Designs, Trademarks and Geographical Indicators, India; Exim Bank Analysis

Table 4.4: R&D Expenditure of Select Indian Pharmaceutical Companies

Company Name	2012-13			2013-14		
	₹ Million		R&D as % of sales	₹ Million		R&D as % of sales
	Sales	R&D Expenses		Sales	R&D Expenses	
Dr. Reddy'S Laboratories Ltd.	83946	6947	8.3	97938	10391	10.6
Cipla Ltd.	82974	3638	4.4	94821	5119	5.4
Lupin Ltd.	71508	7099	9.9	89776	9294	10.4
Aurobindo Pharma Ltd.	55695	2085	3.7	72695	2551	3.5
Ranbaxy Laboratories Ltd.	60615	4491	7.4	68783	5279	7.7
Cadila Healthcare Ltd.	30943	4427	14.3	36916	4358	11.8
Torrent Pharmaceuticals Ltd.	27672	1263	4.6	33586	1455	4.3
Ipca Laboratories Ltd.	28287	887	3.1	32966	1244	3.8
Sun Pharmaceutical Inds. Ltd.	24522	2725	11.1	29959	3752	12.5
Glaxosmithkline Pharmaceuticals Ltd.	27425	24	0.1	26650	26	0.1
Divi'S Laboratories Ltd.	21444	240	1.1	25330	254	1.0
Glenmark Pharmaceuticals Ltd.	20479	929	4.5	24387	1214	5.0
Abbott India Ltd.	16709	13	0.1	23252	16	0.1
Biocon Ltd.	19833	714	3.6	22393	705	3.1
Orchid Chemicals & Pharmaceuticals Ltd.	19183	842	4.4	19183	842	4.4
Sanofi India Ltd.	16128	24	0.1	18549	43	0.2
Alembic Pharmaceuticals Ltd.	15014	743	4.9	18515	1164	6.3
Wockhardt Ltd.	24770	2010	8.1	18108	1985	11.0

Source: CMIE Prowess, Exim Bank Analysis

Patents

The patents filed by, and granted to Indian companies have been increasing significantly. Indian companies have filed a large numbers of Drug Master Files and Abbreviated New Drug Applications (ANDA) with the US-FDA. According to the Indian Patent Office, during 2012-13, a total of 43,674 patents were filed, of which only around 6.8 per cent were filed in the drug and pharmaceutical sector; and of the total 4126 patents that were granted in the year, around 8.3 per cent share was for pharmaceuticals.

R&D

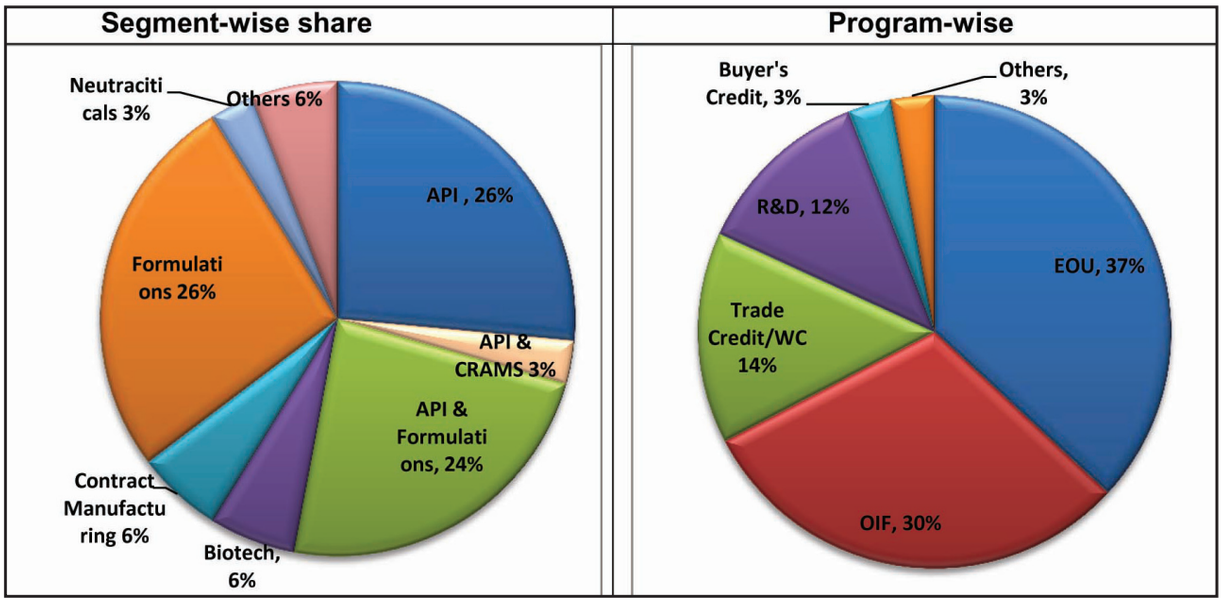
In the recent years, Indian pharmaceutical companies have significantly increased their R&D budgets in view of their growing focus both on regulated markets and complex molecules/therapy segments. In 2013-14, most of the leading pharma players spent anywhere between ₹ 5 billion to ₹ 12 billion on R&D, which represented an increase, both in absolute terms as well as in proportion to net revenues (8-11 per cent of sales).

Role of Exim Bank in Promoting Indian Pharmaceutical Sector

Exim Bank has been closely associated with the export efforts of Indian pharmaceutical industry, in its entire value chain. Exim Bank has been providing support to all segments in the pharmaceutical value chain. A schematic segment wise and program-wise representation of the companies supported by the Bank in this sector is provided in Exhibit 4.7.

Pharmaceutical sector is one of the focus sectors of the Bank. On the whole, Exim Bank's exposure to pharmaceutical industry as on 31.03.2014 is Rs 3,828 crores, a share of 6.24 per cent in total credit exposure. According to RBI's data on sectoral deployment of Gross Bank Credit, as of March 31, 2014, the Indian Banking Sector had

Exhibit 4.7: Exim Bank Supported Companies in Pharmaceutical Industry



Source: Exim Bank Analysis

Table 4.5: Credit Flow to Pharmaceutical Industry

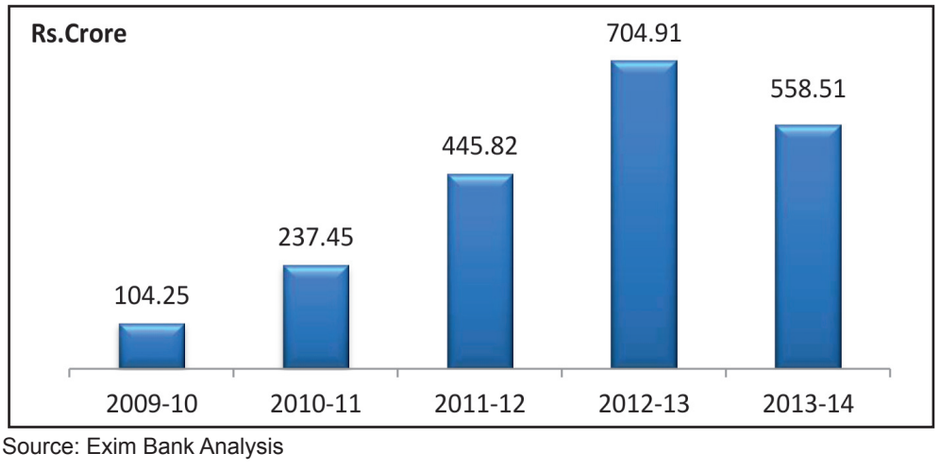
Year	Credit flow to Pharmaceutical Industry (outstanding as on end March)		Exim Bank's Exposure to Pharmaceutical Sector (as at end March)	
	Value (₹ Crore)	Share in Total Gross Bank Credit to Industry (%)	Value (₹ Crore)	Share in Total (%)
2009-10	35,980	2.74	2,112	6.39
2010-11	40,764	2.53	3,733	8.68
2011-12	46,046	2.38	3,587	6.61
2012-13	49,542	2.22	3,854	6.28
2013-14	49,199	1.95	3,828	6.24

