FUTURE OF PHARMA

A FORESIGHT STUDY-2030

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A Report By

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Abbreviations

Abbreviations	Full form
AfCFTA	African Continental Free Trade Agreement
AMA	African Medicines Agency
AMRH	African Medicines Regulatory Harmonization
ANDA	Abbreviated New Drug Application
APEC	Asia-Pacific Economic Cooperation
API	Active Pharmaceutical Ingredients
Asean	Association of Southeast Asian Nations
BSL-3	Biosafety Level 3
CAGR	Compound Annual Growth Rate
(CCCMHPIE)	Chinese Pharmaceutical Association, China Chamber of Commerce for Import and Export of Medicines and Health Products
CDMO	Contract Development & Manufacturing Organisations
CDSCO	Central Drugs Standard Control Organization
CEP	Certificate of suitability
CMO	Contract Manufacturing Organisations
CNS	Central Nervous System
CPhI	Convention on Pharmaceutical ingredients
CRA	Clinical research Associate
CRO	Contract Research Organisations
CTO	Clinical Trial Organisations
DMF	Drug Master File
DPCO	Drug Price Control Order
EAC	East African Community
ECOWAS	Economic Community of West African States
EU	European Union
FDC	Fixed Dose Combination
FDI	Foreign Direct Investment
GCP	Good Clinical Practice
GDP	Gross Domestic Product
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GST	Goods and Services Tax
GCC	Gulf Co-operation Council
HAL	Hindustan Antibiotics Limited
IBEF	Indian Brand Equity Foundation
ICH	International Council for Harmonization
ICMR	Indian Council of Medical Research
IDF	International Diabetes Federation
IDPL	Indian Drugs & Pharmaceuticals Limited
IFC	International Finance Corporation
IOT	Internet Of Things
IP	Intellectual Property
KSM	Key Starting Material
Mercosur	Southern Common Market (a South American trade bloc)

MRA	Mutual Recognition Agreement
MRSH	The Medicines and Healthcare products Regulatory Agency
NCDIR	National Centre for Disease Informatics and Research
NHP	National Health Policy
NPPA	National Pharmaceutical Pricing Authority
NBT	Non-Tariff Barriers
OoPE	out-of-pocket expenses
OTC	Over-the-Counter (Non-prescription medicines)
PANDRH	Pan-American Network for Drug Regulatory Harmonization
PBM	Pharmacy Benefit Managers
PE	Private Equity
PHARMEXCIL	Pharmaceutical Export Promotion Council
PMBJP	Pradhan Mantri Bhartiya Janaushadhi Pariyojana
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PLI	Productivity Linked Incentive
PPP	Public-Private Partnership
QUAD	Quadrilateral Security Dialogue
RCEP	The Regional Comprehensive Economic Partnership
REC	Regional Economic Communities
Rx	Medical Prescription
SADC	Southern African Development Community
SEZ	Special Economic Zone
SME	Small & Medium Enterprises
SPC	Supplementary Protection Certificate
TGA	Therapeutic Goods Administration
TIFAC	Technology Information Forecasting and Assessment Council
UK	United Kingdom
US	United States
USFDA	US Food and Drug Administration
VC	Venture Capital
VUCA	Volatile, Uncertain, Complex, Ambiguous
WHO	World Health Organisation
ZaZiBoNa	Zambia Zimbabwe Botswana Namibia

Executive Summary & Highlights of the Report

Executive Summary

The decade till 2030 can be called the decade of Indian pharmaceutical industry where a lot of convergences are happening which can take Indian pharmaceutical industry to greater global heights. In fact, some sectors of the pharmaceutical industry are the most globally competitive sectors of the Indian economy. However, to take Indian pharmaceutical industry to pinnacle of global heights require a bold vision from the government and the industry and substantial investment in technical education and R&D. India's weakness has always been the low investment in R&D and if this is increased, Indian pharmaceutical industry has the capability to be create new products & efficient production processes. The industry must also substantially increase its revenue streams from diverse sources such as API, CDMO, bio-generics and plant-based health products etc. than only relying upon production & export of generic drugs. This is possible and the preferred route as our insights discover.

Generic exports will come under increased price pressures in developed countries, especially US and non-tariff barriers in developing countries. After Covid experience resulting in shortages of essential drugs, most countries are re-looking at their plans for indigenous production, especially in the light of opening of larger markets due to reduction or elimination of regional trade barriers.

This study largely focuses on the global opportunities that are practically in sight for Indian firms, some of these mentioned above. We have not given detailed analysis of the Indian market. The reason is that a large number of reports have come out recently on the Indian pharmaceutical market and we do not wish to add another me-too report. Indian market is large, diversified and growing at a fast rate. This backbone provides the foundation for faster growth in the burgeoning overseas markets. However, there is little information on India's global opportunities as well as threats and it is here this report has put its efforts. The special focus of this report are the opportunities in Africa. While the African continent accounts for only 0.7% of the world market, with 13% of the world's population and 24% of the world's morbidity against 6% of health expenditure. This will change over this decade. Multinationals are retreating from African markets, at least they are not expanding. Their place is being taken by domestic, Asian and Middle-East firms. Many large Indian firms are not yet represented in Africa which is the last underdeveloped market of the future.

At least four pharmaceutical exclusive cities/zones have been commissioned or under construction on the continent, with the largest pharma city in the Middle East and African continent, in Egypt. A large amount of funding is also available for African industrial development. Besides a host of activities in many other countries have also been reported. Indian companies and the government have to set their vision high and widen their horizon to take India to a dominant global position. It is not impossible to reach a global revenue of $300 billion by 2030.

Highlights of the Report

- Create domestic capabilities for at least 80% of the entire range of formulations value-chain without which the title of "pharmacy of the world" cannot sustain.

- Indian pharmaceutical industry must widen its revenue sources for which a large number of global opportunities are available rather than only dependent of generic drugs.

- Prepare to face increase competition in formulation exports especially from China, Bangladesh, Turkey, Egypt and Turkey.

- After Covid19, more countries & regions will undertake local manufacturing of generics. Develop at least five pharmaceutical clusters abroad similar to one announced for Mexico.

- Take export production of common generic drugs (WHO Model List) to overseas plants and move domestic production into high value segments such as injectables, complex generics & biogenerics (or biosimilar). Large low-cost funding is available from a variety of sources including Impact Investment.

- Africa is the next big market. Indian companies should introduce services such as overseas warehousing, distribution & retail into export strategy for Africa to create an unbreachable competitive advantage. A model is provided here.

- Increase profitability of Jana Aushadhi Kendras. It is unviable in the long-term. Expand reach of affordable pharmaceuticals into rural areas through mobile Jana Aushadhi Kendra and outlets within the government hospitals.

- India is much ahead of China in API manufacturing (except antibiotics). The government should facilitate the growth of API technology through API R&D Centre as well as continuous processing technology development.

- Huge global opportunity for expansion of API industry. Industry should aim for 40% of world's merchant supply of API and it is possible for a global market of $60 billion by 2030 at a CAGR of 16%.

- The government should protect the Indian API industry from predatory Chinese pricing not only in India but also export markets.

- Contract Development & Manufacturing Organisation (CDMO or CRAMS) sector is the dark horse of Indian pharma. Its revenues can rival other sectors. India can build unassailable global advantage

- Create Technology Park for CDMOs around a nucleus of R&D Centres and tertiary pharma focused educational institutions.

- Indian companies should re-examine the cost of bringing out a new drug and not rely upon the ball mark figure $1-1.2 billion given by multinationals. Recent research has shown that the cost is much lower.

- The government should facilitate establishment of biogenerics R&D Centre for a larger number of companies to enter this sector.

- If government invests 10% of the annual space budget for five years, Indian pharma R&D can show equally impressive result.

- Export of knowledge workers for the entire drugs value-chain knowledge can be a big foreign exchange earner by 2030 and also allow transfer of knowledge.

- Major investment rebates & subsidies will be available under European Union's Pharmaceutical Strategy for Europe which will be unveiled in 2022. Indian companies must gear up for increased investment in The European Union and take a sizable market share.

- There are opportunities for India in President Biden's 100-day Supply-Chain Analysis Report entitled "Building resilient supply chains, revitalizing American Manufacturing, and fostering broad-based growth". The government should submit a strategy to the US Administration for collaboration in the pharma sector.

- India must attract a greater share of Impact Investment, both for Indian and overseas operations.

- India must join international harmonisation organisations such as ICH & PIC/S at the earliest

Chapter 1 Introduction

The global pharmaceuticals market was worth $934.8 billion in 2017 and will reach $1170 billion next year in 2021. Growth over past decades means that North America and Western Europe still account for 56% of the global market, but Asia Pacific has overtaken Western Europe as the second-largest region according to The Business Research Company. “Growth in Asia Pacific is fuelled by increased affordability of drugs resulting from the launch of low-priced generics. Other factors that are positive for growth in Asia Pacific are the rise of GDP per capita in the region, government programs to support healthcare, and rapid urbanization, which brings both doctors and pharmacies within easy reach of increasing proportions of growing populations. Pharma sales in Asia Pacific will grow at 8.4% a year to 2021.

India’s pharmaceutical industry has been growing rapidly with a large-scale production ecosystem of low-cost medicines. Covid has brought forth new & expanded opportunities but also certain threats. The opportunities come from the fact that India is largely self-sufficient in meeting over 95% of pharmaceutical needs from domestic manufacturing and beyond that it is major exporter of generic medicines throughout the world. Although India was the largest manufacturer and exporter of vaccines too, this fact was not so well known. During development and marketing of covid vaccines, the entire world now knows this fact. India is not only the largest exporter of generic drugs and vaccines, it is also the lowest cost producer. The government of India is procuring covishield at $2.72 per dose while in 2020, US government signed a deal with Pfizer at USD20 per dose.[1]

Covishield has announced to the world that India is the “pharmacy of the world” and has opened new opportunities for domestic markets and exports. However, the recent decision by the government of India to ban exports has led to realisation by importing countries that they are over-dependent on imported medicines and they must explore establishing their own domestic industry, at least for commonly used drugs. This threat has manifested in both regulated markets such as US and EU and also in other regions such as Africa. However, this threat also comes with an opportunity for expanding the global markets for Active Pharmaceutical Ingredients (API) where for a large number of products, China and the resurgent India are the only source. Many importers, including India, have realised that they cannot depend only upon China and must have diversified sources of supplies and only India can fill in the shoes of China+1 strategy.

1.1 Convergence of events favouring pharma industry

There is a convergence of global events which makes the Indian Pharmaceutical Industry a very exciting sector for the future which not only has high growth potential but also the capability to dominate the global pharmaceutical space over the next decade in several sectors.

The converging events are:

1.1a Covid19 Pandemic – It brought out the fact that no manufacturer in the world can rely upon only one source of ingredients and the Indian pharmaceutical industry can serve the world in China+1 strategy of importers and in many cases replace China.

In 2021, an executive order signed by US President Joe Biden called for the creation of "China-free" supply chains in strategic industries, such as pharmaceutical and bio-pharma products, among others. Firms from the US, the EU, Taiwan, South Korea, and Japan, all active players in these areas, are looking to move portions of geo-fenced operations to India. The Biden administration has made it clear that America plans to put geopolitical considerations ahead of any overarching ideological commitment to free trade.[2]

1.1b Vaccine leadership

India has overtaken China as the principal outsourcing destination for vaccines, not only in efficacy and quantity but also price. Indian vaccine Covishield produced under license from AstraZeneca has been exported to about 30 countries and another vaccine under license from Pfizer may enter market soon. Eight indigenous vaccines are under development in India and Covaxin from Bharat Serum may get the first one to get regulatory approval. Our vaccine cost $2.50 to the government which is the lowest in the world.

India is already world's number one producer of vaccines and the development work done within the country, not only in the vaccine field but allied sectors such as cold chain logistics, transportation boxes (One Indian company has recently received a patent) would have a multiplying effect on the economy as well as creating a R&D & logistics infrastructure which could be used in future outbreaks.

We have seen in the Covid pandemic that even very technologically advanced nations like Japan, South Korea, Taiwan could not produce a vaccine and had to rely on the small number of global manufacturers to vaccinate their population. India is much ahead of these countries and has shown that it has the capacity to develop its own vaccines. If we invest in creating a broad-based biotherapeutic industry which includes vaccines, we can be one of the global powers in this industry of the future.

1.1c China's aggressive postures

China's border aggression has opened our eyes to the fact that we have too much reliance on that country and India has started decoupling from imports of pharma ingredients, not immediately but in a phased manner. Our thriving API industry was crippled by cheap Chinese imports. China's large industrial base is one part of the story for cheap exports. Another side is the opaque government-industrial conglomerate to destroy another country's industry using state subsidies. Our nascent mobile phone industry was nearly wiped out by cheap Chinese imports and prior to the hostilities, China had its eyes fixed on our automotive and networking industry. Many of our thriving small industries like toys, umbrella too were totally wiped out by indiscriminate Chinese imports. Using Covid induced downward valuation of our major companies, China was also creeping into taking stakes into our major companies such as HDFC Bank. The government nipped this in the bud.

We have to understand that in China, there is no private industry as we know in India and western nations. All industries from Huawei to Alibaba have linkages to various organs of the government and they have to follow the diktats of the government. There is no rectification or appeal through judiciary.

On the other hand, China is very cautious about opening its markets to countries which it regards as its rival and India is the top on its list. It uses a variety of Non-Tariff Barriers (NBT) to shut its market to our manufacturing exports.

The aim of Chinese government is to use the state subsidised cheap imports to hook the importing countries in a state of total dependence upon China just like a junkie is hooked on narcotics. India has, at the right time, announced Atmanirbhar Bharat Scheme to reduce this dependence on China for key pharmaceutical ingredients or API. The authors of this report will not be surprised if China uses its old tricks of deep discounts on select APIs, to prevent India from taking foothold in the world API market as a big competitor. China is aware that India is the only country which has the potential to rival China in manufacturing sector. All stakeholders must be alert to this possibility.

Hinrich Foundation, a respected global trade thinktank, in its latest analytical report "India: A 21st century technology hub?" has noted that "India has struggled to develop a solid manufacturing base within its economy. But despite much maligned systemic issues, a combination of geopolitical and internal dynamics suggest that India now faces an historic opportunity to transform into one of the world's most important technology hubs. Geopolitics in the 21st century have handed India a historic opportunity. Washington's technology cold war with Beijing has resulted in strategic decoupling, prompting manufacturing supply chains to shift to new locations. India finds itself well positioned to absorb these supply chains. Its government has responded by rolling out reforms to attract foreign direct investment (FDI), create new infrastructure, and promote special economic zones (SEZs) and technology clusters.[3]

McKinsey & Co., too in its report "India's Turning Point"[4] has identified pharmaceutical industry as one of the six globally competitive manufacturing hubs and has suggested reform themes to make it happen. Some of these are already being unveiled by the government. There is potential to raise Indian manufacturing output in pharmaceutical & medical device industry by additional $60 billion by 2030 and hundreds of small and medium sized firms can scale up to large firms within 10 years.

The pharmaceuticals sector represents a high-potential opportunity for India, both because the COVID-19 pandemic underscores the need for strong medical capabilities all over the world and because India's traditional strengths as a pharmaceuticals export powerhouse can be leveraged to create GDP and jobs. The pharmaceuticals market revenue could reach about $105 billion by 2030 from about $40 billion in 2020 at a compound annual growth rate of 9 percent. The country could also increase its pharmaceutical exports from $20 billion in 2020 to $50 billion in 2030 (The authors of this report estimate is that India should aim for a global market of $70-80 billion with APIs taking the lead over formulations). The key to achieving this will be for India to accelerate Contract Development & Manufacturing Organisations (CDMO), and bulk drug (API) manufacturing and build a strong innovation ecosystem.

Additionally, for India to unlock its full potential, it needs to move towards the more valuable innovation space. The country already has a strong foundation for innovation given its strong domestic market and technical capabilities. However, support from various stakeholders could provide an impetus to grow.[5]

For China, domination in global markets is another form of warfare where it tries to browbeat its rivals just as it has tried to do to all its neighbours. The authors have spent considerable space in analysing these phenomena in the pharmaceutical sector and brough out new insights.

1.1d Strategic convergence of Quad

Chinese aggression, physical, economic and technological. has brought some convergence of interests in a group of four countries, viz. US, India, Japan and Australia which are working together to strengthen supply chains and reduce dependence on China where pharmaceutical would figure prominently.

Japan, South Korea, and Taiwan have been singled out as key strategic partners, but India also stands to gain enormously if it can achieve its manufacturing benchmarks and attract new value chains through its tech-scape. These must continue to involve big firms like Apple and Samsung. New Delhi has an opportunity to work closely with Washington and its allies across Asia. Even if some upstream elements are spread around Southeast Asia, India can still pull downstream portions of those value chains into its orbit. This re-orientation of common interests works in favour of Indian pharmaceutical industry.[6]

Reuters reported on 12th March 2021 that The United States and three of its closest Indo-Pacific partners committed to supplying up to a billion coronavirus vaccine doses across Asia by the end of 2022 at a summit on Friday carefully choreographed to counter China's growing influence.[7] However, recent upsurge in covid cases in India has temporarily derailed India's existing lead in global vaccine supply and provided an opening to China to move into this space.

1.1e Drugs losing patent protection

The global marketing of off-patent drugs has been one of the reasons for India's success in the world markets. With the huge growth in the generic drug market, there is no doubt that generic companies are continuously searching for drugs with a soon-to-be-expired label.

Between 2012 and 2016, drugs with an estimated $117.2 billion in U.S. sales went off-patent. Since then every year 10 or more drugs lose patent protection and it is these drugs which provide the fuel for the growing sales of Indian companies within the country and exports. 43 drugs will lose patent protection in 2021 – 2022 and so on. Now increasingly, biological drugs are also facing patent expiry.

1.1f Rapid rise of Biological Drugs

Biological drugs have shown a rapid increase in share of Top 100 products:

- 2010: 34%
- 2018: 53%
- 2024: 50%

After 2024, the biological drugs will take major share of the market.[8]

This creates a major opportunity for India in biogeneric as fewer small molecules (or synthetic) drugs will enter the generics market in future. There are fewer global competitors in biogeneric space compared to conventional synthetic drugs due to difficulties in their

development and manufacturing. Investment in knowhow and capacity creation would help a greater population in India and elsewhere having access to these drugs, especially cancer drugs.

1.1g Covid induced market growth for nutraceuticals

The nutraceutical market has exploded worldwide since Covid19 pandemic started. A greater number of people are taking preventive healthcare measures, especially fortifying their immunity. The global nutraceutical market size was valued at USD 382.51 billion in 2019 and is expected to expand at a CAGR of 8.3% over the forecast period as compared to 7% in the pharmaceutical sector.

India has a rich resource of plant based raw materials as well as Ayurvedic knowhow. To give an example, India is the largest producer and exporter of turmeric which has great immunity building properties. However, we have not fully exploited these resources and contended ourselves in exporting low-value raw materials rather than high-value consumer products. Yoga is India's best-known soft power globally and more people are aware of Ayurveda than ever before (as evidence in the 100% growth seen in ashwagandha sales in the US for two years in a row). However, to seize this market, R&D to show efficacy, product development and synergistic marketing strategy should be employed. For example, ICMR has rolled out a large clinical study on Ayush ingredient for immunity, which has been tested on over 10,000 police personnel. Some small successes by products developed by the MSME industry have shown the route to gain a large market share.

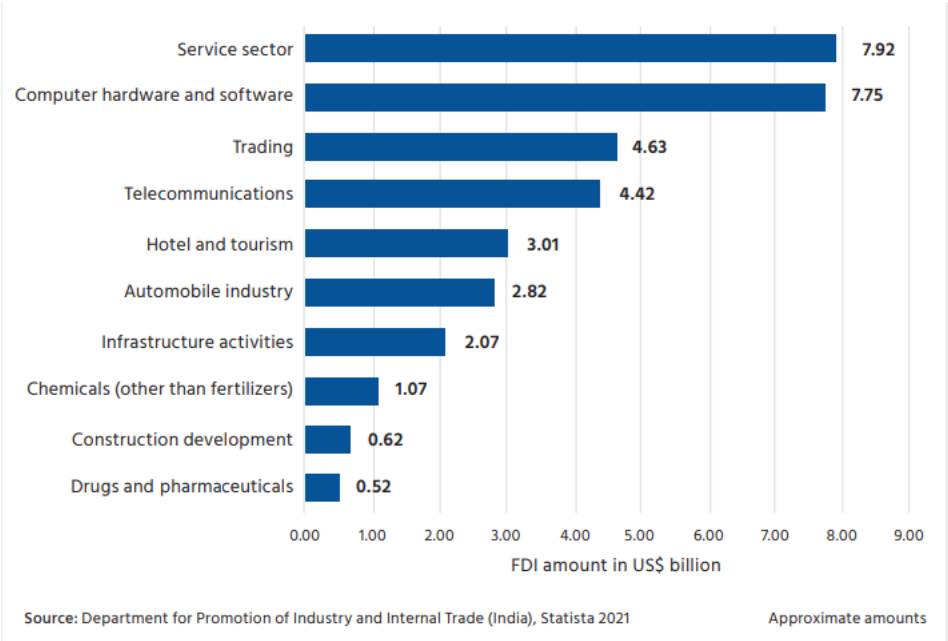
1.1h Information Technology in Drug Development

Big Data, Artificial Intelligence and Machine Learning techniques are being employed not only to speed up drug discovery, but also drug development with the hope that data-driven approaches will help reduce R&D costs and industry failure rates.

India has one of the world's largest information technology (IT) industry and Indians employed in the R&D establishments of global IT giants such as IBM are responsible for producing a very large number of patents. For instance, IBM India was the second highest contributor to IBM's US patents in 2020.[9]

India can be of the centres of the drug discovery & development process through its twin strengths in pharmaceuticals & information technology and opens a vast field for novel drug discovery and contract research.

India has to put in more efforts to reap the benefits of this large market which has opened up. Government has laid out the initial roadmap but not only more efforts are required but these must be accelerated. India should become more attractive for FDI to pour into the Indian pharmaceutical industry. According to the following chart, FDI in pharma is much below potential and it seems some MNC are not yet convinced of India's commercial policies.



FDI distribution by sector in FY 2020

For companies, FDI is a long-term investment and not only they look at the markets but stable & predictable business environment. Therefore, rise in FDI in the pharmaceutical sector will be the proof that India is an attractive destination.

All these events, if viewed in a concerted manner provides an unprecedented opportunity for India to, not only manufacture pharmaceuticals for the world but also partner with other countries to manufacture pharmaceutical formulations, APIs and vaccines. Already some countries such as Egypt and Bangladesh have made their overtures.

Our refusal to sign the RCEP should also be seen in the strategic context of decoupling from China. Any membership of a China dominated body means India would have to play the role of a junior partner. By decoupling, Indian industry can emerge from the shadow of China to become a rival to China.

Since our pharmaceuticals domestic & export markets occupy about 50% share each of the industry, any capacity creation for placing India as the no.1 global sourcing destination would also provide greater and reliable access for providing products for the Indian market, both in time and cost. A larger world market would ultimately benefit the Indian consumer of medicines. The government's policies are also focused in this direction, that is to increase production capacity in India's domestic market, and then expand that capacity to accommodate exports.

According to Deloitte 2019 Global Life Sciences Outlook,[10] India is the world's tenth-largest pharmaceutical market in US-dollar terms. Private expenditure is expected to drive growth by creating a demand for more advanced, costly medicines among India's growing middle class. NCDs account for 53 percent of deaths, while diabetes account for over 80 million patients who require lifelong access to drugs. A majority of these patients may not die of diabetes as such but long-term complications associated with diabetes. In India, ischemic heart disease and chronic obstructive pulmonary, diarrheal, and cerebrovascular diseases are leading causes of deaths. Due to large-scale migration to urban areas, even poor people are developing many of these lifestyle diseases which at one time were associated with the wealthy. This requires

drugs which are cheap but at the same time remunerative to the manufacturers for the investment to pour into the sector. Therefore, a large share of the international market is essential to create scaled up manufacturing.

To leverage these opportunities, we cannot rely on only one strategy which have given excellent dividends till now, that is, producing in India for the world. The global markets are not stationery in time but keep changing due to global, regional and national needs and priorities. Our engagement with the global pharmaceutical market should also anticipate the changing contours of the Indian and global demand and supply. We should not assume that what worked in the past will also work in the future but to be ever ready with an exploring mindset to identify distant signals, understand their relevance as threat and opportunity for the Indian industry and dynamically modify our steering to take to new roads and destinations.

Our aim with this report is not to add to the burgeoning library of well-researched reports which have been issued by the government & private agencies, including globally respected consultancies. Instead, our objective is to sift the data already presented and uncover and highlight those facets of the global markets of the future which will propel our pharmaceutical industry to reach new heights.

One market in particular has drawn our attention and we have spent considerable space on it, that is Africa. With the unified continental market, it has the demographics and rising GDP growth to make it the market for the next decade and beyond. This facet of Africa has not gone unnoticed in the Chinese pharmaceutical industry.

Our pharmaceutical industry has reached a pivotal point where we have to ask what made us global No.1, today and how we can retain a global leadership position a decade from now. Certain weak and distant signals are showing the roadmap. To devise and execute a global strategy where we are leaders in certain segments of the global pharmaceutical market requires deep thinking by the government and other stakeholders jointly and prepare a roadmap for global leadership.

1.2 Objective of the Sector Report

The pharmaceutical industry consists of a vast network of processes and institutions which carry out different drug discovery, development, manufacturing & marketing functions, starting from identifying possible targets for diseases and ending at bringing the medicine in the right dosage and form to the patients.

Many exhaustive reports have been published on India's domestic market by leading consultants and industry associations. The most recent being a detailed report published by Competition Commission of India. We do not want to duplicate their work. However, our international role has been less exhaustively dealt with and it is here that our efforts have been focused.

In this report, we are only concentrating on manufacturing & service functions for our detailed analysis where India has competitive advantage or can take a globally competitive lead within this decade. R&D and Biologics have still a long way to go before Indian companies can be considered globally competitive.

1.3 Research Methodology

Our study is based on the emerging discipline of Foresight. It is the study of weak and distant signals and consists of identifying sources of signals, receiving these signals and interpreting them to understand what will happen and what might happen in the future. In the VUCA (Volatile, Uncertain, Complex, Ambiguous) environment, there is not one route to take but examine many scenarios. To do this, we have cast our net wide to study political, economic, technological & social sources of secondary information. As said earlier, we are not adding to the proliferation of information but to analyse these sources for new insights.

It is usual for such reports to develop a SWOT (Strength-Weakness-Opportunity-Threat) analysis. SWOT was designed for a stable business environment and due to fast changing and uncertainties in today's environment, SWOT is losing its significance. SWOT is based on generation of a mountain of data which gets outdated very fast. Today, in the VUCA age, future is not an extension of the past. With access to big data and huge computing power, we are deluged with information and to find correlation and patterns is becoming more and more difficult. Rather than relying on past data to look into the future, we have tried to look into the distant future, what are the weak signals emanating from the future and to what extent these signals are likely to mature. Therefore, one cannot have a single strategy but a number of different directions which companies can take to ensure their growth a decade from now.

In the VUCA age, it is even more important to test hypotheses and conduct experiments to identify the likely routes to take. Are we testing hypotheses? Perhaps not. Therefore, we have identified some such avenues to explore & experiment further such as end-to-end factory to customer delivery solution for Africa, looking into its huge counterfeit drugs problem, which to a certain extent is perceived to emanate from India. On the surface, it looks inconceivable, but with an explorer's mindset and an experimental approach, can give us an unassailable global position.

In conclusion, through our analysis, we have tried to show that India can be the global leader in certain segments for which we have proposed bold strategies.

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Chapter 2 India Pharmaceutical Sector

2.1 Evolution of Indian Pharmaceutical Sector

The modern pharmaceutical industry in India is over a century old. Bengal Chemicals was established in 1901 and Alembic Pharma in 1907, both companies going strong today. However, till about 1970, foreign multinationals dominated the Indian pharmaceutical market. In 1970, Indian Patents Act was enacted which allowed protection only for the manufacturing process deployed to make new drugs. This laid the foundation of domestic pharmaceutical industry in a big way and most of today's large companies have their origin during this period. From 1990 onwards, the industry was globally competitive, and the country started exports in a large manner, something which is continuing till date with increasing momentum.

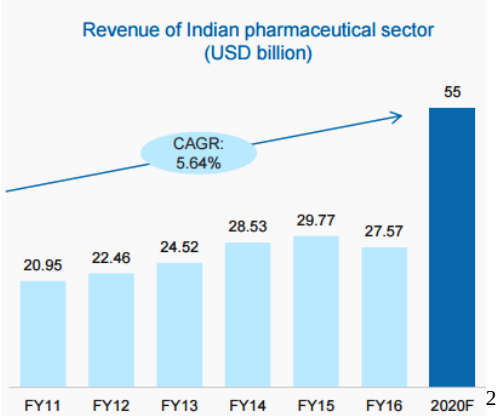
2.2 Pharmaceutical Sector Growth in the last decade 2010-2020

Our country possesses a well-established pharmaceutical industry with a strong network of 3000 drug companies producing a wide range of medicines through several thousand manufacturing units. Out of these, 1,400 units are approved by World Health Organization (WHO) for having Good Manufacturing Practice (GMP); 1,105 have Europe's certificate of suitability (CEPs); more than 950 match Therapeutic Goods Administration (TGA) guidelines; and 584 sites are approved by the US Food and Drug Administration (USFDA).[1]

According to IBEF, India is the largest provider of generic drugs globally. Indian pharmaceutical sector supplies over 50% of global demand for various vaccines, 40% of generic demand in the US and 25% of all medicine in the UK. Presently, over 80% of the antiretroviral drugs used globally to combat AIDS (Acquired Immune Deficiency Syndrome) are supplied by Indian pharmaceutical firms.[2]

According to the Indian Economic Survey 2021, the domestic market is expected to grow 3x in the next decade. India's domestic pharmaceutical market is estimated at US$ 42 billion in 2021 and likely to reach US$ 65 billion by 2024 and further expand to reach ~US$ 120-130 billion by 2030.[2] It is one of the fastest growing sectors of the Indian economy and IBEF predicts a growth rate of 22.4% in the near future. Post Covid19, India's stature has increased and overshadowed Chinese influence in the vaccine field, though there have been recent setbacks. India's advantages are well-known and reported in many studies.

However, the growth pattern is not uniform and there has been considerable volatility in export growth as witnessed in recent years.



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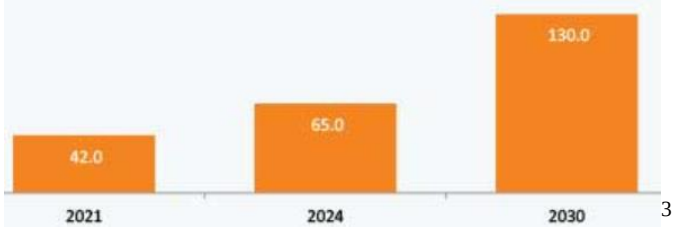


3

The main reasons for the volatility, according to a Deloitte analysis are[4]:

Pricing pressure in the US and Europe – a rapid rise in companies in other countries producing competing generic drugs resulted in a significant erosion of generic drugs prices over the past ten years.

Regulatory compliance issues – India exports 50 per cent of its products to highly regulated markets and, in the past few years, regulators have highlighted issues with quality control and manufacturing slippages.

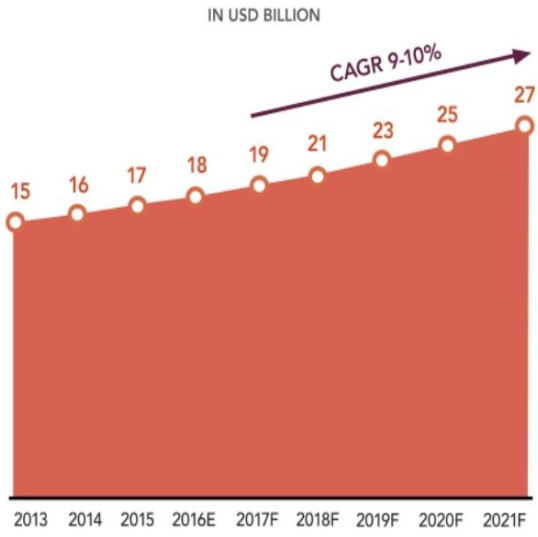
New domestic tax regime – Imposition of GST has resulted in higher manufacturing costs, slow-moving inventory and smaller profit margins. Consequently, the industry grew at only 5.5 per cent in 2017 but recovered to 9.4 per cent in 2018.

Reduction in product launches – in 2011, India launched 3,505 new pharma products, by 2018 the number was 3,150 products (a 10 per cent reduction), due largely to a ban on fixed dose combination (FDC) drugs. There was also a reduction in new acute therapy product launches, due to competing products and price controls by the Indian National Pharmaceutical Pricing Authority (NPPA).

Domestic price regulations – the NPPA's 2012 revised drug pricing mechanism calculates a drug's ceiling price from the mean of the prices of all brands that have more than one per cent of market share for that category. By March 2019, the NPPA had price-capped more than 1,000 drugs, and companies slowed down production of drugs subject to these price controls.

Rising API costs – Rises in the cost of APIs is directly proportional to an increase in the price of formulated drugs. In the past two years, prices of APIs coming from China and other countries (India imports over 60 per cent of APIs) have gone up by 15-80 per cent (depending on the active ingredient). These increased costs of API imports is negatively affecting pharma profit margins. According to a recent news item, China has further increased its prices and upward trend is continuing.[4]

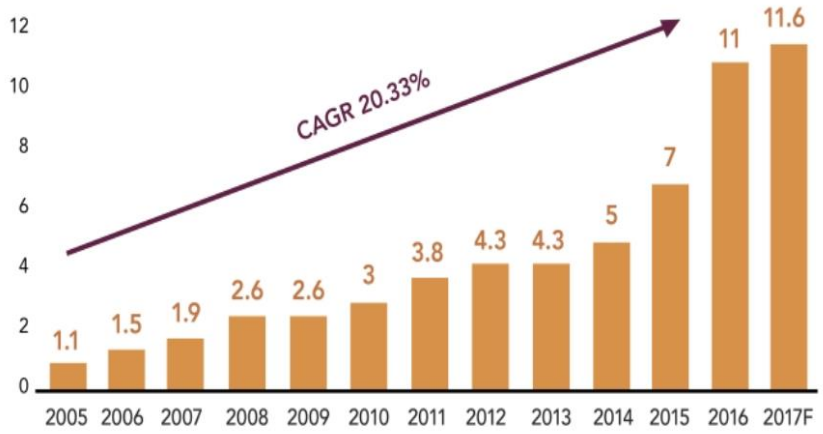
India's domestic pharmaceutical market turnover reached Rs 1.4 lakh crore (US$ 20.03 billion) in 2019, up 9.8% y-o-y from Rs 129,015 crore (US$ 18.12 billion) in 2018.



Indian domestic sales

India’s pharma market has been regularly witnessing 10-11% YoY growth to US$20bn driven by a healthy mix of volume and price-led growth. The industry benefits out of rising penetration of medicines, increasing affordability and a growing incidence of chronic disorders such as diabetes, cardiac, CNS (Neuro) and oncology. In spite of initial disruptions caused by Covid19, Indian pharmaceutical industry gained momentum in later part of 2020 and ended the FY21 with record export of $24.44 with a growth of 18 percent.[5]

At the same time, the Indian biotechnology market, which is much later entrant, grew by a CAGR of 20.33% between 2005 and 2015 and stood at USD 11.6 billion in 2017. India's biotechnology industry comprising biopharmaceuticals, bio-services, bio-agriculture, bio-industry, and bioinformatics. The Indian biotechnology industry was valued at US$ 64 billion in 2019 and is expected to reach US$ 150 billion by 2025.[6]



Indian biotechnology market size ($ bn.)

Covid19 has once again put the spotlight on India being the pharmacy of the world. The speed with which India has been able to produce vaccines for distribution through the world has been the envy of all countries throughout the world. However, this claim was derailed during the second wave of Covid19 which started in March 2021. India is going ahead with efficacy trials of 30 different vaccines for Coronavirus, which are at different stages of development and one of these is already in Phase III trials.

India will have to work hard on regaining the crown of world’s premier vaccine provider. India’s ban on exports have reignited the efforts of many countries and regions to produce their own vaccines and essential drugs.