Source: RBI; Exim Bank Analysis

an exposure of ₹ 492 billion to the drugs and pharmaceutical Industry. This works out to 0.8 per cent of the total non-food credit of the banking system and 1.9 per cent of the total credit to the Industry Sector.

The Bank has been largely supporting the Indian pharmaceutical companies by providing term loans for domestic expansion projects and term loans for overseas acquisitions, besides loans for research and development.

Exhibit 4.8: Exim Bank Support to Pharma Sector for R&D



Source: Exim Bank Analysis

Finance for R&D of Pharmaceutical/Biopharma companies

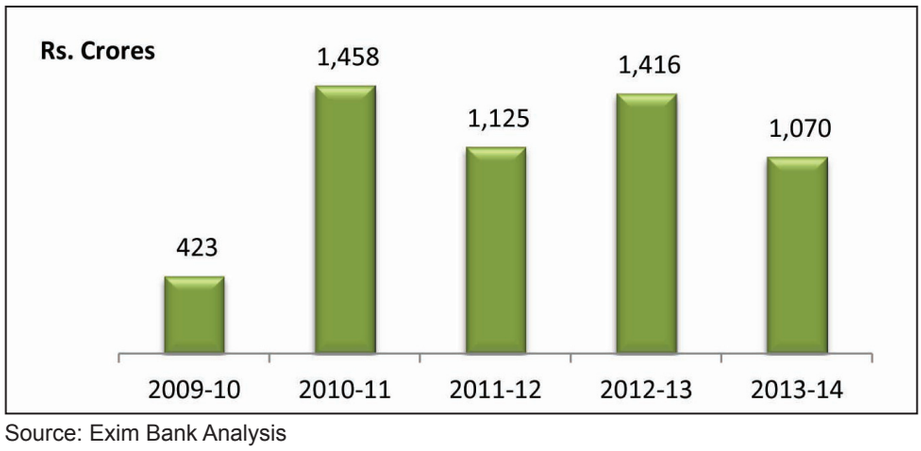
In view of several of the drugs going off-patent and high cost of R&D investment, financial assistance is required by pharma and biopharma companies from banks/financial institutions with longer moratorium period. The need and nature of funding differs for medium and large pharmaceutical companies. Medium-sized companies generally have a pure debt financing requirement to finance research and development costs for obtaining IPRs/regulatory approvals. However, large companies need finance, both by way of debt and equity through special purpose vehicles being set-up which are focused on the activity of developing products, and for basic research work including clinical trials with the objective of obtaining IPRs/ product approvals from overseas regulatory authorities. Accordingly, Exim Bank finances the pharmaceutical or biopharma companies to fund the research and development, new product development and other related costs for obtaining Intellectual Property Rights/regulatory approvals in regulated overseas markets. Financing by Exim Bank is in the form of either term loan/equity participation or a hybrid product.

Finance for Overseas Investment of Pharmaceutical/Biopharma Companies

The pharmaceutical industry is continuing its progress in fundamental restructuring. In this environment, acquisitions and divestments are essential means to achieve strategic objectives. The Bank supports the pharmaceutical companies in their strategic investments abroad for, inter alia, setting up manufacturing units and for acquiring overseas companies to get access to the foreign market, technology, raw material, brand, and IPR.

Exim Bank's support to pharma companies for overseas investments as on end of FY2013-14 was ₹1070.3 crores. Schematic presentation of Exim Bank's support to the Pharma sector for their overseas investment is given in Exhibit 4.9.

Exhibit 4.9: Exim Bank Support to Pharma Sector for Overseas Investment



Source: Exim Bank Analysis

5. CHALLENGES & PROSPECTS

Global pharmaceutical industry, in the recent years, is faced with four key challenges. These are mainly with respect to sailing across the global health care reforms, delivering innovation and value, complying with regulatory changes; and operating in a liberalized connected trade environment.

Global Health Care Reforms

In the recent years, countries including the USA, China, Brazil, Germany, France, and the UK have introduced legislations that have been considerably accelerating the transformation of global health care from a volume-based to a value-based sector, significantly impacting the global pharmaceutical industry. Among the key developments, reducing costs, enhancing innovation and improving market access are the defining goals of healthcare reform. Specific elements of reform vary by country, requiring pharmaceutical companies adopting national approaches. For example, the United States' Affordable Care Act ACA, Britain's Health and Social Care Act, and the laws arising from China's Guidelines on Deepening the Reform of the Health Care System, have many elements that are unique to the countries' national systems.

Cost containment is a common reform objective in both developed and developing pharmaceutical markets. Most national health care systems have been encouraging the use of generic drugs. For example, in the USA, the proportion of prescriptions with generics has risen from 50 per cent to 80 percent over the last decade. Brazil is in the process of making branded generics and proprietary drugs of greater interest to pharmaceutical companies, and in China, recent reforms have put intense pressure on the prices of all drugs, including generic and over-the-counter (OTC) medicines. In Germany and several other European countries, value-based pricing for new drugs have been introduced, which allows a priced differential from existing offerings, including generics, based on a new product's demonstrated superiority. Developing countries, such as India, Brazil and China, have national lists of essential drugs with set prices.

Another emerging health care reform is spurring product innovation, via value based pricing and other methods. For example, China has identified biotechnology as one of the seven strategic industries in its latest five-year reform plan; the Brazilian government is in the midst of a ten-year biotechnology development program; and UK has been incentivizing pharmaceutical companies by way of tax reduction for carrying out R&D activities in the country.

Third major goal of reform is improving health care access, which involves expansion of insurance coverage, and increasing governments' direct purchase of pharmaceutical products. For example, the Congressional Budget Office (CBO) of USA has estimated that, by 2020, approximately 24million people will be covered through the new health insurance exchanges.

While many pharmaceutical companies are addressing these challenges arising out of health care reforms with a reactive approach, many others are considering health care reforms as prominent challenge in the next few years in terms of developing products that meet the goals of reformed systems, such as more patient-

focused care. One of the challenging areas for the companies is coping with the many regulatory environments, which involves interacting with the government agencies (which are created following economic reforms) in various countries, which are in their naïve state of operations.

Innovation and Value Addition

Product innovation and value addition has become one of the compelling challenges for the global pharmaceutical industry. The recent incidents of patent cliffs involving several branded drugs going off-patent have created downward pressure on the revenues of the large pharmaceutical companies, prompting them for increased R&D and new product development. This also implies increased cost on product development and positioning for the companies. In pharmaceutical R&D, productivity is a constant challenge. Main challenges to productivity are managing risk without restricting innovation. Price of failure places increased risk leading the companies to adopt conservative research choices limiting the prospects of discovering genuine 'breakthrough' compounds. Consequently, there is considerable multi-disciplinary activity occurring around in today's pharmaceutical R&D sphere, which requires collaboration and cooperation, both characteristics of new risk-sharing business models, such as joint ventures, partnerships, and acquisitions. This transition of pharmaceutical R&D from its traditional vertically integrated scientific R&D model to the one focused more on asset management has been throwing newer challenges for pharmaceutical companies in human resources management and operations.

The ongoing patent cliff has also opened up opportunities for generic drugs. In addition, several countries, such as the USA and the Europe through various legislations have been encouraging use and manufacturing of generic drugs. While this has resulted in increased opportunity and competition in the generic industry, increased regulatory pressure on the generic industry introduced by the US FDA and similar national agencies is also envisaged to slow down the growth of the industry in the medium to long term.

Regulatory Compliance

Regulatory compliance has emerged as a critical challenge for the pharmaceutical industry, particularly in emerging markets, such as Southeast Asia, India, China and Latin America. Non-compliance is cost intensive, and may expose the companies to revenue losses, reputational risks, patient safety issues, criminal sanctions, and can jeopardize the future of the entire business unit. Compliance issues facing the pharmaceutical industry include government policies, drug safety, counterfeiting, information security and privacy, intellectual property protection, corruption and adulteration, and M&A/joint venture (JV) and other third-party risks.

Policies and regulatory frameworks of the US-FDA and the EU's EMA have strong implications on the global pharmaceutical industry. While each country develops and enforces its own regulations, increasing number of countries are enhancing cross-border agency collaboration to strengthen regulatory decision making and enforcement actions. Drug safety standards, particularly those associated with quality systems implementation, data integrity, and validation of manufacturing and testing processes continue to tighten in countries around the world. The new and stricter Good pharmacoVigilance Practice (GVP) module introduced by EMA is proposed to be implemented throughout the EU; increased inspections by US-FDA on India's FDA approved manufacturing units; are some examples to cite.

Weak or incomplete supply chain security, particularly with multiple supply chains expanding across the globe is exacerbating the spread of counterfeit drugs, particularly in emerging pharma-markets. While the counterfeit market is difficult to quantify, it is estimated to be increasing at 15 percent per year, which is double the expected rate for legitimate pharmaceutical market.

The transforming global health care system is producing immense volume of information, which rides upon its availability, integrity, and confidentiality. The new health care models, health insurance models, electronic medical record (EMR) and other technologies, and permeable boundaries among industry stakeholders have increased the complexities of managing protected health information (PHI), and have compounded an already challenging issue in the pharmaceutical industry.

Ineffective intellectual property (IP) protection in the pharmaceutical industry is regarded as a frequent concern in pharma-emerging markets such as Russia, India, China and the Middle East, which requires the pharmaceutical companies to adapt to local market conditions for product commercialization depending on the level of IP enforcement. Increasingly, pharmaceutical companies are entering into M&A and JV transactions or have key third-party contractual relationships in emerging markets. This has raised considerable cultural and geographical complexities creating operational challenge.

The challenge of operating in a liberalized and connected world involves addressing the demographic trends in the spread of chronic diseases and technological advancements.

Indian Pharmaceutical Industry – Key Challenges

At present, India accounts for about 40 per cent of generic drugs, over-the-counter products and 10 per cent of finished dosages used in the USA. The ongoing and ensuing patent cliff is projected to offer more opportunities for Indian pharmaceutical industry, particularly in generic and biosimilars. The generic market is projected to grow at the rate of 9.5 per cent to US$ 432 billion by 2018. However, recently, the Indian drug industry has come under increased scrutiny by the US-FDA, mainly due to the following two reasons:

Data Integrity – Data integrity practices followed in many the US FDA approved units of Indian pharmaceutical companies have emerged as a major challenge for the industry in the recent times. According to the US-FDA, data integrity matters because properly recorded information is the basis for manufacturers to assure product identity, strength, purity, and safety. Evidences of misrepresented data or problems with batch records found during a preapproval inspections has been the prime factor leading to delays in market approval, and the audits have led to warning letters and black listing of the units.

According to the industry leaders, though data integrity issues have always existed, new mandates by the US-FDA to attain parity in inspection of foreign and domestic facilities have further complicated the picture by expanding oversight of US-FDA to many firms that are less familiar with the US standards. However, according to the sources, quality of finished drugs have not been under the US-FDA scanner; scanning have been mostly with regard to certain CGMP requirements,

and collection and documentation of data, that are raised against the black listed units during the audits (Annexure 2). Multiple data integrity issues reported by the investigators include failure to record activities contemporaneously; document back-dating; copying existing data as new information; re-running samples to obtain better results; and fabricating or discarding data. Further, according to the industry sources, in addition to India, data integrity issues have surfaced in other regions as well. In India the incidence of warning letters have been more due to more number of US-FDA approved units. India has the largest number of US-FDA approved drug manufacturing units outside USA.

Whatsoever, the growth of the Indian pharmaceutical industry, which is one of the largest suppliers of pharmaceutical products to the world, would get affected by such measures arising due to data integrity issues.

Credibility of Clinical Trial Data - Credibility of 'Clinical Trial Data' generated by the Indian pharmaceutical industry has also become a cause of great concern. In many ways India is the ideal location to conduct clinical trials given its diverse pool of patients with diverse treatment needs, and access to a large, scientifically skilled, workforce. This has caused huge growth in the number of clinical trials undertaken in the country; however, capacity to regulate clinical trials has not kept pace with this growth leading to a number of reported unethical practices such as: limited patient compensation for adverse events; approval of drugs without clinical trials; and lapses in informed consent procedures. Though the Government of India has enhanced the regulatory control measures, in the form of mandatory trial registration, and the creation of numerous committees tasked with overseeing trial approval, trial execution, and ethical treatment of patients, the delays in new drug approvals as a result of the new regulatory control regime has been also forcing some multinational pharma companies to rethink their clinical trial activities in India.

IPR - Intellectual property rights (IPR) in the pharma sphere have been a contentious issue globally. The (Indian) Patents Act was enacted in 1970 and inter alia contains provisions relating to pharmaceutical patents. A major change in the patent laws in India was the enactment of the Patent (Amendment) Act, 2005, which made patent laws in India compliant with the TRIPS Agreement. Though there was an overall improvement in patent protection in India, recent issues such as granting of compulsory licenses (CLs) have been contentious. Under the Indian Patent Law, CLs can be awarded, inter alia, if:

- The reasonable requirements of the public with respect to the patented invention have not been met; or
- The patented invention is not available to the public at a reasonably affordable price; or
- The patented invention is not worked in the territory of India.