This industry has gained this stature due to the following reasons:

- Low-cost production capacity with focused target
- A large population needing a wide range of therapeutic treatments.
- High economic growth of the country and rising prosperity of the rural India
- Conducive policy to support 100% FDI, resulted to cumulative FDI worth US$16.39 billon
- Low entry costs and increasing private sector investment
- Increased penetration of health insurance

- Large availability of qualified chemists including PhDs, especially in organic chemistry, the mainstay of our generic industry.[7]

However, this gain has not translated into introduction of novel medicines from India due to the inadequate state of its R&D infrastructure.

Medicine spending in India is projected to grow 9-12% over the next five years (2020-2025), leading India to become one of the top 10 countries in terms of medicine spending.

2.3 India Pharma Vision 2020

The government of India launched Pharma Vision 2020 to make a global leader in end-to-end drug discovery and development as well as the production of low-cost generic medicines. It has definitely achieved its goal of world's no.1 source of low-cost medicines including vaccines. This was a result of building world-scale plants, buying low-cost APIs and low manpower costs. However, solely relying on one global advantage of fast development of generic medicines and low-cost production is not sustainable in the long run as we will show in chapter 7. Therefore, the objective of gaining global competitiveness in new sectors such as bio generics becomes critical.

2.4 Growth of lifestyle diseases in India

According to the IDF Diabetes Atlas, 8th edition (2017), the national prevalence for diabetes (20-79 years) in India is estimated to be 8.8%, much higher than 6.8% in global population. One consideration is certain: the prevalence of diabetes in urban India seems to be higher among those states which are economically stronger. An important observation seems to be the fact that in some of the economically well-to-do states, the prevalence of diabetes among the urban poor appears to be going up. Unhealthy diet of the poor migrants could be a contributory factor.

The treatment of diabetes is a great burden on the poor since these have to be paid through out-of-pocket expenses, upwards of Rs.10,000 per head per annum.

2.5 Indian Biosimilar Market

The global biosimilar market is expected to reach $35.7 billion by 2025, up from $11.8 billion in 2020, at a CAGR of 24.7 percent. According to the Association of Biotechnology Led Enterprises, India's biologics market will grow at a compound annual growth rate (CAGR) of 22 percent to hit $12 billion by 2025.The market currently is dominated by simple biologics, such as therapies for the treatment of diabetes (insulin), oncology (EPO and mAbs), autoimmune, and cardiovascular diseases. Similar biologics for insulin and EPO enjoy 80 to 85 percent market share in India. However, complex biologics such as mAbs in Asia Pacific is estimated to be $5.94 billion in 2020 and is expected to reach $10.9 billion by 2025 at CAGR of 4.52%, in that landscape India is the fastest-growing country.[8]

However, because the manufacturing process of these drugs are more complex than other medicines and more expensive to store and transport, their unit costs are high, especially if seen in the light of their consumption for a longer period, if not lifetime.

For example, filgrastim, one of the most common and earliest biosimilar has an average unit cost of Rs. 2500. The annual drug cost per patient based on a regimen of 6 cycles of 10 days each would be Rs.1,50,000. With a per capita income of Rs.1,35,000 per year, this essential treatment to support cancer therapy is beyond the reach of 95% of Indians. There is a need for creating a mechanism for reducing the price of biosimilars. One route could be the government sponsoring an institute for development of bio generics where knowhow can be

licensed out to a larger number of companies for commercial production. Today, there is little competition in the market.

According to the latest cancer report released by the Indian Council of Medical Research (ICMR) and National Centre for Disease Informatics and Research (NCDIR), Bengaluru confirms the sharp increase in India's cancer cases, estimating that it could further increase by 12% in the next five years. Going by the statistics revealed in the National Cancer Registry Programme Report 2020, the cancer incidence in men is estimated to be 679,421 in 2020 and 763,575 in 2025, while among women, it is estimated to be 712,758 in 2020 and 806,218 in 2025. If the current rate continues, we could be witnessing an epidemic of cancer by 2050.[9]

In spite of price controls, these medicines are beyond the affordability of a majority of its citizens, since a majority of medicines, up to 80%, are bought from out-of-pocket expenses. To increase the domestic market, manufacturers, should employ differential pricing mechanisms. To those patients who have life-long need, such as insulin, there can be a subscription system where substantial discount is provided for tying up with a particular supplier on annual intake.

Being a price-sensitive market, India had taken a lead in introducing biosimilars. The first biosimilar was introduced in India in year 2000, 15 years before this happened in the United States. The cold-chain requirement has been a major deterrent in its wider use and hence the high cost. It is expected that the cold-chain investment for covid19 vaccination would go a long way in providing a fillip to the wider use and, hence reducing its price. This had been a neglected sector of the logistics industry.

The rise in health insurance coverage will also bring more patients within the coverage of such expensive drugs. In the fiscal year of 2020, nearly 500 million people across India were covered under health insurance schemes. Of these, the highest number of people were insured under government-sponsored health insurance schemes. Overall, the penetration of health insurance in India stood at just around 35 percent in financial year 2018.

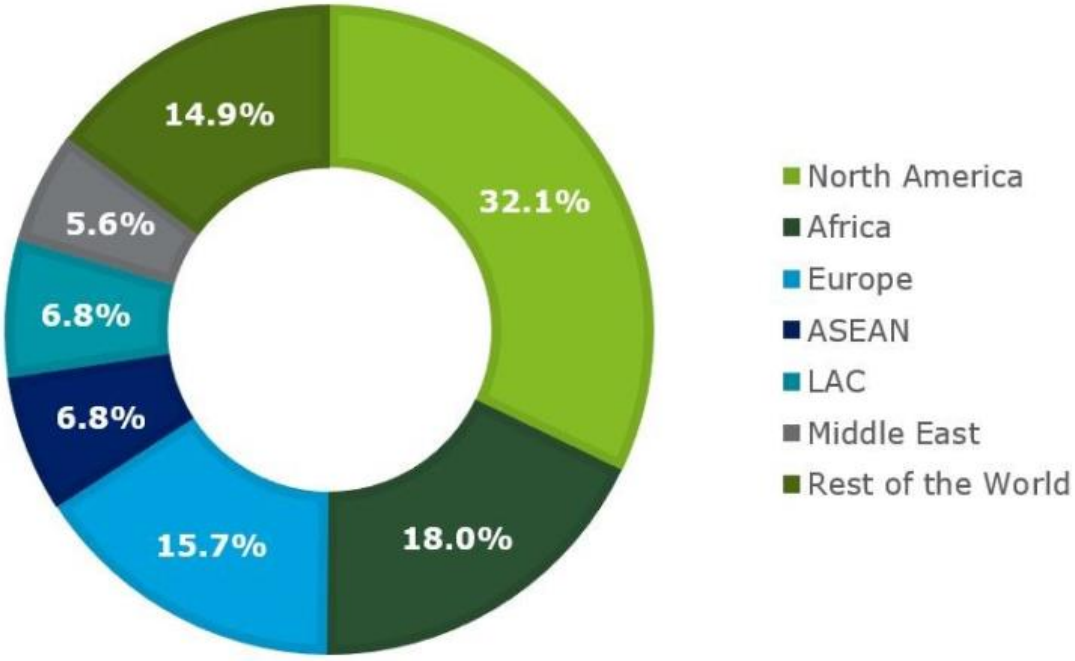
Our low public investment in healthcare was visible in the inadequate state of infrastructure during the Covid pandemic. The 2021 Economic Survey set out the importance of increasing public health spending and discusses in detail market failures in health. It showed that an increase in public health expenditure from the current levels in India to 3% of the GDP can reduce out-of-pocket expenses (OoPE) from 60% currently to about 30%. As is well known, the OoPE on health burdens not just the poor but also the middle class of this country.

The Economic Survey therefore makes a case for increasing public spending on health from current 1.3% to 2.5-3% of GDP, as the National Health Policy (NHP) 2017 states. This is necessary to improve India's poor standings on various indicators of health, such as share of OoPE, equitable and good quality access to healthcare, availability of infrastructure and human resources for health. For example, India currently ranks 145 out of 180 countries on quality of and access to healthcare, and 179 of 189 countries in prioritisation of health in government budgets.[10]

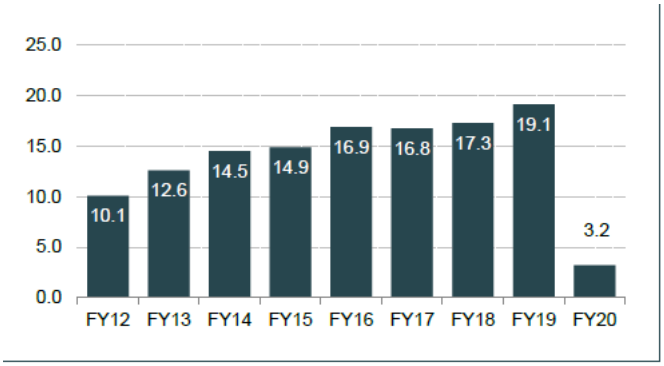
If India is able to double the healthcare expenditure, this will also increase the market of pharmaceutical products and the above forecasts may have to be revised upwards. This will also lower the cost of biosimilars. The overall results of a study conducted in the United States strongly suggest a positive correlation between healthcare expenditure and the economic indicators of income, GDP, and labour productivity. The study shows that an increase in healthcare expenditure has a positive relationship with economic performance.[11] Therefore a greater investment in healthcare in India will also help in the growth of its GDP.

2.6 Indian Pharmaceutical Exports

India has made remarkable progress in the export sector, especially in the high regulated markets of US and EU and is currently growing at 20% per annum.



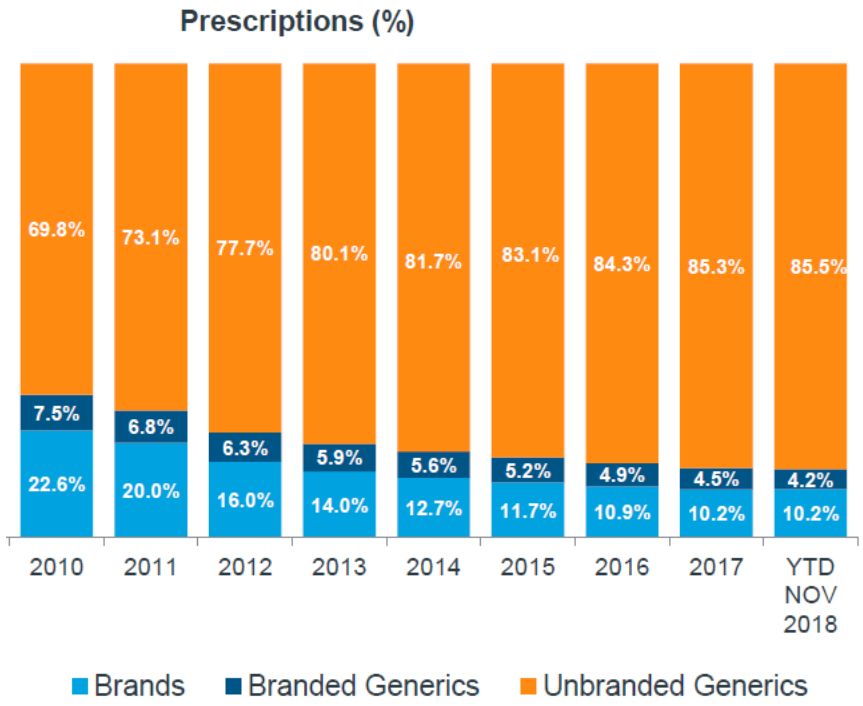
Indian export geographical dispersion-2019 (Pharmexcil)



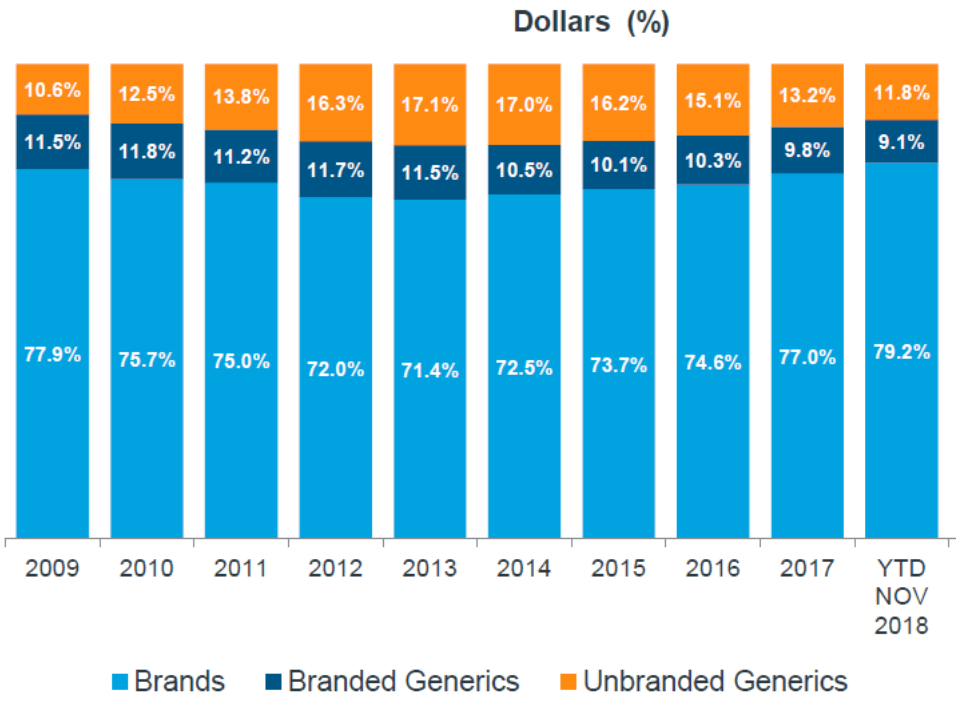
Indian exports (IBEF)

However, there is considerable scope for increasing exports through entry into new markets and harmonisation of Indian regulatory environment with the global trends (see chapter 3).

No doubt, it is largely due to efforts of Indian exporters that the share of generics in world markets is steadily growing and has crossed 85% in USA.



However, it also underscores the fact that though volume-wise, generic penetration is overwhelming, but the innovator drugs still command most of the value and thus take away a greater share of the revenue and profits.



The profitability in me-too drugs is unlikely to improve and India will have to revise its strategy to maintain its market share and profitability.

Indian generic formulations export will come into increasing competition by 2030 due to the following reasons.

1. More countries undertaking greenfield and brownfield pharmaceutical projects restricting Indian exports. Some may even ban certain pharmaceutical formulations to encourage domestic production.
2. Some countries such as Turkey, Ethiopia, Saudi Arabia and Russia are aligning their policies for creating regional pharmaceutical hubs
3. Rising Chinese threat for expansion of generic exports
4. Rising exports from new and brownfield projects in regional markets
5. Effect of Regional Economic Agreements such as African Continental Free Trade Agreements (AfCFTA) on import of pharmaceuticals
6. Post covid development in regulatory markets such as US and EU in re-shoring their generic industry
7. Closing of markets for Indian pharmaceutical due to global harmonisation such as PIC/S (Pharmaceutical Inspection Co-operation Scheme)

These issues with be discussed in detail in this and following chapters.

2.6a Competitive landscape in generics exports

India took an early lead in the export of generics when many nations in Asia, Africa, Central Asia and Latin America did not have a sizable indigenous industry to meet domestic demands. Exports were necessary to scale up the industry where domestic demand is small. Here, India had an advantage with a large domestic market as well as a rising per capita income during the last decade to meet out of pocket expenses.

The global environment is different today with many emerging nations building up their pharmaceutical industry and some of them also exhibiting ambitions of a regional hub. Today, over 30 countries (see annexure 1) are creating pharmaceutical infrastructure through attractive policies and building exclusive manufacturing zones to feed demand beyond their borders.

Argentina, Bangladesh, Indonesia and Jordan demonstrate that a second tier of countries such as these are well poised to take on the role of supplying cheaper medical products to poor people across the developing world. Firms in these countries have attained the economies of scale required to produce drugs competitively and will expand over the next decade.

Some of the notable developments are:

Ethiopia & Egypt in the East and Morocco & Tunisia in the west of Africa undertaking large scale pharmaceutical infrastructure. South Africa already possess a sophisticated pharmaceutical industry in the Southern Africa, their aim is to take a share of the growing African market due to

- Implementation of a continent-wide African Continental Free Trade Agreement for n creating a single market of 1.2 billion people where large-scale pharmaceutical manufacturing can take roots.
- Rising GDP growth and consequently higher per capita income of African nations.
- Pharmaceutical industry being seen as a core industrial activity in many nations.
- Growing urbanisation in African nations with increasing per capita income and access to drugs.
- Notable changes have made the continent a much more viable market for manufacturing pharmaceutical products than it was a decade ago. Many countries now have social security systems and insurance systems that pay for health care, so it is a more structured market, with people able to afford longer term treatments.

All these developments point towards a large growing pharmaceutical market of $45-60 billion by 2030.[12]

Looking at this large market, both China and Bangladesh have entered the market. China has two manufacturing plants for billion tab/cap and recently a Bangladesh firm is building its first pharmaceutical plant overseas, in Kenya at an investment of USD25 million. The plant will be capable of manufacturing two billion tablets and capsules and 60 million bottles of liquid formulations.

2.6b India's global competitiveness

According to CPhI Insights USA (7.04) takes the top spot for Competitiveness in the pharmaceutical sector. India took second place in global competitiveness. Surprisingly, given its strong showing in other categories, Germany (6.47) has slipped from second to fourth, with a decrease of 1.3%. Moving up to third is China (6.56) with the largest increase in growth (3.9%) for competitiveness. This may stem from executives' belief that the Chinese government is actively increasing standards throughout its pharma sector and becoming increasingly competitive across more sectors than ingredients. At the opposite end of the table, Italy falls to last position, with a score of 5.25. The UK also slides down the rankings scoring 5.77, down 2.8% on last year's score of 5.94. Competitiveness was assessed through respondent's evaluation of each country's tax environment, quality of employees, infrastructure, research potential, labour costs, accessibility, and access to funds.

CPhI Insights, New modalities, new methods and new thinking to solve old problems, CPhI Annual Industry Report, 2019

India should be wary of China entering into the global formulations market in a big way by 2030, especially in markets where India has a definite traditional lead.