In the context of the pharmaceuticals, the conditions for grant of a CL are aimed at preventing a situation where the public health is prejudiced by the exclusivity granted to the patented product. Recently, the Supreme Court of India dismissed a Special Leave Petition for reversing the CL awarded to an Indian company, since all the grounds for granting a CL under the (Indian) Patents Act, 1970 had been met.

While CLs have been viewed as a necessary evil, in a developing country, like India, they have also caused grave concerns in the industry due to the

revenue loss that CLs tend to cause. In a recent order by the Controller of Patents, it has been held that granting a CL should be the last resort and efforts for obtaining a voluntary license should be made first. This order provides some comfort to the industry, as it clarifies the legal position that so long as the patentee does not meet the conditions for grant of CLs under the Patents Act, 1970, its patent rights would not be interfered with.

Another observable trend in the IPR sphere is the stricter enforcement of trademark contraventions in India. In the pharma sphere this trend is comforting as trademark contraventions may lead to use of wrong drugs.

Over Dependence on China for Bulk Drug and APIs – India is heavily dependent on China for bulk drug intermediates and APIs. Indian pharma industry imports metformin, analgestics paracetamol, ranitidine, vitamin C and its intermediates from China in large quantities. India is largely dependent on China for almost all APIs by fermentation route, such as penicillin, cephalosporins and macrolides. The large scale imports have led to shutting down of several API units (Annexure 3). A similar trend is also evident in the case of many large volume imports of chemical synthesis-based API's or intermediates, such as paracetamol, metaformin, ibuprofen, and quinolones. Imports of these APIs have grown at a CAGR of 18 per cent over the last decade. Currently, China contributes 58 per cent of all such imports by value and almost 80 per cent by volume.

The over dependence situation on China for important bulk drugs and APIs is of significant concern for Indian pharmaceutical industry as any shift in Chinese policies or eco-political conditions between the two countries may result in a significant setback for the Indian formulation industry, which are heavily dependent on the API imports as raw materials.

BOX 2:

API/Intermediate Imports from China by Value in 2014

API/Intermediates	Value in USD million
Paracetamol	116
Metformin	63
Ranitidine	12
Amoxicillin	104
Ciprofloxacin	59
Cefixime	16
Acetyl salicylic acid	5
Ascorbic acid	13
Ofloxacin	23
Ibuprofen	16
Metronidazole	14
Ampicillin	92
Levofloxacin	23

Source: Indian Drug Manufacturer Association (IDMA)

R&D

The R&D profile of Indian pharmaceutical industry includes development of generics, new drug delivery systems and new drug development. The data on patents granted to leading Indian pharma companies by Patent & Trademark Office (PTO) shows that patents on new products account for only 5 per cent and the rest has been on new processes, new dosage forms and drug delivery systems. It appears that the growth in R&D intensity of Indian pharma companies has been the outcome of the fear of shrinking market opportunities, as they will no longer be able to reverse engineer and produce new drugs, rather than induced by the incentives of the new patent regime. In the R&D for new drugs, the analysis

of new drug pipeline of leading Indian pharma companies shows that the new patent regime has not been able to become the driving force; the R&D activities of Indian firms are increasingly getting concentrated on life style diseases of global nature and they find little opportunity in addressing the drug delivery requirements of local diseases such as TB and malaria.

The policy reforms, however, paved the way for the "globalisation" of Indian pharmaceutical industry; it has now become a part of the global production and development network of MNCs. Participation of Indian firms in the global network has come more of an income generation opportunity than a means for competence building.

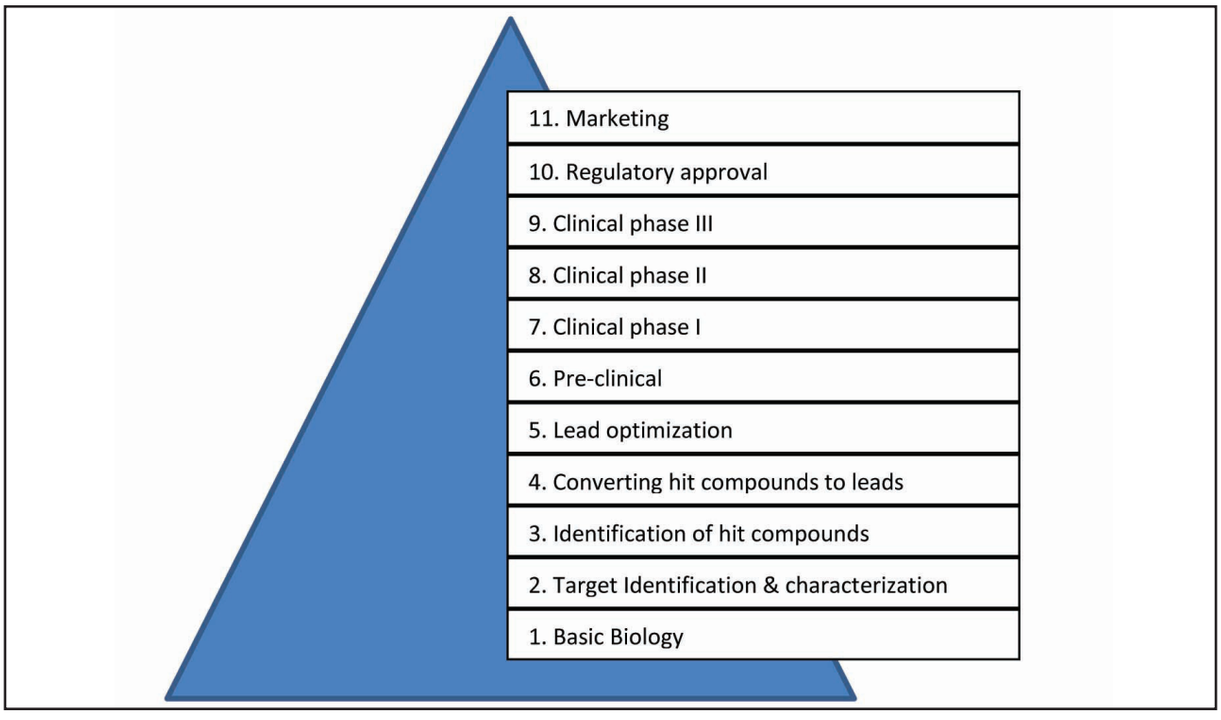
In contract research, collaborative research projects, out-licensing and in-licensing partnerships Indian firms have been partners of subordinate status who perform piecemeal projects in drug research and they are not exposed to the whole process of new drug development. In these collaborations, the scope for transfer of technology and joint ownership of technology is also very limited. The subordinate status of the Indian firms in the long run may result in a dependency relationship of Indian firms with the MNCs. This may have deleterious consequences to the industry in many ways. Being trusted allies in the global strategy of MNCs, Indian companies may lose interest in those therapeutic areas which do not have global presence (for example, tropical country diseases). These allies might also withhold themselves from: exercising compulsory licensing provisions, the TRIPS instrument to counter abuse of patent monopoly rights as well as to address national health emergencies.

The limited capacity of Indian firms in developing new drugs, both in terms of S&T skills and financial resources leave them with no other option but to collaborate with MNCs. In the earlier policy regime, the public sector companies and public sector laboratories had played a major role in augmenting the S&T skills of the private sector industry. Under the new policy regime, the public sector companies have been relegated and a few of them have already been closed down. The aversion to indigenous innovations at the regulatory approval stages and at promotional stages further encourages Indian firms to develop new drugs in collaboration with MNCs.

The liberalisation measures, on the other hand, have attracted foreign investment in pharmaceutical R&D in India. But it has been observed that bulk of foreign investment in R&D in the pharma sector has been in the clinical phase, especially in phase III trials and not much in the biology and chemistry research for new drug development. Phase III requires a large number of human subjects in the trials. MNCs are attracted because India provides a large size of population which is ethnically diverse and suffering from various ailments. The English speaking human power and a well-developed communication network with information technology capabilities are also advantageous for India in clinical trials.

In addition, the Indian pharmaceutical industry is also witnessing regulatory challenges with respect to uncertainties over the FDI policy, the new pharmaceutical pricing policy, a uniform code for sales and marketing practices and compulsory licensing. These challenges have been slowing down the growth of the industry. The recent developments in domestic regulatory framework and their implications on the pharmaceutical industry are provided in Annexure-4.

Exhibit 5.1: R&D Process for Developing New Drugs



Source: Kettler, White and Jordan

Way Forward

Manufacturing of Bulk Drugs and Intermediaries

Increased production of essential drug intermediaries and APIs at competitive prices should be the current focus of the Indian pharmaceutical industry to ensure adequate supply of essential raw materials and attain self-sufficiency and reduce dependence on imports. These primarily include:

- First-line antibiotics (e.g. SSPs, SSCs, Fluoroquinolones)
- Analgesics (e.g. Paracetamol, Ibuprofen)
- First-line cardiovascular drugs (e.g. ARBs, Ace Inhibitors)
- First-line anti diabetes drugs (e.g. metformin)
- Anti-cholesterol drugs (e.g. statins)

Bulk drug or API industry is capital-intensive with environmental implications. Towards this, there is need to have in place a long-term policy for sustaining the growth of the bulk drug industry. This may include encouraging PPP model in pharma manufactufring or establishing JVs with overseas manufacturers. This may also require dismantling sick bulk drug units and setting up of modern plants with higher capacity. Industry sources suggest the following capacity requirement of essential raw materials (indicative) in short to medium term for the India's pharma industry:

- Penicillin plants with minimum capacity of10,000MT per annum

- Macrolides plants with minimum capacity of 2000 MT to 3000 MT per plant per annum
- Cephalosporin with minimum capacity of 2000 to 3000 MT per annum.

Regulatory Compliance

CGMP and data integrity are other key focus areas for Indian pharmaceutical industry. In order to address GMP and data integrity issues, emphasis of Indian pharmaceutical companies should be on pursuing stronger compliance risk management capabilities, rather than to merely satisfying the emerging legal requirements. Indian pharma companies are required to re-evaluate their organization's approach of managing compliance risks; applying methodologies used for financial reporting to compliance issues, such as putting formal governance and organizational structures in place; forming freestanding compliance and risk committees at the board level; and more. Taking a risk-based approach to compliance planning, execution, and monitoring may help in a heightened regulatory environment. It may enable companies to focus on critical risk areas that need attention while reducing emphasis and effort on less critical ones.

To document that manufacturing processes comply with GMPs, pharmaceutical companies are required to retain complete and accurate production information and make it available to agency inspectors and auditors. It has been often pointed out by the agency inspectors that pharma companies regard contract testing and production operations as one way to alleviate their involvement in inspections and dealings with regulatory authorities. However, they have emphasized that licensed manufacturer remains responsible for products meeting all GMP standards. Thus, drug manufacturers should not totally look at contract manufacturers to reduce their responsibility for data accuracy and reliability.

Preparedness and skill development on documentation, statistical techniques as per regulatory requirements are other important areas where Indian pharma companies need to invest.

Research and Development

The present R&D efforts of the Indian pharmaceutical industry are mainly targeted towards therapeutic areas of global interest like diabetes, cardiovascular diseases, central nervous system disorders and oncology. However, diseases local to India and other tropical countries, for example tuberculosis and malaria, are getting less attention due to economic reasons. To promote the novel research and development in these areas, there is a need for short/medium/long term policy to further incentivize the private sector for new drug development and bringing down the commercialization barrier in these areas.

Presently, apart from strengthening intellectual property protection system, the Government of India is providing soft loans, grants and tax benefits to promote R&D activities. Public-Private Partnerships (PPPs) initiated by the Department of Science & Technology (DST) and Council of Scientific and Industrial Research (CSIR) are providing avenues for risk sharing and better collaboration between public research facilities and private sector for development of National College of Engineering (NCEs). These partnerships need to be more commercially oriented and proactive in bringing innovations to market. To commercialize new drugs developed for neglected tropical diseases, there is also a need to promote them by providing incentives to the private sector in the form of subsidies or drug

assistance programmes, or by reviving public sector manufacturing for these drugs.

IPR

There has been a growth in patent activities in India after TRIPS Agreement came into existence. Most of the patent activities in the Indian pharma industry are carried out by large pharmaceutical companies in India and MNCs, and further, a greater number of applications are related to new or improved processes for products rather than products themselves. The products related to applications are concerned with intermediaries and formulations with maximum contribution in modified-release dosage forms. Further, R&D intensity of SME pharmaceutical companies is too insignificant in comparison to large companies; because of lack of technology support and resources for upgradation and expansion of their internal R&D facilities, SME firms have low to nil participation in IPR activity.

To promote IPR activity in the Indian pharmaceuticals industry, the pharmaceutical companies need to be encouraged to undertake new drug discoveries, innovate new dosage forms, and new uses of existing drugs. This may be done through subsidizing the cost of filing and maintenance of patents, and supporting the cost of litigations and other legal formalities. There is an urgent need for SMEs to develop collaborative research culture with public and privately funded research organisations for their survival and increased participation in IPR activities.

Clinical Research & Trials

To address unethical practices in clinical research and encourage clinical trials in India, the approval mechanisms for protocols need to be more transparent and time efficient. In addition, a policy promoting clinical research and innovation needs to be supported by action at various levels:

- Rational regulations: Regulations and guidelines developed through a multi stakeholder consultative approach that are based on science and highlight a commitment to patient safety, ethics and confidentiality, in line with globally accepted practices are the need of the hour. There are situations unique to India like literacy, socio economic considerations and social cultural norms, which must also be taken into cognizance in the development of guidelines so that no one is denied the right to participate in research because of these challenges.

- Capacity building: There is a need for more trained resources within Central Drugs Standard Control Organization (CDSCO) to ensure the smooth roll out and governance of clinical research in the country.

- Accreditation: To address the concerns that have been raised about the conduct of clinical research in India, there is a need for an objective system to accredit investigators, sites and ethics committees. The accreditation should be provided by an independent third party and reviewed at periodic intervals.

- Infrastructure development: For sustained growth of clinical research in the country and to ensure a healthy balance of research across geographies, the investments are needed in bettering infrastructure particularly at government run hospitals and institutions. Many patients do not have the option of participating in clinical research in many areas of India, because, majority of these sites being ill equipped and most of the investigators are not trained in clinical research.