2.6c African - Market of the future

India is now Africa's third largest trading partner, accounting for 6.4 percent of African total trade for a total value of $62.6 billion in 2017-18. By comparison, China, having surpassed the United States, is Africa's largest trading partner; the value of Chinese-African trade in 2018 was $185 billion. Chinese overseas investment in Africa, in all sectors, as of 2020, totalled $147.66 billion. India cannot hope to compete dollar-for-dollar with Chinese spending power.

However, healthcare is one area where, with judicious use of foreign aid and a joint government-industry strategy in the healthcare area, India can consolidate its position as the no.1 supplier of healthcare products & services to the African continent, both as a direct exporter, as major investor in domestic industries and positioning of aid where India has competitive advantages. Investment in Africa's healthcare would make India a major supplier

of intermediates from APIs to processing chemicals, machinery and consultancy & training. Amidst growing rivalry with China for influence in African, pharmaceutical industry, with strategic inputs from the government, can play a big positive role.

India's engagement with Africa which has focused on "capacity-building." That is, building local capacity to increase leverage and agency among African nations, to be largely directed against Chinese interests. With his interactions with African leaders Prime Minister Modi also stated that India was looking to "liberate" Africa's potential, by creating local opportunities to enable such an end.[13] This capacity building engagement strategy is ideally suited to present the Indian healthcare expertise as a key differentiator to build African healthcare sector. This strategy should include not only pharmaceutical but the medical device, hospitals and training industry inputs. Our strategy is outlined in chapter 7.2

2.6d Gulf Countries

Elsewhere too, larger markets are building up due to establishment of regional economic communities such as Asean, Mercosur, Pacific Alliance, Eurasian Economic Community, and Gulf Cooperation Council. These regional markets are leading to the establishment of large-scale pharmaceutical plants even in countries such as Qatar. Qatar already has a plant with an investment of $50 million and another is being built with a total investment of $350mn. Qatar is looking forward to export drugs to over 20 countries.

Saudi Arabia has plans to become the main pharmaceutical hub for the Middle East and North Africa and is well positioned to achieve its goals and develop this sector. It is considered one of the most stable areas in the Middle East, with strategic location and a close access to the regional market. Part of the transformation plan for Saudi Arabia is to raise the percentage of total pharmaceutical production from 20% to 40%. Foreign pharmaceutical manufacturers are being actively encouraged to establish plants in Saudi Arabia through a combination of public and private partnerships as well as joint ventures with national entities. Efforts by the government to curb pharmaceuticals expenditure and promote local production has resulted in generics becoming a fast-growing product.

Under the Kingdom's long-term development plan, Vision 2030, and its shorter-term goals, set out in the National Transformation Programme (NTP), which runs through 2020, a major shift towards locally produced drugs and medicines is set to take place. Examples of this include Pfizer, which began production at its new, $57m plant at King Abdullah Economic City (KAEC), on the Red Sea coast north of Jeddah, in January 2017. Some 16 products will be manufactured at the facility, building on a 2014 deal the US giant struck with local Tabuk Pharmaceuticals, giving the Saudi company exclusive rights to manufacture and sell "second brand" Pfizer drugs in the Kingdom.

2.6e Looming threat from China & other countries

Therefore, we foresee serious competition to India generic exports by 2030 and erosion of the markets as well as profitability for Indian exporters. The competition will come from three directions

1. China
2. Bangladesh, Turkey, Egypt etc. which will make inroads into African markets.
3. Rising indigenous manufacturing and consequently ambitions for capturing a slice of the regional markets.

None of these are serious challengers today. But we see major headwinds by 2030.

The most important threat is from China.

China will start offering serious competition to our generic exports for the following reasons.

- Lower profitability in domestic markets

Since 2018, Chinese government has launched centralised procurement policy to drive down generic prices. In a pilot project, tenders for 31 drugs were issued for all government procurement in 11 cities, comprising around 30% of the total government purchase. The result was an average of 52% drop in prices. This reduced the outsized profitability of domestic firms and will continue to do so as the scheme brings other regions into its sphere gradually.

This has put pressure on Chinese companies to expand their operations to overseas markets where sizable profits are still possible. This is Africa which will double the pharmaceutical market by 2030 and where there is little price control.

In 2018, The Chinese Pharmaceutical Association, China Chamber of Commerce for Import and Export of Medicines and Health Products (CCCMHPIE) commissioned a study titled *21 Country Profiles* which has identified 21 countries in Africa with pharma manufacturing potential and highlights vast opportunities for Chinese pharma companies to expand and relocate their manufacturing to African countries.[14]

In 2018, China made its first foray into overseas manufacturing when Sansheng pharmaceuticals inaugurated its $85mn plant in Ethiopia to serve domestic, regional and eventually global markets. According to The China-Africa Project, “So, if African countries can go from buying medical products from abroad to producing them domestically, there is potential for significant health and economic benefits. Foreign investment can support this process by providing capital, technology, and expertise to build pharmaceutical plants and factories on African soil. And as Chinese influence on the continent grows, there are increasing hopes that China has a major role to play.”

It was followed by two more companies Humanwell Pharmaceutical Ethiopia PLC and Sino-Ethiopian Sunshine Pharmaceutical PLC setting up plants in Ethiopia.[15]

Taking advantage of Covid19 pandemic, Chinese company Sinovac has signed an agreement with Egypt to produce its covid19 vaccine locally for distribution throughout Africa. This has presented China with a major geopolitical coup.[16]

- **Increase political & economic influence**

While countries like Russia and India are producing low-cost C19 vaccines, it'll be difficult for those suppliers to pull off the kind of logistics operation that is required to get the vaccines into the market. The Chinese, in contrast, have turned to e-commerce giant Alibaba and its powerful logistics division Cainiao for help. It has created a cold chain bridge linking Shenzen with Addis Ababa to distribute vaccines coming from China.

China has the capability to seize the opportunities wherever these occur and in Africa, they are slowly but surely expanding their reach. This is only the beginning. We should expect more project announcements in future.

China's global share of formulations exports trebled from 0.4% in 2009 to 1.2% in 2018, while India's doubled over the same period from 1.5% to 3.6%. Remarkably, 36% of China's exports are to the EU and North America, where regulations are the most stringent, compared to 19% in 2009. Beijing's "Made in China 2025" policy has identified pharmaceuticals as one of its strategic industries. The aim of this strategic plan is:

- Develop new medical products using chemicals and biotechnology to address critical diseases, including antibody drugs, antibody coupling drugs, new structural proteins, polypeptide drugs, and new vaccines.
- Develop innovation traditional Chinese medicine with prominent clinic advantages.
- Develop technologies to support individualized drug treatments.
- Improve the innovation capability and industrialization level of medical apparatus and instruments, focusing on efficient diagnosis and treatment equipment (imaging equipment and medical robots), high-value medical supplies (fully degradable stent), and mobile medical products (wearable and remote diagnosis equipment).
- Make breakthroughs in new technologies like 3D bio-printing and induced pluripotent stem cells.

Therefore, Indian government and pharmaceutical stakeholders must take serious note of China's incursions can include not only territory but markets as well.

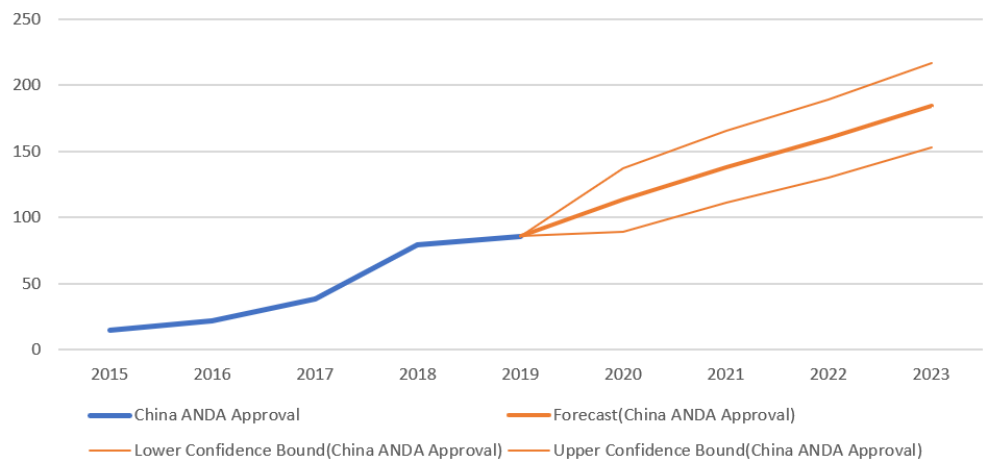
- **Improving the quality of its medicines for export competitiveness**

The reputation of Chinese medicines is quite low, and it is a major source of counterfeit drugs, especially in Africa. Therefore, Chinese companies are improving the quality of their medicines.

China's rising share of formulations has been aided by improved standards that appear to be making the world less apprehensive about Chinese medicine quality. Notably, the China Food and Drug Administration issued guidelines in 2013 to make generic medicines bioequivalent to the originals, and in 2016, the government made them mandatory.

According to a recent article in China News Daily "Chinese pharmaceutical and healthcare companies are seeing an increasingly stronger presence in the global market with effective strategies, reflected by more new drug registrations abroad, diversified international mergers and acquisitions and product licensing progress".[17]

As part of this strategy, Chinese companies are applying for greater number of USFDA ANDA approval for generic drugs.



China USFDA ANDA approvals-forecast

Beyond increasing its inroads in the regulated markets, USFDA approvals has two other advantages. It brings faster approval from Chinese regulatory agency. Therefore, the number of Chinese ANDA approval is steadily rising every year.

Chinese domestic approvals can take up to three years. However, for certain categories of drugs, which have been previously been approved and marketed in United States, European Union or Japan in the past 10 years and not yet been approved in China they are eligible for the breakthrough, priority, fast-track or special designation for approval, shortening time by up to 50%.

The third benefit is raising the quality profile of Chinese drugs in their export markets such as Africa. Chinese drug makers can increasingly showcase their rising approvals in regulated markets to reassure governments about the high quality of Chinese drugs. Over 40 percent of all counterfeit drugs land up in Africa and it is widely believed that most of these originate in China, including those with Indian labels.

Indian government and drug makers should take Chinese generic threat seriously since their attention is largely focused on API import dependency.

2.6f Bangladesh

Bangladesh presents an interesting case study for establishing a largely self-sufficient domestic generic formulation industry but also scaled up for significant exports. Today, BD meets 97 percent of its demand through locally manufactured drugs and expanding rapidly in export markets. BD is the example which many larger countries such as Egypt, Kenya and Ethiopia are likely to follow in developing their indigenous industry.

To allow local industry to flourish, Bangladesh progressively restricted and banned the import of generic drugs. Some countries in Africa are also likely to follow the same practice. For instance, Algeria prohibits the importing of any drug that can be manufactured locally. Kenya may be the next to ban some common drugs such as paracetamol for which adequate local supply is now available. As local supplies increase and as African Continental Free Trade Agreement starts taking concrete shape, there will be pressure from the governments and African Union to source from indigenous sources as the first choice.

No large-scale domestic pharmaceutical industry can exist without export markets and Bangladesh is now aggressively promoting its pharmaceutical exports. According to a Pharmexcil report, Bangladesh is poised well to take advantage of increasing global demand

for generic medicines Produced in low-cost economies and is forecasted to see their export footprints rise over the next few years.[18]

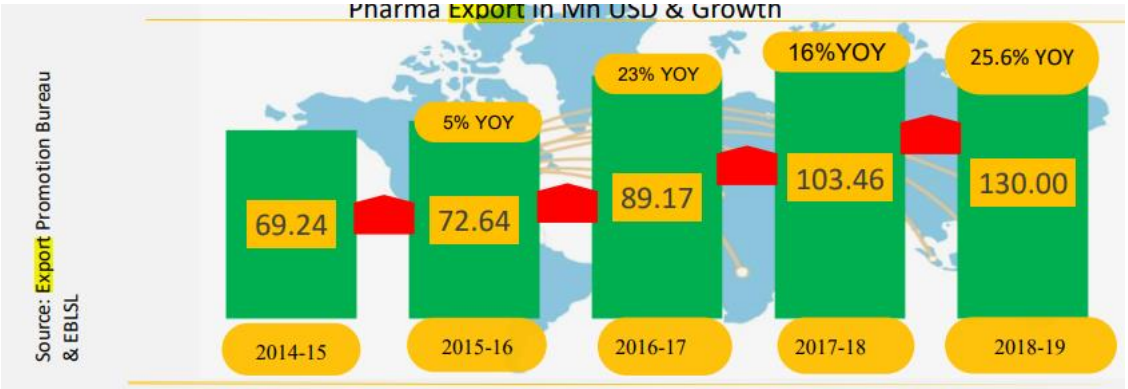
BD Export earning $mn. (Dhaka Tribune)

Bangladesh has all the ingredients for a large & growing pharmaceutical industry such as large population (10 crores), high GDP growth of over 8% for the last decade and a responsive government resulting in a domestic market of $3.5 billion which will reach over $6 billion by 2025.

Bangladesh's pharmaceutical industry has developed steadily for the last 30 years with the result it imports of pharmaceuticals is much less than comparable countries. Nigeria imports US$ $859 million and Vietnam imports $1,775 million worth of medicines -- 3.2 and 6.6 times higher respectively compared Bangladesh's $ 270 million import a year. This large domestic industry is poised not only to challenge India's exports by 2030 but also make investment in local pharmaceutical industries, especially in Africa.

According to Export Promotion Bureau (EPB) data, Bangladesh's medicine exports registered a 25.60% rise to $130 million in FY19, which was $103.46 million the previous year. Bangladeshi pharmaceutical makers are now compliant and regulated as some leading companies have received certification from US FDA and UK MHRA. According to Bangladesh Association of Pharmaceutical Industries (BAPI), approximately 1,200 pharmaceutical products received registration for export in the last two years. At current growth rate,

As an LDC (least developed country), Bangladesh will not need to pay royalty for producing patent drugs till 2033, which is a great opportunity for Bangladesh to improve its export share. At current growth rate, BD exports will cross $ one billion by 2028.



BD pharma exports

Not only generic formulations, but Bangladesh also has an ambitious plan for developing its API industry, particularly its under construction API manufacturing Park. It has already started export of APIs.

2.6g Turkey

Turkey's Vision 2023 is aimed at making Turkey a global centre for pharmaceutical R&D and production. The Turkish Government aims to make Turkey one of the world's top ten economies in health services by 2023 by increasing R&D expenditures to 3% of GDP and by increasing total exports to USD 500 billion. Moreover, according to the Turkish Ministry of Science, Industry, and Technology (AIFD)'s Strategy Report, Turkey should become the Eurasian production base for medium- and high-level technology products. The export target for 2023 is $7.3 billion compared to $1.8 billion in 2020.

2.6h Jordan

Jordan has few natural resources and pharmaceutical sector is one of the shining examples of its export revenues. Jordan was among the first manufacturers of branded generics in the Arab world—producing common medicines such as acetaminophen that have been sold with Arabic packaging to customers throughout the region. The Middle East and North Africa region has long depended on Jordan which exports 75% of production. Jordan pharmaceuticals are now distributed worldwide in more than 87 countries and 90% of the exports are going to Arab countries. Jordan pharmaceutical companies have joint ventures and subsidiary companies in 8 Arab and foreign countries.

2.6i Threats from European Union

German chancellor Angela Merkel and French president Emmanuel Macron – presented a jointly developed five-point "Health Strategy" on May 18 2020, a plan which aims to increase EU sovereignty on pharmaceutical products and reduce its dependency on the import of medicines and active pharmaceutical ingredients from other countries. Rather than continuing to rely on China for 70 per cent of its active ingredients and on India for formulations, Merkel and Macron's initiative would pave the way to bring the production of pharmaceutical ingredients back to Europe, avoiding bottlenecks and drug shortage issues in the future.[19]

The European Union too is perfecting its pharmaceutical strategy which will identify strategic dependencies and propose measures to reduce them. These may include diversifying production and supply chains, ensuring strategic stockpiling, and fostering production and investment in Europe.

As part of The Pharmaceutical Strategy, Generic and biosimilar medicines provide a large number of patients with accessible and affordable treatments. They also allow health systems potential savings in costs through their positive effect on pricing competition. The Commission will consider targeted policies that support greater generic and biosimilar competition, based on the sound functioning of the single market, appropriate market protection mechanisms, the removal of barriers that delay their timely entry to market and increased uptake by health systems. This may include further clarifying the provisions for the conduct of trials on patented products to support generic and biosimilar marketing authorisation applications (the so-called 'Bolar' provision).

The policies will be accompanied by enforcement of the EU competition rules. The Commission's Report on competition enforcement in the pharmaceutical sector has shown that originator companies sometimes implement strategies to hinder the entry or expansion of the more affordable medicines of their generic and biosimilar competitors and that such

strategies may require competition law scrutiny. The Commission will also continue to carefully review mergers between pharmaceutical companies to avoid distortion of competition.

Some initiatives resulting from the Pharmaceutical Strategy, with completion dates, are as follows:

- Propose to revise the system of incentives and obligations in the pharmaceutical legislation considering the relationship with intellectual property rights, to support innovation, access and the affordability of medicines across the EU – 2022.
- Review the pharmaceutical legislation to address market competition considerations and thus improve access to generic and biosimilar medicines, including interchangeability and the 'Bolar' exemption – 2022.
- Initiate a pilot together with the EMA and Member States, with the engagement of future marketing authorisation holders, to understand the root causes of deferred market launches – 2021.
- Encourage buyers from the health sector to cooperate in view of implementing innovative procurement approaches for the purchases of medicine or medical devices, in the framework of the Big Buyers initiative – 2021.[20]

Further, the strategy focuses on the affordability of drugs.

A mix of policy levers can support this goal, including ensuring value for money through health technology assessment; exploiting potential savings from generics and biosimilars; encouraging responsible prescribing; and improving patient adherence.

Certain conditions such as newly launched niche products for a small number of patients or the absence of automatic substitution rules for biologicals, can create market barriers. This means that competing generics, biosimilars and 'older' products may find it hard to enter or stay in the market. This lack of competition thus inhibits price savings once innovative products lose their market exclusivities. Rules that do not directly regulate prices or reimbursement levels may nevertheless have a bearing on the affordability and cost-effectiveness of medicines through indirect effects on the contestability of markets or the economic viability of products in more mature markets. The Commission will take this into account in the review of the pharmaceutical legislation, to see how sound competition can best be fostered, leading to downward effect on prices of medicines. It will also continue to work, including through the exchange of best practices, on the uptake of biosimilars, in order to stimulate competition.