- Public education and awareness: Mis-reporting and sensationalism of clinical research in India has created fear and suspicion amongst the public at large. A key requirement is public education and awareness not just about clinical research in general but also about the rights and responsibilities of those who participate in a clinical trial. There is a need to create an environment where patients have the confidence and trust that their participation in a trial is not only beneficial to them, but also to other patients in the world.

- Transparency and Openness: Greater transparency and openness by the regulators will go a long way in restoring trust amongst various stakeholders.

Pharma-SME Development

There are over 9000 pharma SMEs in India, which include manufacturers of formulations, APIs, and nutraceuticals. Pharma SMEs are cost-effective vital resources of skill, knowledge and employment and have been instrumental in reducing prices of drug manufacturing and in increasing rural penetration. Indian pharmaceutical SMEs have a great potential for transnationalization through exports and outward FDI, but are constrained by limited financial, technological capabilities and inadequate policy support. There is an urgent need for provision of sufficient low cost finance, strengthening access to national research laboratories, promoting pharmaceutical SME clusters, and continuous training and skill development programmes in transnationalization.

As per the Pharma Vision - 2020 of the Department of Pharmaceuticals, following goals have been set for the 12th Plan Period with respect to SMEs:

- Upgradation of SMEs to WHO-GMP and training of professionals therein; and

- Establishment of Pharma Growth Clusters.

To achieve these goals, there is a need for expedited approach.

Cluster Development

Setting up of pharma specific clusters in SEZ formats may help the industry in addressing the regulatory requirements and resultant costs. Common facilities, including common patent libraries, provision of International Pharma-copoeias in identified clusters; establishing quality control labs; developing world class quality control labs in the clusters will provide support for primary characterization and testing in a cost effective manner.

Utilities are the single largest contributor to the running costs of a plant in India, which include power and pollution control measures. Cluster development may address the need for reducing the cost of utilities by establishing common captive power plants and by way of creation of Common Effluent Treatment Plants (CETP).

Skill Development and Training

There is a need to focus on skill development and training of personnel for the pharmaceutical and lifesciences industry. Skill development is required in various functional disciplines in the industry, such as analytical, manufacturing and quality management. There is an acute dearth of qualified personnel in regulatory norms governing the pharmaceutical industry, e.g. filing of New Drug Application (NDA), negotiation skills, documentation, regulatory requirements and statistical techniques. Hence, it is important that

these disciplines may be introduced in academic syllabus of pharmaceutical training institutions. In addition, National Institute of Pharmaceutical Research and Education (NIPER) and the National Skill Development Council (NSDC) may develop training centres and modules particularly catering to the pharmaceutical industry.

Trade issues

Indian pharmaceutical trade quite often faces trade barriers in overseas markets, such as delayed approvals, severe administrative requirements and sanctions, drop in approval rates, delay in consignment clearances, rejection of consignments, and higher fees and commissions. These may be addressed through diplomatic channels, in addition to negotiations between the trade players; besides, such issues may be diligently pursued during bilateral and multilateral trade agreements.

Pricing of Formulations

Industry is of the opinion that frequent changes in pricing policy may be counterproductive and restrict long-term growth of the formulation sector. Also New Drug Delivery Systems (NDDS) for already marketed formulations need encouragement through proper fiscal measures. A stable pricing policy or market based price control may continue to encourage the formulation industry to invest in R&D in NDDS and dosage forms. Industry is further of the view that prices of patented products may be regulated on Purchasing Power Parity basis.

Combination products (Fixed Dose Combinations-FDC) are India's indigenous contribution to the world, with considerable approvals by regulators in the overseas markets. However, FDCs faces stringent regulations in the domestic markets. FDCs contribute substantially to the pharma companies' turnover. Having a rigid stand on this issue may diminish chances to attract FDI. Thus, depending on efficacy testing and patient compliance, FDCs may be supported and encouraged.

Outlook

Indian pharmaceutical industry is in the process of developing many potential new pharmaceutical products for world markets. While some of them are in the early stages of development, others are well on their way to commercialization. Many pharma companies have altered their drug portfolios from primary care driven blockbusters towards specialties, such as oncology, immunology and inflammation, where the medical needs are so high that prices are more easily accepted by the regulators.

The Indian pharmaceutical industry is projected to grow steadily in the medium term. In terms of volume, the Indian pharmaceutical market is forecast to be a major market, second only to USA, by 2020. The combination of value and volume growth is anticipated to provide ample opportunities for the industry for upgrading therapy and treatment levels. The mix of therapies is projected to continue to gradually move in favour of specialty and super-specialty therapies. Notwithstanding this shift, mass therapies are forecast to constitute half the market in 2020. Metro and Tier-I markets are projected to make significant contributions to the growth, driven by rapid urbanisation and greater economic development. Rural markets are projected to grow faster driven by step-up from current poor levels of penetration. On balance, Tier-II markets are projected to get marginally squeezed out. The hospital segment is envisaged to increase its share, growing to 25 per cent of the market in 2020, from the current 13 per cent.

The affordability of drugs will rise due to sustained growth in incomes and increases in insurance coverage. Private insurance coverage is projected to grow by nearly 15 per cent annually till 2020. However, the largest impact will be seen through government sponsored programmes that are largely focused on the 'below poverty line' (BPL) segment, and are expected to provide coverage to nearly 380 million people by 2020.

The global market for pharmaceuticals is forecast to register a steady growth. A recent report from IMS Institute for Healthcare Informatics had forecast that global spending on medicines is expected to increase by 4 per cent to 7 per cent CAGR (compounded annual growth rate) between 2014 and 2018. The USA is expected to drive the growth, with its spending expected to increase between 5 per cent and 8 per cent. Emerging markets too are expected to register healthy growth, with projected growth rates in the range of 8 per cent to 11 per cent.

A large number of patent expirations continue to offer strong growth prospects for Indian generic players in the developed markets, steadily driven by USA. Most developed markets continue to move away from branded generics to commoditized un-branded generics and lower margin tender based business; amongst new frontiers, Japanese generic market offers considerable potential for Indian generic companies, though there are significant challenges. Price erosion, especially through regulatory interventions, remains a foremost challenge in the European markets. However, presence in limited competition product segments and over-the-counter (OTCs) segments offer some protection to the margins for the Indian pharmaceutical companies.

Apart from the developed markets, the Indian pharmaceutical companies are also increasing their presence in the emerging markets. Indian pharmaceutical companies have strengthened considerable presence in Russia, South Africa, Brazil, Mexico, and South-East Asia. These emerging markets with some of them being branded generics offer strong growth prospects for Indian players given the high out of pocket expenditure on healthcare in these markets and relatively easier regulatory pathways.