Some initiatives on the accessibility & affordability of drugs are as follows:

- Propose to revise the pharmaceutical legislation addressing aspects that impede the competitive functioning of the markets and to take account of market effects impacting on affordability – 2022.
- Develop cooperation in a group of competent authorities, based on mutual learning and best-practice exchange on pricing, payment and procurement policies, to improve the affordability and cost-effectiveness of medicines and health system's sustainability, including on cancer treatment – 2021-2024.

Judging from the recommendations put forward by European associations representing drug and pharmaceutical chemical firms, the commission's approach will differ significantly from the tack taken by the outgoing Trump administration. Rather than spending millions of euros launching made-in-Europe ventures, the EC will likely leverage a sizable established

manufacturing base. Likewise, industry guidance for Europe's plan places greater emphasis on making its supply chain more secure rather than less global, while maintaining and expanding the region's manufacturing footprint.

Adrian van den Hoven, general director of Medicines for Europe, an association of generic-drug and API makers recommended that proposals to the EC include a change to generic-drug pricing, which individual countries currently set at the lowest possible levels to reduce the cost of subsidized health care. The association proposes a scheme that would allow prices to be negotiated from the bottom up based on a supplier's cost of goods, regulatory costs, and other considerations.

For hospital and retail purchases, van der Hoven says Medicines for Europe favors "multi-winner tenders," in which buyers are required to purchase from several suppliers as opposed to awarding contracts to the lowest bidder, a practice that has fuelled consolidation among drug suppliers.

Medicines for Europe also advocates global coordination of drug supply as opposed to rampant reshoring. "It is important that we maintain critical technologies in Europe," van den Hoven says. "That said, we don't believe we can or should produce everything in Europe." No decision has been taken by the EU as yet.

However, Europe's overreaching regulation for the manufacture & distribution of chemicals may come in the way of large-scale reshoring of APIs.

Pharmaceutical chemistry presents a significant hurdle given that many of the reactions involved have disappeared from Europe in the wake of the region's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) legislation and other environmental tightening over the past 2 decades. For example, REACH required expensive environmental controls on reactions such as nitration, fluorination, and bromination, which are critical to making certain drug ingredients. REACH created an incentive for production of these chemicals to move to other places, especially Asia, but that doesn't mean they cannot be manufactured again in Europe.[21]

This will create a technological space for green chemistry as well as Continuous Processing Technology and EU may provide funds for it. Already, Graz University's Center for Continuous Flow Synthesis and Processing (CC Flow) at its Research Center of Pharmaceutical Engineering is the center of continuous technology development in Europe.

Some of these provisions may be favourable to India as it aims to simplify the regulatory process of registration of medicines and diversifying sources, both within Europe and outside Europe. The Indian stakeholders, that is the government, export promotion bodies and trade associations should keep a close on these developments as these are discussed within the EU bodies to be ready to take immediate remedial actions.

The government should also show a roadmap to European decision makers before they take a decision as to how India could be that diversified China+1 source. It is important not only to show the size of our industry, especially API but also the reliability of safe & consistent quality manufacturing. It is possible to get loan too for Indian industry to ramp up its API production from EU for China+1 strategy.

2.6j Threats from USA

In August 2020, President Donald Trump on Thursday signed an executive order aimed at boosting U.S. production of both generics and API aimed at protecting the United States against shortfalls in a future pandemic. It also provided $800 million to Phlow Corporation, US company to produce generic drugs for government stockpile.

This was followed by a letter of intent for a $765 million loan to Eastman Kodak to convert a specialty chemical plant at the company's headquarters in Rochester, New York, into an API manufacturing complex dedicated to "reshoring" pharmaceutical chemicals from China and India.

No doubt, India's ban on the export of certain drugs during Covid could have prompted such immediate reaction but this proposal has been in circulation within both US and EU for some time now.

The goal—to rebuild America's lost drug-manufacturing capacity—is critical. COVID-19, which has unleashed a global scramble for essential medicines, has crystallized the potential life-and-death consequences of these countries' unhealthy dependence on low-cost generic drugs manufactured overseas. To date, amid a flurry of industry and legislative efforts, Trump's order is the most high-profile effort to support "reshoring," the return of drug manufacturing to the United States.[22]

If the US order is strictly adhered to, it will heavily affect Indian pharma. More than half of India's pharma sales are from exports, and US has bought 37% of them over the past three years.

Access to the US market is also critical for leading firms to maintain profit margins. For example, when Dr Reddy's secured 180-day exclusivity in the US for selling the antidepressant fluoxetine 40mg in 2001-02, it increased the company's annual sales of generic drugs by 81% and operating profits by 50%.[23]

It remains unclear what kind of effect the executive order will have. Unlike other countries with nationalized health systems, where governments are the predominant pharmaceutical procurers, America's federal government directly procures only a small percentage of medicine taken in the U.S., through the Veterans Health Administration and Department of Defence. To really restore U.S. drug manufacturing, there need to be incentives for the private sector that purchases medication to "actually value American-made."

According to Time magazine, this is where the American consumer comes in. Most of them have little say in what kind of medicine they get. Many Americans receive their drugs in the mail from pharmacy benefit management companies, which make drug-purchasing decisions through an opaque system that relies on rebates. Or Americans go to big pharmacy chains whose buying decisions are guided by cost.

The executive order acknowledges that price is an issue: it states that federal procurers would be allowed to prioritize the purchase of American-made drugs that are up to one-quarter more expensive than foreign-made versions. But if employers or chain drugstores gave their employees or customers a choice—to fork out a slightly higher co-pay for a drug made in America, at a plant with higher standards that was better inspected— many of us would jump at the opportunity.[24]

2.7 API-Active Pharmaceutical Intermediates

There is a myth that Indian API industry is not competitive compared to China. Nothing can be farther from truth and facts prove otherwise. China is only ahead of us in antibiotic production due to the large-scale fermentation plants producing antibiotic APIs at a much lower cost. There are other causes for lower costs which have been discussed in many industry and consultants report such as lower utility costs etc.

Taking Drug Master Files (DMF) filing in the US as a benchmark of API technological superiority, India is consistently filing up to 50% of the total DMF filed with the UAFDA much ahead of USA and China.

Country	2019	Jan-Jun 2020
India	331 (54%)	155 (55%)
China	113	45
USA	57	30
Italy	22	8
Taiwan	18	
Japan	8	
Germany	7	
Israel	7	
Switzerland		9
Spain		7
Total	616	283

If we look at the DMF filed by top companies in following tables, a majority of companies are from India, again demonstrating Indian technological superiority as well as speed to market.[25,26]

S. No.	Company	Jan-Jun 2020
1	MSN India	40
2	DRL India	7
3	Metrochem India	7
4	Biophore India	5
5	RN Lab Europe *	
6	Alembic India	3
7	Aurisco China	4
8	Aurore India	4
9	Century India	4
10	Innovare India	4
	* RN Lab is an Indian HQ co.	

S. No.	Company	2019
1	MSN India	42
2	Aurobindo India	16
3	Biophore India	12
4	Biophore India	5
5	Sun Pharma India	13
6	Lupin India	12
7	Mylan*	10
8	Aurore India	9
9	Fuxin Long China	9
10	Unichem India	9
	* Although Mylan is an international company, it has several API plants in India	

Chapter 5.7 provides our analysis of the future scenario of global demand for APIs and it is possible for India to take a 30-40% share of the global market compared to present export of $5 billion, that is 8% . The global API market for merchant supply is 40% of the total global production, the balance being captive production for internal use by pharmaceutical companies. The total global demand in 2020 is $190 billion and 40% of this is $76 billion. India's current production is $11.73 billion.[27] It imports another $3.5billion worth of APIs, over 70% from China.

Since the current trend shows, as described in chapter 5.4, global multinationals will progressively shed their internal API production and source from contract producers. The first to do so, AstraZeneca moved 90% of its generic API supply to Chinese manufacturers but looking at post Covid scenario, India should have a strategy of bringing API captive manufacturing to Indian suppliers.

In spite of re-shoring efforts by some countries, outsourcing trend is likely to continue, and Indian government and the industry should ensure that a significant share of the API outsourcing comes to India.

Over the past 25 years there has been a significant shift by innovator biopharmaceutical companies away from in-house manufacture of APIs to predominantly outsourced manufacture at CDMOs. Even in cases where the innovator company might use in-house manufacture to prepare the materials to supply clinical development studies and launch supplies of an asset, having a parallel supply network with CDMOs is an important part of ensuring a robust supply chain of material.

Another significant change in recent decades is the shift away from blockbuster therapies for a wide patient population toward more targeted precision medicines. The emergence of precision medicine has two important effects that dramatically shrink the annual demand for a given API. First, the patient population is smaller. Second, precision medicines often have a low daily dose since the underlying biological target is clearly identified. The combination of these factors means that annual API requirements for a precision medicine can be as low as a few hundred kilograms per year, even for medicines that aren't classified as highly potent.[28]

This trend suits Indian API manufacturing as most of the units are small-scale producers below Rs.100 crores turnover. However, there should be incentives in place for foreign partners to share technology and skills.

According to some estimates, India's API industry will double to $21 billion at a growth rate of 8.6% by 2026 and with the same growth rate, it should rise to $29 billion by 2030. PLI scheme will give a boost to indigenous production. The global demand for APIs will grow to $264 billion by 2025 at a growth rate of 6.24%. By same calculation, the global demand will go up to $360 billion by 2030 and 40% share of merchant producers will be $144 billion, even taking into consideration that no further transfer of captive production to contract suppliers take place. To obtain a 40% share of this global merchant market, India must produce $58 billion of API by 2030. That is, Indian industry must double its production by 100% over the next decade at a CAGR of 16+%. It is a tall order but not impossible.

We suggest the following strategy considering, the government has already announced certain positive policy measures.

2.7a Incentives Schemes.

PLI scheme is essentially tailored towards import substitution and cover 53 APIs and KSMs which are presently imported from China. Simply creating capacity for indigenisation, will again force companies to small scale trap which has been the bane of Indian industries for long. Indian companies and the government must visualise global demand for the foreseeable future, of which India is a part, though an important one, then look at the global market share, India would like to achieve and create capacity to match our global ambitions. Only then, we can create globally competitive industry. In our opinion, India must aim for meeting a minimum of 40% of global API demand by 2030.

Only large companies can take advantage of PLI scheme although a large number of MSMEs are engaged in API production. With focus on export rather than only import-substitution,

Government should formulate a scheme where MSMEs can also produce for domestic and export markets.

The scheme looks more attractive to fermentation products (tailored for import substitution only) than chemical synthesis products although the number of chemical synthesis APIs outnumber fermentation process. Fermentation APIs are high volume-low value products which require very high investments, approximately Rs.750 crores and upwards. Therefore, there is little incentive for greenfield plant unless prices can be protected by the government. Though, antibiotics are one of the largest group of medicines required, their prices also the most controlled under DPCO.

Therefore, the drawback of the PLI scheme is its limited approach of only looking at import substitution rather than capturing a large global market share. The government should look at the value-addition of Indian manufacturing throughout the pharmaceutical value-chain rather than piecemeal intermediate action.

The API manufacturing requires a host of other processing chemicals which are also imported from China. As Dr Gurpreet Sandhu, President, Council for Healthcare & Pharma noted in his recent article, most API syntheses require pharmaceutical solvents such as methanol and isopropanol, among other chemicals such as acid base, reaction promoter, catalyst, surfactant etc. used in the manufacturing of drug, extraction, and purification processes. We are dependent on China for these too.[29]

PLI should be holistic in approach so that it helps create a specialty chemicals industry around the manufacturing of APIs and which could cater to other industries as well.

Just like the policy for the manufacture for mobile phones also includes the incentives for manufacturing its components, so should be in the case of APIs too.

The recent shortages in ingredients for vaccine production has clearly demonstrated that the government should look at the indigenous supply of the entire value chain and not one component of it. Our claim for being the largest vaccine manufacturer was proved hollow when we could not obtain essential ingredients from US.

A typical vaccine manufacturing plant will use around 275 different consumables, according to a report by the World Trade Organization. These materials are sourced from suppliers across the world. However, the major raw materials impacted will include items such as bioreactor bags, cell-culture media, reagents and lipid nanoparticles etc.

Still, a good beginning has been made and with time and hindsight, the government should modify the scheme to make India not only globally competitive but the first choice of the global customer, if not in antibiotics, at least in other APIs.

Bulk Drugs Parks – There is no facility envisaged for R&D which is essential for new product development. It is essential that a R&D Project for bulk-drugs be initiated through the Central Government policy of aiding under Common Facilities centre for a R&D Centre.

As early as 2013, an Inter-Ministerial Committee for Accelerating Manufacturing in Micro, Small & Medium Enterprises Sector made the following recommendations[30]:

- Enabling the Indian pharmaceutical industry to develop competence in advanced areas of drug manufacturing like dedicated research facility in bulk drugs, improving processes of manufacturing generics and new Active Pharmaceutical Ingredients (APIs).

- Developing common infrastructure in drug discovery and development, such as,

manufacturing, distribution, exports and medical devices

2.7b Use synergy with India's vast specialty chemicals industry

Without R&D support, SMEs cannot effectively contribute towards ambitious manufacturing & export targets. We have a vast & diversified specialty chemicals industry producing over 80,000 products supported by a large pool of organic chemists. The Chemical Industry of India ranks 6th in world and 3rd in Asia after Japan and China. In terms of global shipments of chemicals, India ranks 10th in the world. Our chemical exports are growing at 20% per annum.

API is an important part of India's specialty chemicals industry. Many of our companies are world leaders in several types of chemical reactions and resultant products. The following examples provide the range of expertise available in the Indian specialty chemicals industry which is a source of depth of knowledge in the Indian industry.

Like Indian generics industry, the agro-chemicals sector has also taken advantage of products where patents have expired and has taken a large share of the world market. India is the fourth largest producer in the world with 50% output going to exports of $3.14 billion. India is also a strong global dye supplier and according to Invest India, it accounts for nearly 16% of world production of dyes and dye intermediates.

One Indian company, Aarti Industries, which also operates in the API segment ranks among world's top three companies in chlorination, top 2 players in ammonolysis and hydrogenation and among top 4 players in nitration.

Similarly, Fine Organics is among world's top six global players in food and plastics additive industry and Vinati Organics has 65% of share of world's Isobutyl benzene (IBB) market, 55% share of -2-Acrylamido 2 Methylpropane Sulfonic Acid (ATBS) market and 70% share of Isobutylene (IB)market.

These are some of the Indian leaders in specialty chemicals which have created a significant space in the world market in spite of global competition, especially from China.

However, most of our specialty chemicals industry is MSME which do not have the capacity to build up a strong R&D base. With strong R&D support from the government, our specialty chemicals industry which includes API industry can be a prime mover toward the cherished goal $5 trillion Indian economy by 2025.

In terms of support for R&D, the government provides Weighted tax deduction of 200% under section 35 (2AB) of the Income Tax Act for both capital and revenue expenditure incurred on scientific research and development. However, all such incentives only favour large-scale industries which have the required infrastructure for innovation.

According to Mr. Ravi Kapoor, former President, Indian Chemicals Council, the government should engage with industry and academia for technology adoption and research, developing IP among MSMEs. So, the government needs to add value because it is tough for MSMEs to do that by themselves," he added.[31]

It is one area, where more than seeking FDI, greater efforts should be undertaken to create our own Intellectual Property(IP). While foreign companies are attracted to the large Indian market while our industries can become outward driven with a research-oriented business environment to achieve our potential to reach world scale capacity.

Besides R&D, Indian government should ensure that Indian producers & exporters are protected from Chinese predatory pricing.

2.7c Revive HAL and IDPL bulk-drugs under PPP model

As long back as 1954, India started manufacturing of antibiotics at HAL Plant in Pimpri, Pune which has since closed. Besides the plant at Pimpri-Chinchwad, it has two other plants at Nagpur and the company was profitable till 1973-74 but due to DPCO price controls, it could not raise prices and subsequently went into losses and overall continuous decline till date. Later many other companies in the private sector also closed down as they could not compete against Chinese imports.

It is our suggestion that HAL be converted to Public-Private Partnership to resume production of antibiotics APIs, including new generation APIs as a greenfield project. It is unlikely that the present plant is capable of resuming production in a globally competitive environment without extensive investment. Swiss drug maker Novartis's Sandoz division will invest about 150 million euros (Rs. 1326 crores)) to shore up antibiotics production at their Austrian plant with one third cost coming from the Austrian government.

We also doubt, under the current environmental laws, possibility of getting permission to resume production of a large-scale chemical plant at Pimpri, even if investment was forthcoming. We suggest that the project may be shifted to one of the bulk-drugs parks. The government can sell the present land at the three sites. At present, over 400 employees are still on rolls and these can be either be given VRS or shifted to new company. The government can plough back the funds from land sale as equity in the PPP project. It can take back a certain quantity in the form of dividend and sell to units producing Janaushadhi drugs at a subsidised cost.

The plant is still producing formulations but at a high cost and it is unlikely that, looking at the ageing of the plant and its design for a bulk-drugs plant and not formulations plant, it can cost-effectively produce generic formulations and compete in the market.

Many proposals for rehabilitation Hindustan Antibiotics Limited were brought to the attention of the government as late as January 2021.[32]

However, all these proposals are on the lines of rehabilitation in present sites which in our opinion is not cost-effective. The company still has several assets such as land, R&D, experienced people etc. and they can be put to good use in the PPP mode. Although PPP does not have a great success history in India, it can succeed with the right approach.

The government has announced annual incentives for four fermentation plants to the tune of Rs.720 crores. One of these could be proposed HAL PPP project.

2.7d Continuous Processing Plants

API production has traditionally been undertaken in batch processes. However, over the last few years, some companies have started to explore the potential of continuous processing, specifically flow chemistry, for producing APIs. Despite its potential to offer safer, faster and more sustainable processes, the production method remains relatively untested by the industry. This is in part because manufacturing pharmaceuticals is far more complex than say, manufacturing commodity chemicals where continuous processing has been widely used for many years. In addition, skilled people are not available.

In continuous processing, reactions run on a smaller scale repeatedly until the entire volume of API is produced. This contrasts with the traditional batch production, whereby a step-by-step approach is taken to manufacturing API in huge volumes.

Because it takes place on a smaller scale, continuous flow processing gives the operator greater control over parameters and can allow them to achieve conditions that were previously unattainable. This is also particularly useful when handling hazardous materials, not least because bi-products can be quenched in real time as opposed to at the end of a batch cycle. Continuous processing also allows immediate immobilisation of any catalysts, meaning operators can limit the probability of any adverse reactions. [33]

Commencing & shutting down batch process production is costly and 24x7 processing can maximise yield and ensure quality and process reliability. Quality parameters can be more strictly adhered to than in batch processes. This can result in savings in raw material & labour costs and better regulatory compliance.

Continuous flow processing is more suited to certain APIs than others. Before companies decide to explore continuous processing, it is essential that they take the time to weigh the potential benefits against the required investment. They should also consider the various challenges, such as product suitability and equipment availability. Assessing the viability is the first step to accessing the full potential of continuous processing.

The result of an industry survey has shown that the industry has been increasing, and will continue to increase, the portion of total manufacturing executed as continuous processes with a decrease in batch processing. In general, most of the experience with continuous processing on scale have been enabling reaction chemistry, while postprocessing and analytical remain in the very early stages of development and implementation.[34]

Therefore, it is essential that primary research towards continuous processing be undertaken at a central facility such as Indian Institute of Chemical Technology, Hyderabad. The government should fund a facility which can sell the technology to private companies and recoup government investment. Universities such as Rutgers and MIT have constructed solid-dosage continuous manufacturing lines and transferred the technology to pharmaceutical industry partners.

In a reaction brought about by Covid19, disruption of supply-chain from China, US government put forward a proposal for re-shoring of manufacture of generic medicine within the country. As a first case, the government awarded $800 million contract to Phlow Corporation to manufacture generic drugs. These drugs will be made in USA through continuous processing.

United States Pharmacopeia Chief Executive Officer Ron Piervincenzi, whose organization helps drugmakers meet quality standards, said in an interview that investments in continuous manufacturing would go a long way toward encouraging drug companies to invest in infrastructure in countries with higher quality standards. It was unsaid that the finger was pointing at China and India which are perceived to have lower quality standards.

Many experts believe that continuous manufacturing technology will play a role in developing efficient and green manufacturing.

We do not know how successful continuous processing will be in diverting production away from batch process. We also do not know how much re-shoring would take place as a result of continuous processing. However, this process must be researched further in India to provide knowhow to the industry. as it represents both an opportunity and threat. A facility should be established in India that will pilot the manufacture of both APIs and finished drugs in a fully continuous fashion. Unless we begin to develop technology when it is still in its infancy stage, we will continue to follow other countries in the race.

GSK has made a commitment to move toward continuous processing. The idea is to apply as much continuous processing as possible to new drug filings. Its first pilot plant is running in the US. It has been designed to be as flexible as possible — to be able to host any future unknown piece of continuous processing equipment for small molecule organic flow chemistry. So as technology evolves, the plant will be able to host it without any major modification.

One EU country has floated a Phlow-like venture with a view toward securing domestic supply of acetaminophen. The government of France is sponsoring a partnership with the French drug firms Sanofi, UPSA and the French API maker Seqens to establish domestic supply of the analgesic, which currently comes mostly from China. Seqens manufactures bulk acetaminophen there. UPSA and Sanofi manufacture most of the finished drug used in France, but they source API from China. The plan, still at a preliminary stage, would have Seqens add capacity for the API in France. There is a lesson for India in fostering tripartite cooperation to create large & diversified API capacity with the government facilitating this cooperation.

Looking more at the opportunity it offers rather than the threats, India must have its own dedicated R&D Centre for APIs which can undertake study of synthesis of chemicals through various processes and also produce through green chemistry.

We cannot allow degradation of environment. In India too, environmental regulations and control will be stricter in future as we are seeing in China. We must take proactive steps that new plants and expansions must be based on green chemistry. This too requires a major R&D base. With R&D on these lines, not only India can deflect the perception of poor quality but also take a lead over China in API production.

In the various policy interventions made by the government for API manufacturing, R&D is not given the attention it deserves. Unless we have R&D as a pivotal for API manufacturing, we cannot take a global leadership role which is very much within our grasp.

It is also to be noted that established US multinationals have not warmed up to reshoring of generic manufacture and it is the new companies which are taking the lead.

2.7e Cost Control

Many of the larger Indian companies drive significant revenue from the US market. Their profitability has come under pressure, largely from two development.

Consolidation of US Consolidation of firms of Pharmacy Benefit Managers (intermediary between drug companies and customer) in the US is starting to hurt revenues of Indian generics players, whose sales come mainly from US market. The PBMs in the US which purchase drugs from manufacturers and sell them to retail drugstore chains which actually fill the patient prescriptions.

IQVIA Global/US Generics & Biosimilars-Trends, Issues and Outlook, 2019

The PBM market is approximately worth $300 billion and is growing at a CAGR of about 6 percent. The three major players account for 90% of the total market. There have been several multibillion-dollar acquisitions in 2017, as an attempt by the top players to consolidate their position in the market. Market share for top players in this industry is expected to increase even further to about 75-80 percent following market consolidation.[35]

This would have its repercussion on the me-too generic export prices, unless the companies have products which provide distinct competitive advantage.

In the year 2019, Indian pharma companies have secured 336 ANDA approvals as compared to 290 in 2018. Pharma players also received 76 tentative approvals in 2019. The US FDA approved total 837 ANDAs in 2019 as compared to 813 in the previous year. Similarly, total tentative approvals were at 165 in 2019 as against 194 in 2018. Indian pharma companies secured 40 per cent of total final ANDA approvals in 2019 and 49 per cent of total tentative approvals.

The US FDA approved total 5,768 ANDAs during last decade i.e 2010-2019 and 1,351 tentative approvals. Indian companies remained dominant and grabbed over 35 per cent approvals. During the last 10 years, Indian companies received 2046 ANDA approvals on account of investments in R&D activities. With higher approvals, Indian players were able to launch new products in leading market like US & Europe. Indian companies have given tough time to major international players by launching affordable products in these markets.

To supply drugs to the US, India has 665 USFDA-approved manufacturing plants outside the US, the highest in the world.[36]

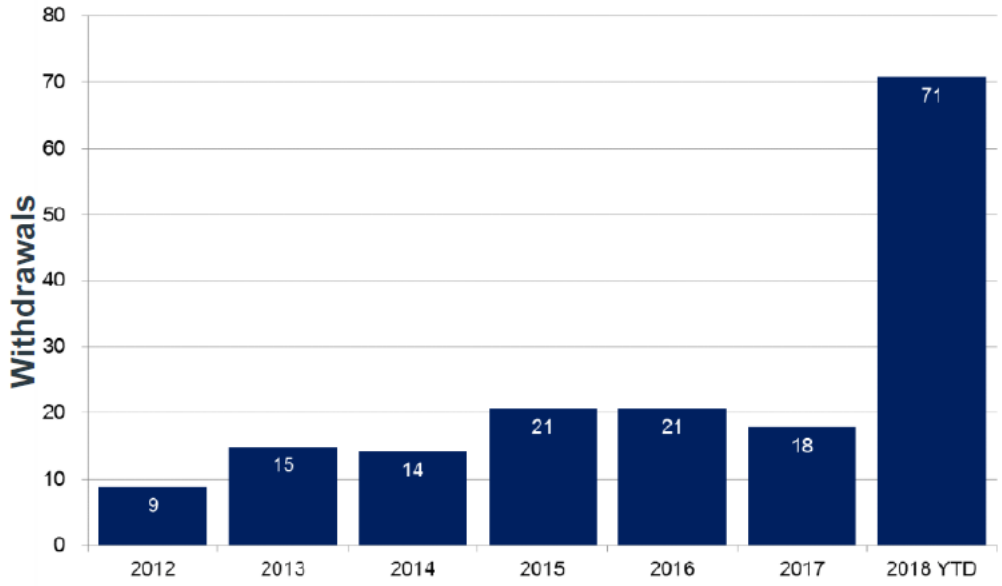
For many companies, their major source of revenue is domestic market and exports is “icing on the cake”, and they cut the price down to up to 90%. Smaller Indian firms that previously had little presence in the U.S. are also seeing approvals surge. Their expansion is boosting competition in the U.S., where mergers among pharmacy chains and pricing wars between drugmakers had already been driving down the cost of generics and USFDA is handing down rising approvals every year. The agency has said it will specifically favour generic drug applications for products that have few competitors to drive down prices further.

With so many rivals in the generics space, Cadila’s pipeline needs to broader, said Patel (Pankaj Patel, Chairman of Cadila), whose father founded the company. “It will be crucial to look beyond pure generics at specialty products if we need to stay ahead of competition,” said Patel. “We have a large pipeline of products which are under approval, and the attempt has been to create a judicious mix of generics, specialty and niche products”[37]

Today, Indian companies have a 30% share of the US generics market with nine companies in the top 20 generic companies.

Rank	Corporation	Unadjusted Rx		Rank	Corporation	Unadjusted Rx	
		MAT NOV 2018 Total (MNs)	Market Share (%)			MAT NOV 2018 Total (MNs)	Market Share (%)
1	TEVA	484.0	12.7%	11	HIKMA	104.8	2.7%
2	MYLAN LABS	240.0	6.3%	12	SUN PHARMA	101.0	2.6%
3	AUROBINDO	230.7	6.0%	13	CIPLA	94.3	2.5%
4	LUPIN	223.9	5.9%	14	SOLCO HEALTHCARE	92.0	2.4%
5	SANDOZ	177.9	4.7%	15	ENDO	89.5	2.3%
6	AMNEAL	151.1	4.0%	16	LEGACY PHARM PKG	85.7	2.2%
7	APOTEX	126.8	3.3%	17	GLENMARK	77.9	2.0%
8	ZYDUS	122.3	3.2%	18	TORRENT	74.1	1.9%
9	ACCORD HEALTHCARE	119.9	3.1%	19	LANNETT COMP	70.0	1.8%
10	DR REDDY	105.5	2.8%	20	HETEROPHARMACEUTICALS	69.4	1.8%

Along with continuous growth of ANDA applications, a new trend is the rising withdrawal from the US market.



ANDA withdrawals spiked in fiscal 2018 as companies realized that “me too” type products, which make up a portion of the FDA backlog, are unlikely to be financially viable.

All this churning is happening when we have not yet factored in the entry of new countries such Bangladesh, Turkey, Jordan etc. which have been discussed elsewhere in this report. Since this is a commodity market, it is our assessment that more companies from the emerging nations would enter the largest market in the world over the next decade, putting prices under greater pressure.

Therefore, to drive decent profits, Indian manufacturers must cut costs and bring higher-value products into the markets faster than ever before including take in First-to-file and enter new markets. Some of these strategies are discussed here as well as in other chapters.

2.7f Vertically integrated manufacturing

With the new thrust of indigenous production of APIs, companies should again think of vertically integrating their API and formulations manufacturing. Almost 60% of APIs are produced for captive use worldwide.

In India, only some companies practice vertical backward integration. Since the global market for APIs will increase substantially, more companies should take a look at backward integration of API with generics production. Taking into account, both captive utilization and exports, the companies can create a larger API capacity which is necessary to sell in the global market, especially compete with China.

The following reasons provide a case for backward integration.

1. Reduce production costs considerably by eliminating the margins that are usually left in the hands of third parties.
2. Ensure continuity of supply and product quality, allowing a competitive advantage.
3. With cost competitive operations, companies can go for higher global market share.

Backward integration can also be realised by investing in API business of another company to ensure supplies.

This is one area where even mid-sized Indian companies can take competitive lead in the international markets as many formulation competitor countries cannot create a large & viable API business.

2.7g Industry 4.0 in pharmaceutical manufacturing

Another source of cost reduction as well as keeping control over supply-demand mismatch is through introduction of Industry 4.0 in pharmaceutical manufacturing. Besides, above, industry 4.0 is helpful in quality control, a common occurrence in plant & product rejections from India.

The term "Industry 4.0" was coined by the German government in 2011 in a national strategy to promote application of converging technologies like IOT (Internet Of Things), Robotics, Artificial Intelligence and other related fields as a key resource to gain and maintain global industrial competitiveness. The 4.0 designation represents the fourth evolution of the industrial revolution. The first three were steam power to drive production rather than human power; Industry 2.0 was powered by electricity which increased production manifold compared to steam. This period also brought great advancement in transportation with large scale locomotive trains systems. Industry 3.0 was the digital revolution brought about by large scale use of computers and communication technologies in manufacturing. Now, Industry 4.0 is convergence of four technologies which are disrupting the manufacturing sector. These are communication technologies which make possible the transfer of large amount of data over vast distances such as 4G which is being supplanted by 5G communications. This has made many functions possible such as remote monitoring of production processes; robotics, the use of automated machines to greatly reduce cost of manufacturing; Artificial Intelligence & Machine Learning and finally IoT which describes the network of physical objects such as embedded with sensors, software, and other technologies for the purpose of connecting and exchanging data with other devices and systems over the Internet. The whole gamut of Industry 4.0 is also termed as "smart factory."

The goal of Pharma 4.0 is to create the intelligence needed for engineers and operators to make smarter decisions that increase operational efficiencies, improve yield and engineering productivity and lastly, substantially drive business performance. Pharma 4.0 applies Industry 4.0 concepts to the pharmaceutical setting. Within modular structured smart factories, cyber-physical systems monitor physical processes, create a virtual copy of the physical world, and help make decentralized decisions. With the connected devices of the Internet of Things (IoT), cyber physical systems communicate and interoperate with each other—and with humans—for real-time control and data collection that contributes utilizable information shared among participants of the overall pharma manufacturing value chain.[38]

In practical terms, it means more connectivity, more productivity, simplified compliance, and the marshalling of production information to respond to problems as they emerge.
It changes the response from reactive to predictive, such as address potential challenges in the overall supply chain as well as maintaining the integrity of production data through tools like blockchain and more definite prediction of market demand & supply. At the same time, we should not be blinded by the range of technologies but gain the expertise to choose and integrate these. According to experts, the reluctance to change is rapidly diminishing given the FDA's and EMA's initiatives to move towards a scientifically based definition of product quality.

According to Society of Pharmaceutical Engineers, the advantages in a highly regulated industry such as pharmaceutical manufacturing are many:

- The elimination of data silos with better communication across the lifecycle of drugs
- A lower-touch relationship with regulatory bodies as data collection and sharing improves
- The elimination of paper-based processes
- A shift to risk-based regulation
- Improved agility, connectivity, and productivity--even in highly regulated facilities

2.8 Increase profitability of Janaushadhi Stores

Prescription medicines are largely bought from out-of-pocket funds. The government's flagship scheme to push medicines to urban and rural poor is Pradhan Mantri Bhartiya Janaushadhi Pariyojana (PMBJP) which today has over 6600 stores. It will rise to 10,000 soon. The total sales of these stores were Rs.419 crores in 2019-20.[39] This comes to a monthly sale of only Rs.6000 per month. A gross margin of 20% brings gross profitability to Rs.11,000 per month. If we take into account the overheads such as rent, utilities etc. there is very little profit left for long-term viability (after the subsidy provided by the government is exhausted.)

A cursory survey has shown that these stores are not located in areas of high footfalls due to the high rentals. However, to make the Kendra viable, each shop must attain higher sales. We have two suggestions to do that.

One suggestion to increase sales is to open one kendra in all government hospitals to take advantage of high footfalls and thus compete against the private medical stores which are found at the gates of all hospitals. There are over 11000 government hospitals in India. The existing Kendra owners should be given the first option to move to the government facility.

	The other suggestion is to open Kendras on wheels and the government subsidy can go towards the down payment of the retail van. These vans can travel within a convenient geographical distance and bring medicines to rural areas. It can visit haats (rural markets) and other high-traffic destinations. Here, government should even allow provision of vans for janaushadhi stores under Corporate Social responsibility (CRS).

Rural population is the major victim of counterfeit medicines and this wider accessibility will fight this menace too. Higher sales through Janaushidhi Stores would increase the overall market for high quality but low-cost drugs.

There is a bright future for Indian Pharmaceutical Industry but in a VUCA environment, it must study global trends, make sense of distant signals and evolve in a proactive manner. There is little long-term future without strong foundation in science & technology. With significant investment in R&D, Indian industry can stay globally competitive, both from onslaught of generic competitors and development in US and EU to re-shore the pharma supply chain.

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We anticipate certain developments taking place in the overseas markets which should be taken note of. The important one is the movement towards global or regional harmonisation of regulatory processes. With globalization creating opportunities for pharma companies but increasing the workload of regulators, a demand for regulatory harmony has arisen for national regulatory bodies to cooperate regionally and globally. As the nature of industry has evolved, the need for a global view of regulatory oversight has arisen.[1]

Till a decade back, national regulatory authorities developed their systems and processes independently to ensure that products on their markets are safe, efficacious and manufactured in accordance with prescribed quality standards. Today's system is characterized by increasing levels of harmonization – from collaboration on selected topics, to Mutual Recognition Agreements (MRAs), all the way to full integration, as with the European Union. Key organisations which oversee this global regulatory landscape are World Health Organization (WHO) and the International Council for Harmonization (ICH), which work to achieve global scientific consensus in developing regulatory guidelines.

It is important in the light of both China and India being seen by overseas regulatory bodies as source of poor-quality drugs.