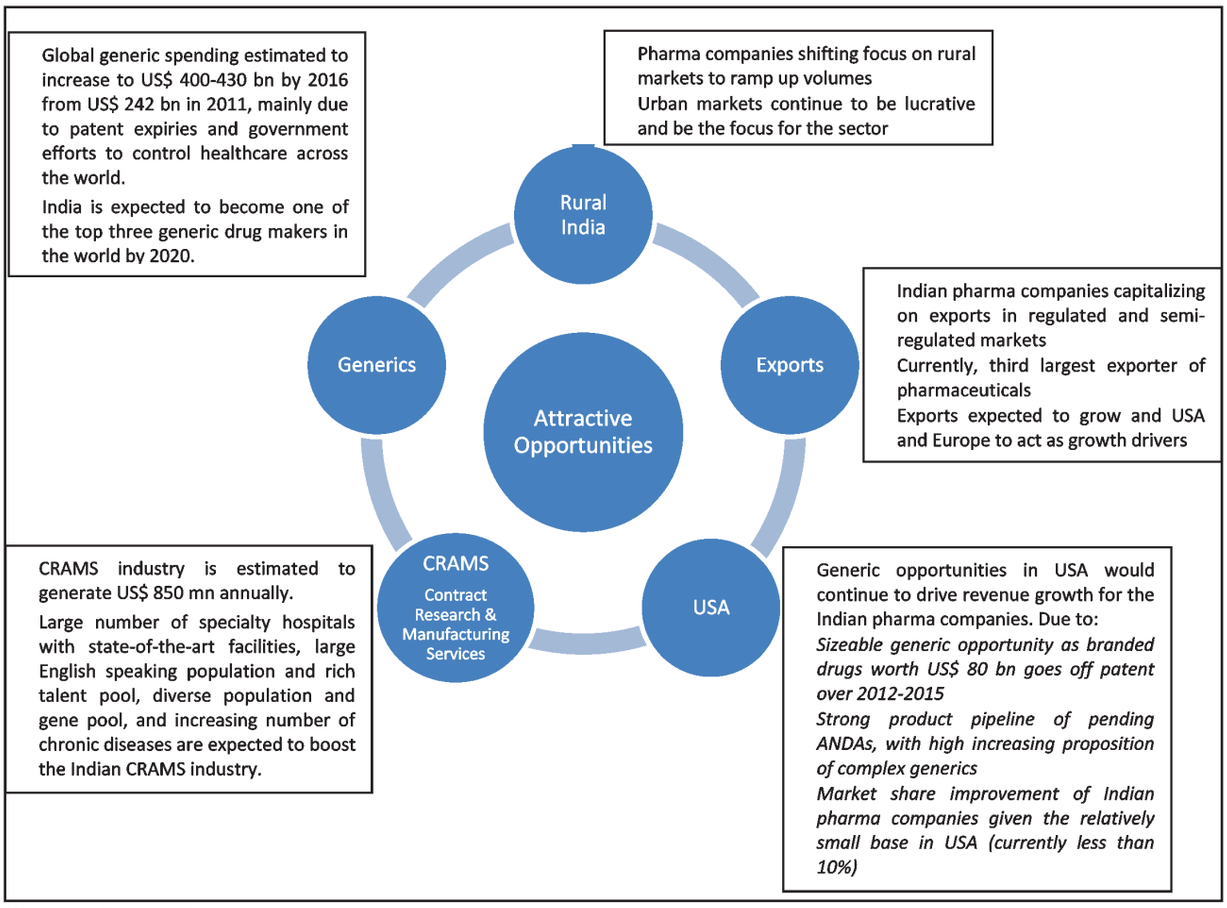
Besides new markets, Indian pharmaceutical companies are also tapping new areas, such as biologics/biosimilars for long-term growth avenue. As per the industry estimates, the biopharmaceuticals market was estimated to be around US$ 100 billion in 2010 and is estimated that almost 85 per cent of the existing biologics would face generic competition over the next ten years. The global biosimilars market is estimated to grow to US$ 3.7 billion by 2015 from US$ 243 million in 2010. The rapid growth in biosimilars is expected to be driven by patent expiries for more than 30 biologic medicines, with sales of US$ 51 billion in the next five years.

Despite challenges, leading Indian pharmaceutical companies is envisaged to continue to exhibit strong profitability indicators (excluding one-time instances like exclusivity-related aberrations or impact of foreign exchange fluctuations) and credit metrics. These strengths are also reflected in their strong credit profile. Outlook for the Indian pharmaceutical companies remains favourable as companies are forecast to continue to benefit from recovery in the domestic market, strong growth potential for generics in developed markets, and potential outsourcing opportunities. Overall, investments including capital expenditure are likely to remain buoyant over the medium term. Balance sheets of major pharmaceutical companies remain strong providing adequate room for fund raising.

In order to support the Indian pharmaceutical industry in its growth endeavour a 'Pharma Vision 2020' has been prepared by the Department of Pharmaceuticals, for making India as one of the leading destinations for end-to-end drug discovery and innovation, and for that purpose, the Government has proposed to provide requisite support by way of world class infrastructure, internationally competitive scientific manpower for pharma R&D, venture fund for research in the public and private domain and such other measures.

On the back of a high middle-class population base, improvements in medical infrastructure and the establishment of intellectual property rights are also anticipated to help the Indian pharma industry to grow manifolds. With the focus of companies shifting to smaller deals catering to niche segments and markets, partnerships seems to be the new norm in the pharmaceutical sector. The strategic execution of maximising on the available resources, both human and financial, will be the way forward for clinical and contract research building capabilities through strategic partnerships.

Exhibit 5.2: Opportunities for Indian Pharmaceutical Industry



Source: Express Pharma, Aranca research

ANNEXURE - 1: SIGNIFICANT PATENT EXPIRATION 2014 THROUGH 2015

Product	Company	Month of Patent Loss/Geography (US unless otherwise stated)
Micardis	Boehringer Ingelheim	January
Nasonex	Merck & Co	January (Paediatric)
Trilipix	AbbVie	January
Sandostatin LAR	Novartis	January/June
Maxalt	Merck & Co	February
Temodar	Merck & Co	February
Evista	Lilly	March
Avelox	Merck & Co	March
Viracept	Pfizer	April
Celebrex	Pfizer	May (Nov'14 in Europe)
Nexium	AstraZeneca	May
Copaxane	Teva	May
Herceptin	Roche	July (Europe)
Cymbalta	Lilly	August (Europe; Dec'13 in US
Remicade	Merck & Co	August (Europe)
Exforge	Novartis	October
Lantus	Sanofi	November (Europe)
Integrilin	Merck & Co	November
Abilify	BMS	Europe; April'15 in US
Agenerase, Infanrix/Pediarix, Relenza	GSK	Europe
Lyrica	Pfizer	Europe
Rituxan	Roche	Europe
Lemtrada	Sanofi	Europe