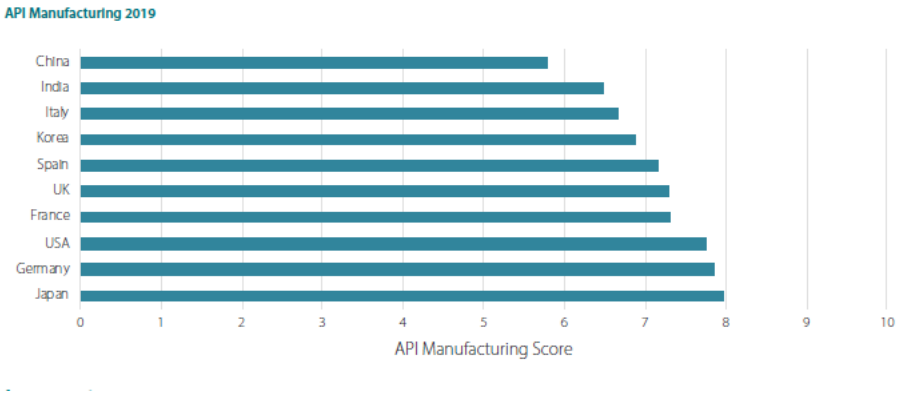
Issue of substandard drugs is not new in India and has wider impact including recalling of 632 medicines from Jan Aushadhi Kendras in Karnataka after failed drug quality standard test and recalling 106 batches of 52 drugs in last 4 years by Bureau of Pharma PSUs of India (BPPI). WhatsApp group of Jan Aushadhi Kendra owners has several complaints of shortage of supply and of not-of-standard-quality (NSQ) drugs.[2]

Obviously, our regulatory system needs upgradation which can be undertaken by linking it to international regulatory harmonisation systems which are being adopted by an increasing number of countries. This will give the confidence to the authorities in importing countries about the high quality of our medicines as well as provide access to quality drugs in the Indian market.

Since China is a major source of our APIs, the poor quality of their APIs (which is one of the reasons for cheaper prices) reflects in our formulations.

3.1 Quality Manufacturing Rankings

According to the CPhI Insights for 2019, API manufacturing quality is a key indicator for the performance of pharmaceutical markets – with many of pharma's developed markets still perceived as ahead of the large volume producers. With a respectable growth of 2.5%, Japan (7.97) has pushed ahead of Germany (7.85) to the number one spot for API manufacturing quality. But it is Spain (7.16) and Korea (6.89) that are the big movers, with scores increasing by 6.4% and 5.5% respectively overtaking Italy (6.7). Korea's performance sees the country improve its perceived quality of manufactured APIs, which could be a positive response from the market of recent government efforts to repatriate manufacturing and the desire for generic companies to source locally manufactured APIs. In Europe, Germany (7.85) retains its position as the preeminent API Manufacturer (7.78) ahead of France (7.31) and the United Kingdom (7.30). China followed by India are perceived as those with poor quality.[3]



Many Indian companies have been fined heavily by USFDA for serious lapses such as falsifying and destroying documents & data, changing samples etc. Some years back Ranbaxy, the largest Indian pharmaceutical company at that time was fined US$500 million and very recently, in March 2021, Fresenius Kabi Oncology Limited, Indian affiliate of the German multinational was fined $50 million after pleading guilty to concealing and destroying records at an API plant in Bengal, prior to a 2013 US Food and Drug Administration plant inspection in India.[4]

Such cases which are widely published and discussed internationally present a poor image of India's quality control in pharmaceutical manufacturing.

President Trump's executive order on the manufacturing of generic drugs and APIs on the US soil calls on the Food and Drug Administration (FDA) to conduct more unannounced inspections of drug plants overseas, a tacit acknowledgement of a failed inspection system that has allowed companies operating abroad to prepare for pre-announced inspections, turning their plants into veritable charades of compliance. Falsified results have allowed generic drugs with toxic impurities and dangerous particulates, or that are not bioequivalent to brand-name drugs, to enter our supply.[5]

Since API is the major and most important ingredient of formulations, the evidence of high and consistent quality is important for India, not only to seize markets for APIs and formulations but also to take the lead from China. Therefore, the PLI thrust of the government must include regulatory interface to ensure that our quality is at par with the best in the world. This can only happen when India joins international cooperative efforts on harmonisation.

3.2 Formulations Manufacturing Ranking

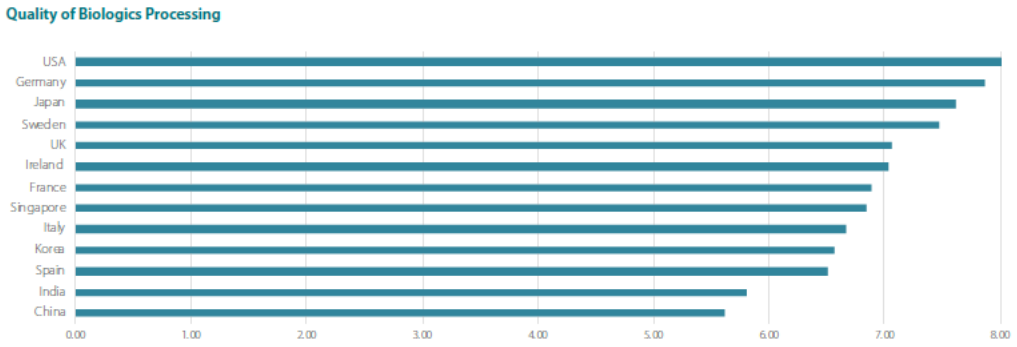
According to CPhI Insights, Germany (8.17), the U.S. (8.11) and Japan (7.97) are again ranked, as tier one nations, above all other major pharma economies in terms of the quality of finished formulations. Interestingly, CPhI Worldwide 2020 host country, Italy has grown by almost 14% over the last two years, emphasizing the strength of market conditions in Italy in the finished product manufacturing sector. A separate report by Farmaindustria provides some context to this, with the findings showing that, in the last year, Italy has equalled Germany in total production, as well as production per unit. All markets except the UK showed growth. Korea registered the biggest percentage growth rate in this category. Reporting, a healthy 3.72% increase, which sees it rise above Spain (6.79) – a nation that recorded a marked decrease (-3.10%). Spain's performance may be a consequence of German

and Italian improvements in finished product perception. India (5.86) and China (5.28) – who both see notable decreases in score from last year – remain at the bottom of the rankings.[6]

It is obvious that any improvement in the quality of both APIs and formulations would benefit Indian companies to take a lead in global supply and widen the lead with China.

3.3 Biotherapeutics Manufacturing Perception Ranking

Perceived quality of bioprocessing seems to closely relate to the results for innovativeness of bio markets. Once again, the USA (8.01) lead tier-one, followed by Germany (7.86) and Japan (7.61). Sweden (7.48) leads the 'best of the rest', with the UK (7.05), Ireland (7.04), France (6.89) and Singapore (6.84) a little behind. Despite its impressive results in the innovativeness category, China has not mirrored those improvements in perceived quality of bioprocessing, which has remained flat year-on-year – suggesting that whilst the market is acknowledged to be strongly growing some executives still have reservations about bioprocessing techniques.



CPhI Ranking-2019

The pharmaceutical companies are the main beneficiaries of harmonisation. the main driving force behind harmonisation in the pharmaceutical industry is cost. The companies have to produce different and unique dossier for each regulatory environment. Some national regulatory authorities also require companies to conduct additional clinical trials on their population such as Japan. This regulatory divergence is also costly for patients. Japan is one case where the patients have to wait at least three years after a drug has been approved in US or EU. Japan entered a Good Manufacturing Practice (GMP) MRA with the EU in 2012 to reduce the time-lag.[7]

Another key patient benefit is more effective pharmacovigilance because of international cooperation. Sharing data among different countries is crucial to being able to improve signal detection and act quickly if there's a problem. We need international agreements on rapid data sharing, as well as harmonized standards so that the various databases can talk to each other. Such activities are hugely important to keep patients safe.[8]

Another advantage is fewer "non-tariff barriers" to pharma trade, such as divergent standards and customs checks.

Today, the demand for harmonisation is rising, both in the developed and developing world, as a regional as well as global initiative.

Among the regional initiatives, the best known is European Union, but there are a growing number of additional groupings, including the Pan-American Network for Drug Regulatory Harmonization (PANDRH), the Gulf Cooperation Council (GCC), the Southern African Development Community (SADC), the Association of Southeast Asian Nations (ASEAN), and Asia-Pacific Economic Cooperation (APEC). If we take APEC as an example, its Life Sciences Innovation Forum has managed to coordinate multi-country clinical trials, the implementation of good clinical practices, efforts to combat counterfeit medicines, and more. By 2020, APEC is seeking to "achieve convergence on regulatory approval procedures."

3.4 African Drug Harmonisation Initiative

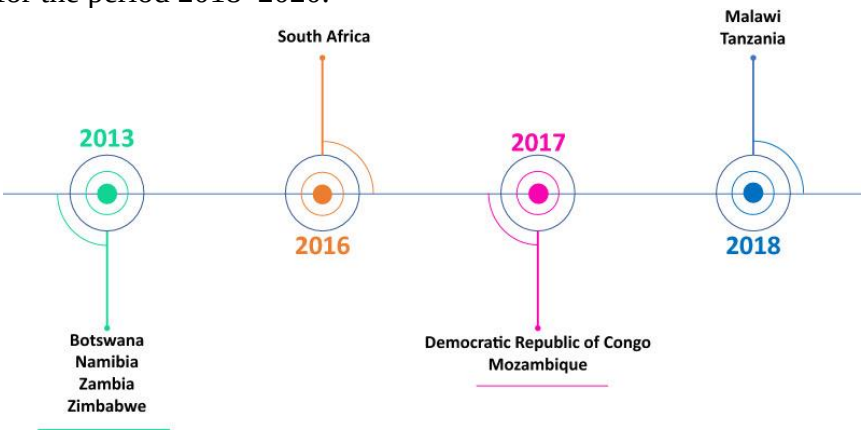
WHO is also working with NGOs like Gates Foundation to bring drug harmonisation to the African continent. The unanimous decision in 2019 by the African Union Assembly to adopt the treaty to establish an African Medicines Agency is a turning point to enhancing regulatory oversight and facilitating access to safe and affordable medicines across the continent.
As of March 2020, the Treaty for the establishment of the AMA has been signed by fifteen (15) countries.

There are eight regional economic communities (RECs) recognized by the African Union, such as the East African Community (EAC), the Economic Community of West African States (ECOWAS), and the Southern African Development Community (SADC) and it should be noted that several countries belong to more than one regional economic block. Through the work of the AMRH, three of the RECs have developed regional policies and guidelines for the regulation of medicines and reduced timelines for registration, and 17 countries have adopted or adapted the African Union model law. The AMRH was also responsible for establishing a task force to develop a legal and institutional framework for the establishment of the African Medicines Agency (AMA) which is expected to address the challenges faced by the African continent in medicine regulation.

At present, only a few harmonisation initiatives can be called successful. The Southern African Development Community (SADC) collaborative medicines registration initiative ZaZiBoNa is a successful regional work-sharing initiative on the African continent.

The ZaZiBoNa collaborative medicines registration initiative was established in 2013 by four countries, Zambia, Zimbabwe, Botswana, and Namibia, with technical support from the WHO Prequalification Team (PQT). The acronym ZaZiBoNa was derived from the first two letters of the founding countries, and although the initiative has expanded beyond these four countries. ZaZiBoNa is an advisory body and individual countries have to decide on its implementation.

The initiative has grown, and 13 of the 16 SADC member countries are participating either as active or non-active participants, based on their internal capacity to conduct assessments and inspections. The ZaZiBoNa initiative was later absorbed by the SADC Medicines Registration Harmonisation project, launched in 2015 and currently being funded by the World Bank for the period 2018–2020.



Angola, Seychelles, Swaziland, and Madagascar participate in ZaZiBoNa as non-active members and Comoros Islands, Lesotho, and Mauritius are the few remaining SADC countries not yet participating in the initiative.

As of October 2019, a total of 289 products had been considered under the initiative, 203 have been finalized and 86 are pending. Of those that have been finalized, 56% received a positive recommendation, 20% received a negative recommendation, and 24% were withdrawn voluntarily by the applicants. Of these 289 products, 274 (95%) were generics, 4 (1%) were innovative products or new chemical entities and 11 (4%) were biologicals or biosimilars.

As an example, to show the effectiveness of regional harmonisation processes, recently, Ugandan drug maker - Cipla Quality Chemicals – was granted permission to export antiretrovirals and malaria medicines such as efavirenz 600mg, lamivudine 300mg, tenofovir 300mg, and Artemether 20mg. to about 30 African countries through common harmonised regulatory process for ECOWAS (West Africa) and ZAZIBONA (Southern Africa). This is the first approval for a plant located in EAC (East Africa).[9]

In line with the implementation of African Continental Free Trade Agreement, African Medicines Agency will also see accelerated progress in the next five years. The Indian government should encourage the common harmonisation initiatives in Africa.

3.5 Global harmonisation Initiatives

At a global level, International Council for Harmonisation (ICH) was initially formed by the regulatory authorities of US, EU and Japan which are the founding members. It aims at development of common technical guidelines and requirements for pharmaceutical product registration. The organization currently has 16 members and 32 observers. India with observer status can attend meetings and nominate members to the expert groups but no voting rights. There was an announcement by India's Central Drugs Standard Control Organization (CDSCO) in 2020 that India will soon join ICH as a full member. China became a member in 2017. To become a member of ICH, the country needs to follow certain guidelines on good

manufacturing practice (GMP), Good Laboratory Practice (GLP), Good Clinical Practice (GCP), etc as well as good regulatory practice.

3.5a Pharmaceutical Inspection Co-operation Scheme (PIC/S)

Another important development in international harmonisation schemes is the rise of PIC/S. The Membership of PIC/S will reduce the burden on drug regulators in terms of decreasing the repeated inspections by various drug regulators on drug units. the Pharmaceutical Inspection Co-operation Scheme (PIC/S) develops and provides standards and guidelines for the harmonisation of Good Manufacturing Practice(GMP) in the global pharmaceutical industry.

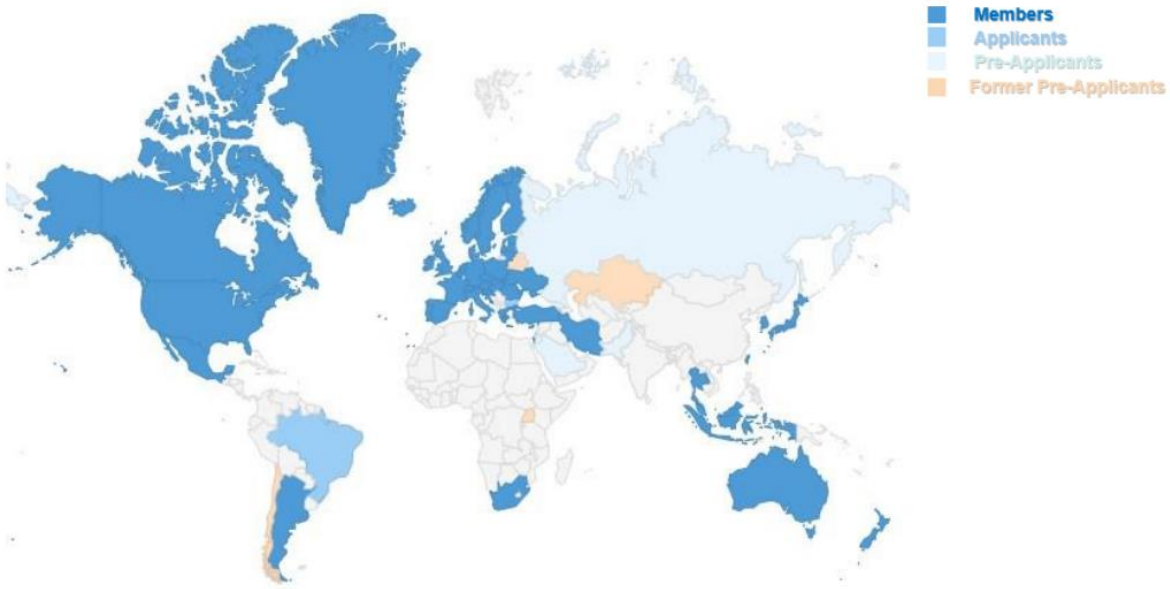
Unlike FDA or other national inspections which inspect individual company's manufacturing plants for export to their countries, PIC/S members are required to harmonise their respective drug control bodies' activities.

PIC/S is aimed at the removal of non-tariff barriers in the trade of pharmaceuticals in member countries through recognition of inspection reports and certificates on Good Manufacturing Practice (GMP). It essentially means that if a country joins PIC/S they will recognise GMP inspections and assessments done by other PIC/S member countries – without the need for another inspection (audit). Note that product registration is still required in each country.

A company manufacturing and supplying pharmaceuticals to multiple countries would be subjected to audits from the regulatory bodies of each country. For those countries who are members of PIC/S, an audit by another PIC/S member country will be accepted without the need for a further audit. This reduces compliance costs and increase exports between member countries.

For example, Company X in Indonesia exports product to Australia, Brazil, and South Africa. The company has been audited by the Australian regulatory body, the Therapeutic Goods Administration (TGA) and have been granted a GMP licence. As Australia, Argentina and Indonesia are all members of PIC/S, Indonesia and Argentina will accept Company X's products without their regulatory bodies performing separate audit on Company X. Once one PIC/S member country has confirmed that a manufacturer meets GMP requirements then all other PIC/S member countries will usually accept the GMP certification without performing and inspection and assessment themselves. So, being assessed as PIC/S GMP compliant will significantly reduce your compliance burden and costs if you are supplying product to multiple countries.

With over 50 countries being members of PIC/S, most of the Western world, and more than 75% the pharmaceutical spend, is represented. More countries have applied for membership and it is expected that by 2025, over 70 countries will be members, the latest to join is Brazil which became a member in October 2020. . India's membership will significantly increase its exports and take a big lead over its competitor countries such as China and Bangladesh. Today several countries, among them Saudi Arabia, Russia, Bulgaria, Italy, Jordan, Bangladesh and Pakistan have applied for membership.



From PIC/S Annual Report 2019

The process of accession to membership can take several years. Even if India decides to join in 2021, its acceptance to the PIC/S community may take several years for successful conclusion.

If India has to become a global power in pharmaceutical sector, it must ensure that the global health community has trust in the quality of products coming out Indian industry. This can happen only by adopting evolving global standards and harmonisation and become an active member of the consultative process. It is all the more important in the global market competitive scenario since China is not a member of either ICH and PIC/S and has not taken any steps to join.