Source: IHS, 2014

ANNEXURE - 2: WARNING LETTERS ISSUED TO SELECT INDIAN PHARMACEUTICAL COMPANIES BY THE USFDA

Companies	Date of Issue	In Focus
Apotex Research Private Limited	01/30/2015	Unauthorized "trial" High Performance Liquid Chromatography (HPLC) injections prior to additional injections that were used in the reported test results. Failed to "exercise appropriate controls" - The company's computer systems were apparently configured such that data could be over-written.
Micro Labs Limited	01/09/2015	Potential testing 'fraud' - "reporting only those results" which were favorable to the company
Cadila Pharmaceuticals Limited	10/15/2014	Proper controls … unauthorized manipulation of [its] electronic raw data. "failed to have a back-up system for the data generated"
Marck Biosciences Ltd.	07/08/2014	Falsified data CGMP Violations: Hygiene - Serious mould and decaying frogs at the unit premises
Apotex Pharmachem India Pvt Ltd.	06/17/2014	Lack of control over its data – unauthorized manipulation
Sun Pharmaceutical Industries	05/07/2014	Physical data of trials destroyed
Canton Laboratories Private Limited	02/27/2014	Fabricating data, depriving quality data
USV Limited	02/06/2014	Fraudulent testing practices
Wockhardt Limited	11/25/2013	Testing results manipulated
Posh Chemicals Private Limited	08/02/2013	CGMP Violations; Sterility issues - inadequate monitoring of aseptic processing areas, air samples taken at inadequate times, uninvestigated batch failures and components, and failure to properly clean manufacturing areas.
Wockhardt Limited	07/18/2013	Efforts to delay and disrupt Inspection
Fresenius Kabi Oncology Ltd	07/01/2013	Significant deviations from CGMPs for active pharmaceutical ingredient. Manipulation of testing results
RPG Life Sciences Limited	05/28/2013	Deficient testing practices Falsified records

Source: Regulatory Affairs Professionals Society

ANNEXURE - 3: NON-FUNCTIONAL API/ BULK DRUG MANUFACTURING PLANT IN INDIA

Name of Bulk Drug	Producers	Commencement of Production	Present Status
Penicillin G/V	Alembic, Sarabhai, IDPL, JK Torrent, Ranbaxy, Standard	In early 60's	Plant Stopped
Streptomycin	Alembic, Sarabhai, IDPL	In early 60's	Plant Stopped
Tetracycline	Sarabhai, IDPL, Pfizer	In early 80's	Plant Stopped
Oxytetracycline	Sarabhai, IDPL, Pfizer	In early 80's	Plant Stopped
Kanamycin	Alembic	In early 70's	Plant Stopped
Erythromycin	Alembic, Themis, IDPL, Standard	In early 80's	Partially in operation for captive production for safety
Rifamycin	Themis, Lupin, Sandoz	Late 80's	Protection, captive
Gentamycin	HAL, Themis	Late 80's	Closed
Sisomycin	Themis	Late 80's	Closed
Vitamin B12	Themis, Alembic, MSD	Early 70's	Closed
Cephalosporin 'C'	Alembic	Early 90's	Closed
Lovastatin	Themis, Biocon, Kreb	Early 90's	In operation
Pravastatin	Themis, Biocon, Mylan	Late 90's	Closed
Griseofulvin	Glaxo	Late 80's	Closed
Cyclosporin A	Biocon, Mylan	Late 90's	Closed
Bleomycin	Themis	Early 90's	Closed
Mitomycin 'C'	Themis	Early 90's	Closed
Citric Acid	Citurgia, Citric India, Themis	Early 80's	Closed
Ephedrine	Malladi	Early 80's	In operation
Ascorbic acid	Sarabhai, Jayant Vitamin	Early 80's	Closed

ANNEXURE - 4: KEY DEVELOPMENTS IN REGULATORY ENVIRONMENT AND ITS IMPLICATIONS ON INDIAN PHARMACEUTICAL INDUSTRY

Particulars	Description	Implications
National Pharmaceutical Pricing Policy (NPPP) 2012	• The Indian Government introduced NPPP in 2012 to regulate the prices of 348 essential drugs, based on their strengths and dosages. • Manufacturers are allowed to sell these drugs at or below the ceiling price fixed by the government. • The policy is applicable to imported drugs as well.	• Implication of NPPP resulted in decline of profit margins for products under regulation from 20% to 16% and 10% to 8% for retailers and stockists, respectively, during 2012-13. • The policy has resulted in significant uncertainty among stockists on whether to continue with the business amid low profit and margin reduction.
Foreign Direct Investment (FDI) Policy	• The FDI Policy in the pharmaceutical sector allows 100% FDI under the automatic route for Greenfield investments and 100% FDI are allowed for brownfield investment under the government approval route. • Further with a view to protecting the domestic pharmaceutical sector, including the production of generics, the Government has decided that 'non-complete' clause would not be allowed except in special circumstances with the approval of Foreign Investment Promotion Board.	• As per the Department of Industrial Policy & Promotion (DIPP), the pharma sector attracted cumulative FDI investments of approximately USD 12.7 billion during the period January 2000 to November 2014.
Medical Council of India (MCI) guidelines on sales and marketing practices	• MCI guidelines were issued to ensure transparency in sales and prevent unethical practices of some doctors. • MCI aimed to stop medical professionals from prescribing drugs in exchange of enticement from drug manufacturers.	• Tax authorities use the Central Board of Direct Taxes (CBDT) circular based on MCI guidelines to decide on permissible sales and marketing expenses.
Department of Pharmaceuticals (DoP) uniform code on sales and marketing	• In 2011, DoP laid down a code of marketing practices for the pharma sector to streamline marketing efforts. • The DoP code lays down guidelines for exaggerated claims; audiovisual promotions; activities of medical representatives; and provision of samples, gifts, hospitality and sponsorships by pharma companies.	• The adoption of DoP code is voluntary. However, in recent times, the pharma sector has agreed to enforce the code. • DoP review its implementation and after a set interval of time it is discovered that the code has not been implemented by pharma associations or companies, it would consider making it a statutory code.

Compulsory Licensing	• India has adopted compulsory licensing on the following grounds under Section 84 of the Indian Patent Act: (1) The drug did not mean reasonable requirements of the citizens, (2) the drug was not reasonably priced and (3) the patent was not locally manufactured.	• The imposition of this regulation paved the way for production of low-cost generic medicines of the branded patent drugs. Thus, costly branded lifesaving drugs is available at cheaper rates to the Indian population. • The regulation affects the brand value of branded drugs manufactured by MNCs and thus has been opposed by them.
Clinical Trial Regulations	• As per new regulations introduced in 2013, all clinical trials need to be approved by a government committee and at least half of each trial needs to be run in government–run hospitals. • Pharma companies need to have the videotaped consent of each test subject.	• Stringent regulations increase the duration of the approval process; hence, the number of clinical trials has dropped to 19 in 2013 from 500 in 2011. • It also projects India as a less favourable option to conduct clinical trials.
Bio similar Guidelines	• The 'Guidelines on Similar Biologics' prepared by the Central Drugs Standard Control Organisation and Department of Bio technology in 2012 laid down the regulatory pathway for a biological claiming to be similar to an already authorized reference biological. • The guidelines address the regulatory pathway regarding manufacturing process and quality aspects for similar biologics. • These guidelines also address the pre-market regulatory requirements including comparability exercise for quality, preclinical studies, and post-market regulatory requirements for similar biologics.	• The new guidelines create a pathway for local and international companies to invest in bio similar development with manufacturing in India. • The introduction of a similar biologic or bio similar into the market would result in significant reduction in cost. • The introduction would also help address local patient's access to expensive drugs.

Source: Sun Pharma Annual Report 2013; PWC