According to a news item, a section of the industry is not in favour of India joining PIC/S and enforce stricter standards of Good Manufacturing Practices (GMP) as most manufacturers will not be able to comply with new rules which will replace the current GMP rules. At present, less than 15% of manufacturers are WHO-GMP compliant. PIC/S will impose a higher standard than even WHO-GMP.[10]

At present, from around 15000 manufacturing sites in India, 1,400 units are approved by World Health Organization (WHO) for having Good Manufacturing Practice (GMP); 1,105 have Europe's certificate of suitability (CEPs); more than 950 match Therapeutic Goods Administration (TGA) guidelines; and 584 sites are approved by the US Food and Drug Administration (USFDA). Many of these approvals are overlapping. Therefore, we already have a core strength in gaining foreign approvals.

The Indian government has often reiterated India's resolve to join PIC/S but it has to sell the scheme to the drug industry. Those who oppose are the ones which do not export and only cater to the domestic markets and would like fewer controls on the quality of medicines being produced. However, export bodies such as Pharmexcil has advocated the joining of PIC/S.

All major Indian exporters are in favour of joining PIC/S as not only its membership will open more markets but in the absence of membership, the cost of registration in PIC/S member countries will go up and may even close or restrict access to these markets. The advantages for India are:

- Reduced duplication of inspections;
- Cost savings;
- Export facilitation;
- Enhanced market access.

When we look at India's exports to PIC/S member countries, we find that it is significantly lower than its similar neighbours which are not members of PIC/S.

The government also has to view the implications of joining PIC/S for the manufacture of herbal and alternative medicine products such as Ayurveda which are rising in exports and have a high growth future.

The lack of Chinese or Indian participation in ICH and PIC/S is particularly concerning as the number of FDA and other regulators' warnings, Form 483s, import alerts and banned products in both countries continue to increase.

The US and EU lawmakers and the governments had been concerned about Indian and Chinese quality for over a decade.

Under these close scrutiny, no doubt, in part encouraged by multinational drug companies' vast resources and their effective lobbying power, it become more important for India to engage with multilateral agencies such as ICH and PIC/S as members. Only as a member, can India influence the outcome of these deliberations which have implications for the country.

No doubt, the membership and resultant changes in Indian regulatory system would prove onerous for many pharma companies which do not, as yet, follow WHO-GMP. In such a situation, either these manufacturing sites can close down (as hundreds of Chinese chemical companies have done so as compliance cost of new environmental protection laws take effect) or the government can fund their compliance costs to ensure that the vast domestic drug market is protected. Unlike inspections by FDA, MRSH and other agencies which only inspect export-oriented manufacturing sites, membership of PIC/S would require the entire Indian regulatory system to comply, both export and domestic. This would be a strong incentive to overhaul the drug regulatory systems and minimise the flow of sub-standard drugs.

The major impact of the membership would be the burden of compliance for the large MSME sector in the pharmaceutical industry. According to TIFAC, approximately 24,000 units in MSME's sector accounting for 70% of production by volume and 50% by value on ex-factory basis with an annual turnover of approximately Rs.60,000 crores which is an integral part of predominantly formulations. MSMEs contribute almost 50% to exports. The MSME-Pharma sector is facing many challenges as mentioned below:

• Lack of proper industrial infrastructure, capital, compliance with environmental laws, regulatory stringencies.

• Lack of awareness about regulatory compliance of stringent quality norms, ever changing technology in the drug making procedures, meeting international standards requirements.

• Lack of VC, PE or foreign funding for capital investment.

Probably, likely closure of this vast sector may be a major cause of the government moving cautiously and slowly on international membership. However, it has to take a call and time is running out. Even USA, with its most sophisticated and extensive regulatory body USFDA, took over 5 years to become a member after filing its application.

Pharmexcil in its report on PIC/S has concluded that the implementation of PIC/S has brought a harmony among PIC/S members. It has brought a uniform understanding among member countries regarding Good Manufacturing Practices for medicinal products. PIC/S has brought an understanding among drug regulatory authorities in bringing high standard, uniform acceptable quality standard medicines that can be permitted into the member countries. PIC/S has benefited the pharmaceutical manufacturers, inspectors, inspectorate and governments in saving time, cost for drug approval procedures and enhance the pharmaceutical market.[11] Moving forward, quality of drugs should be the paramount objective of the government and it should ensure that a majority of drug manufacturing units at least attain WGO-GMP status

3.6 European Union

In Europe, the likely introduction of the Supplementary Protection Certificate (SPC) manufacturing waiver will further expand the market for generic drug firms and their suppliers. Allowing generics firms to manufacture for export and stockpiling while the SPC is in place will accelerate market entry on patent expiry.

3.6a Supplementary Protection Certificate waiver for EU based Generic Manufacturers

The term of protection of a patent is 20 years from the date of filing of the application. In the life sciences industry, however, the period of effective patent protection is significantly less than in other industry sectors, because of the need to satisfy certain regulatory requirements and obtain marketing authorisation before medicinal products (both human and veterinary) can be placed on the market. Supplementary protection certificates (SPCs) were introduced in Europe to compensate, at least in part, for the investment made in these areas of life science research.

The EU is taking measures to foster the competitiveness of EU producers of generic medicines and biosimilar products. The Council, in May 2019, adopted a regulation which introduces an exception to the protection granted to an original medicine by a supplementary protection certificate (SPC) for export purposes and/or for stockpiling.

Thanks to the exception, EU-based manufacturers of generics and biosimilars will be entitled to manufacture a generic or biosimilar version of an SPC-protected medicine during the term of the SPC either for the purpose of exporting to a non-EU market where protection has expired or never existed or (during the six months before the SPC expires) for the purpose of creating a stock that will be put on the EU market after the SPC has expired.

The new regulation will enable generics manufacturers based within the EU to compete with non-EU manufacturers on equal terms.

The EU harmonised SPC system was introduced in 1992. It sought to compensate for the loss of effective patent protection due to the time required in order to obtain marketing authorisation (including research and clinical trials).

Global demand for medicines has increased massively (reaching €1.1 trillion in 2017). Alongside this, there is a shift towards an ever-greater market share for generics and biosimilars. Assuming an annual growth rate of 6.9%, by 2020 generics and biosimilars represent 80% of all medicines by volume, and about 28% by value.

With the expiry of industrial property protection, over €90 billion of the first generation of blockbuster biologics has become open to biosimilar competition by 2020.

The adopted regulation should contribute to Europe's competitiveness as a hub for pharmaceutical R&D and manufacturing. It will help new pharmaceutical companies start up and scale up in high growth areas, and is projected to generate, over the next 10 years, additional net annual export sales of well more than €1 billion.

3.6b Regulatory aspects of the proposed Pharmaceutical Strategy for Europe

One of the four goals of the proposed Pharmaceutical Strategy for Europe, a draft of which is being discussed and may be finalised by 2022 is to **influence other countries to harmonise international standards of quality and safety of medicines.**

As a response to the draft circulation, one trade association, SICOS (Syndicat de l'Industrie Chimique Organique de Synthèse et de la Biochimie). the national industrial sector group representing the manufacturers of APIs, excipients and intermediates in France, has (among other recommendations) has proposed that

- Give priority to European sourcing of raw materials for public tenders and reimbursable medicines (without hindering free trade). In all cases, priority should always be given to suppliers who comply with EU quality, safety, sustainability and environmental standards.
- Strengthen more specifically the qualification criteria for foreign suppliers in terms of quality, safety and respect for the environment.

Obviously, India being a major supplier of both APIs and formulations would come under pressure from The European Union to take membership of drug harmonisation initiatives. India should not wait for any regulatory directions from other countries but should voluntarily take steps to join international harmonisation initiatives.

In addition, looking at the overall concern for the environment in the EU, it is imperative upon India to take steps to create capability for development of APIs and KSMs through green chemistry route.

Looking at the various statements being issued by various trade bodies; the overall focus is to incentivise production of APIs and formulations rather than national protectionism. Any potential measures will have to comply with EU competition and World Trade Organization (WTO) rules. This creates space for a larger number of Indian companies to move into Europe and take advantage of the likely incentives for local production. One strategy could

be to take over some or many of the 400 off-patent medicines manufacturing sites in EU and increase supply of APIs from India.

3.7 United States

According to an analyst report, India is an increasingly important supplier of drugs to the U.S. market. In 2018, 12% of drug manufacturing sites for the U.S. market were in India, surpassing any other foreign country including China. As of August 2019, 72% of the active pharmaceutical ingredient (API) manufacturers supplying the U.S. market were located outside the United States, with 18% of them located in India.

As India has taken on an essential role in the U.S. pharmaceutical supply chain, Indian companies exporting drugs to the United States are experiencing greater scrutiny from Congress and U.S. regulators including the Food and Drug Administration (FDA). For example, Congress has held multiple hearings to address the safety of imported drugs in response to the recalls of angiotensin II receptor blockers (ARBs) (i.e., valsartan, losartan, and irbesartan) and the heartburn drug ranitidine, all due to potentially dangerous impurities. Congress has focused on India and China as manufacturers in both countries were implicated in the recalls.

Congressional scrutiny is likely to continue due to the recent outbreak of the novel coronavirus originating in Wuhan City, China, which has disrupted pharmaceutical supply chains in China, India, and the United States. In remarks at an oversight hearing on FDA foreign inspections on December 10, 2019, House Energy and Commerce Committee Chairman Frank Pallone indicated that the committee will be focusing on foreign manufacturers, stating that "manufacturers have the first responsibility to guarantee their products are safe and effective," and "FDA must ensure that any company, whether brand or generic, that wishes to market drug products in the United States adheres to the same quality standards." Congressman Pallone's statement is not surprising, as certain members of Congress now consider the United States' reliance on foreign manufacturers—particularly China—to be a national security issue.[12]

3.7a Application under Section 505(b)(2)

Till recently, introduction of pharmaceutical generics in the US was only possible under Abbreviated New Drug Application (ANDA) route. Generics approved via ANDAs are common, with hundreds of approvals coming each year (India being a major recipient of approvals), whereas examples of drugs approved under the 505(b)(2) pathway may be less well known.

The number of ANDA approvals are rising every year and competition in the generic industry is increasing rapidly eroding the profitability substantially. Some generic firms have sought to increase profitability by diversifying into modified products using the 505(b)(2) pathway.

Unlike ANDA which is specific for generics approval, the 505(b)(2) pathway, in contrast, is not specifically intended for generics. Instead, it is designed to encourage development of modified versions of approved drugs that provide additional benefits. Applicants must show the product is safe and effective, but, like ANDA applicants they can use data generated by other parties. However, the major difference between an ANDA and approval via the

505(b)(2) pathway is that the latter affords three to five years of exclusivity. In effect, generics firms using it will be free of competition for longer periods.

The 505(b)(2) new drug application (NDA) is one of three U.S. Food and Drug Administration (FDA) drug approval pathways and represents an appealing regulatory strategy for many clients. The pathway was created by the Hatch-Waxman Amendments of 1984, with 505(b)(2) referring to a section of the Federal Food, Drug, and Cosmetic Act. The provisions of 505(b)(2) were created, in part, to help avoid unnecessary duplication of studies already performed on a previously approved ("reference" or "listed") drug; the section gives the FDA express permission to rely on data not developed by the NDA applicant.

A 505(b)(2) NDA contains full safety and effectiveness reports but allows at least some of the information required for NDA approval, such as safety and efficacy information on the active ingredient, to come from studies not conducted by or for the applicant. This can result in a much less expensive and much faster route to approval, compared with a traditional development path [such as 505(b)(1)], while creating new, differentiated products with tremendous commercial value.

FDA explains that Both ANDA and 505(b)(2) applicants have significant flexibility in the types of studies, data and information they may submit, the guidance says, although ANDA applicants should not submit clinical investigations to establish safety and effectiveness.[13]

Thus, there are three pathways for introduction of drugs in the US:

1. 505(b)(1) NDA Full application – Data predominantly obtained from studies conducted by and for the sponsor.
2. 505(b)(2) NDA - Hybrid between an ANDA (505(j)) and full NDA (505(b)(1))
3. 505 (j) ANDA - Appropriate for drug products that are the same as approved products

Thus 505(b)(2) provides another significant route for introduction of generics in the US and exporters can evaluate the suitability of each in individual cases. Some examples are:

A company may wish to create a new dosage form that is faster acting, combines two active ingredients in a novel way, or provides a route of administration or mechanism of drug delivery that patients or doctors prefer over previous versions. Also, a company may wish to seek approval for a new indication for an already-approved drug or carry out an Rx-to-OTC switch. Such new products often contain well-understood active ingredients that are present in existing, approved drug products (reference drugs); so, companies must only create a bridge between what is already known about the previously approved reference drug and the novel drug product or indication. The 505(b)(2) NDA pathway makes this possible. In Europe, a regulatory approval route similar to the 505(b)(2) pathway is the hybrid procedure based on Article 10 of Directive 2001/83/EC.

BENEFITS OF 505(B)(2)

505(b)(2) is particularly valuable for pharmaceutical and generics companies looking to alleviate competitive forces in their environments while still wanting to benefit from a development process that eliminates most nonclinical studies as well as extensive safety and efficacy tests.

- Relatively lower risk because of previous drug approval

- Lower cost, accelerated development due to fewer studies
- May qualify for three, five or seven years of market exclusivity[14]

Increased interest in the 505(b)(2) pathway has been accompanied by a diversification of finished dosage forms and the technologies used to produce them. Varying a formulation so it changes how a drug's active pharmaceutical ingredient is released is precisely the type of modification the 505(b)(2) pathway is designed to encourage. Likewise, producing a finished dosage form that requires fewer pills than rival products is another strategy generics firms are using to try and differentiate themselves from competitors.

This is a good opportunity for Indian manufacturers as such capability is not available in rival exporting countries such as Bangladesh, Egypt and Jordan etc.

3.7b Complex Generics

According to a CPhI paper, in addition to encouraging use of generic drugs, the US Government is also trying to support development of non-branded products. In January 2019, FDA Commissioner Scott Gottlieb outlined the agency's efforts to advance the development of complex generics to improve patient access to medicines. Complex generics, as the name suggests, are drugs that as a result of their formulation, delivery systems or their active ingredients, are harder to "genericize" under traditional manufacturing approaches.

Gottlieb's concern is that "there are a number of complex drugs that are no longer protected by patents or exclusivities that would forestall generic approval, yet they continue to face no generic competition owing to the difficulty of developing generics." A lack of competition will mean that prices remain at their current level. To address this the FDA will issue specific guidance documents for complex generics outlining the scientific challenges involved. It also plans to make "recommendations on establishing active ingredient sameness and help advance the development of new analytical tools able to reduce development time and cost and inform regulatory decisions".[14]

To sum up, there are many regulatory developments taking place at national, regional and international levels and these represent both opportunities and threats. Considerable opportunities can come India's way, giving it an advantage over looming competitors provides it brings its regulatory framework in line with international conventions.

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Chapter 4 Future Growth Opportunities to 2030

There are many sectors which India should aim to grow in the next decade.

4.1 Increase intake of generic medicines in European countries

Covid has put pressure on European Union and other European countries to increase the intake of generic medicines. The EU's regulatory response in this regard is discussed in chapter 3. The future of regulatory directions seems favourable to India. However, to keep strong control over the manufacturing process, it is likely that EU may facilitate greater share of the manufacturing within its boundaries.

According to the latest annual survey by the Pharmaceutical Group of the European Union (PGEU), which represents pharmacists in European Union countries as well as the United Kingdom, drug shortages across Europe worsened in 2020.The therapeutic areas worst affected by shortages, according to the survey, were:

- cardiovascular medicines
- vaccines,
- respiratory disease medicines, and
- medicines to treat nervous system disorders.

Approximately 65% of the respondents (representing individual countries) reported shortages of more than 200 medicines during 2020, up from 58% in 2019.[1]

Action by India in banning certain drugs have at the time of outbreak in March 2020 has strengthened the resolve in the EU to have greater control over the manufacturing of APIs and formulations.

Some countries like France and Germany are actively considering reshoring of generic manufacturing in their respective countries, starting with paracetamol. Since these are the largest economies in Europe, any reshoring would also affect the market share of other generic producers and exporters within the entire EU as these medicines move beyond France and Germany.

"As a result of the Covid-19 pandemic, French pharmaceutical companies and political leaders are in agreement about the importance of repatriating production to France or Europe, especially those that manufacture drugs….. health has become a question of sovereignty and national security."[2]

In June 2020, President Macron was one of the six UE leaders who wrote to the Head of European Commission for incentives for European companies to develop critical ingredients and medicines.

The coronavirus pandemic has reinforced Sanofi's vigour. On February 24, 2020, the company announced the creation of a new offshoot with the ambition of becoming the world's second largest manufacturer of active pharmaceutical ingredients (APIs), after world leader the Swiss Lonza Group. They are currently predominantly manufactured in Asia. This new company has its headquarters in France and has six European plants with more than 3,000 employees. It is targeting sales of one billion euros and an IPO on the Paris stock exchange by 2022.

"Our calculation is strategic before being economic," insists Luscan. "Admittedly, our manufacturing costs here will be higher than in Asia, between 10 and 15 percent higher, but that's the price we have to pay to maintain a pharmaceutical industry in Europe."

This is an interesting development to watch for since other companies buying API from Sanofi may not wish to pay the higher costs. Besides, drugs sold in Sanofi's overseas markets such as Francophone West Africa may not be able to absorb the higher costs providing opportunity for India to increase its market share.

Other companies have different views. For manufacturers, the Covid-19 crisis illustrates the limits of a model based on unbridled globalisation. *"It is dangerous to be dependent on a single production site," says Jacques Zagury, director of health policy, public affairs and communication at the MSD laboratory (Merck Shape & Dohme, a subsidiary of Merck & Co) speaking with FRANCE 24. "However, it would make no sense to simply repatriate everything to Europe. We just need to diversify our suppliers."*[3]

It is unlikely that many companies would go to the extreme of Sanofi. Companies such as AstraZeneca have already outsourced 90% of their captive API production. It is here that Indian industry can play the part of convincing European manufacturers to relook at India's API sector for diversifying supplies, especially with the launch of three API Parks and the government's PLI scheme. We have the necessary knowhow, people and a large domestic demand to rejuvenate the API sector. However, as we have noted in a later part of this chapter, China will do everything to derail India's API push including reducing prices substantially so that India is not able to take a solid foothold and is priced out of international markets. However, political and strategic conditions are in favour of India provided we speed up and widen the scope of API production beyond Atmanirbhar objective.

Therefore, Indian companies should scale up and provide a large product portfolio and give reliability of a viable, high-quality and cost competitive alternative to China in APIs.

4.1a European Generics Market

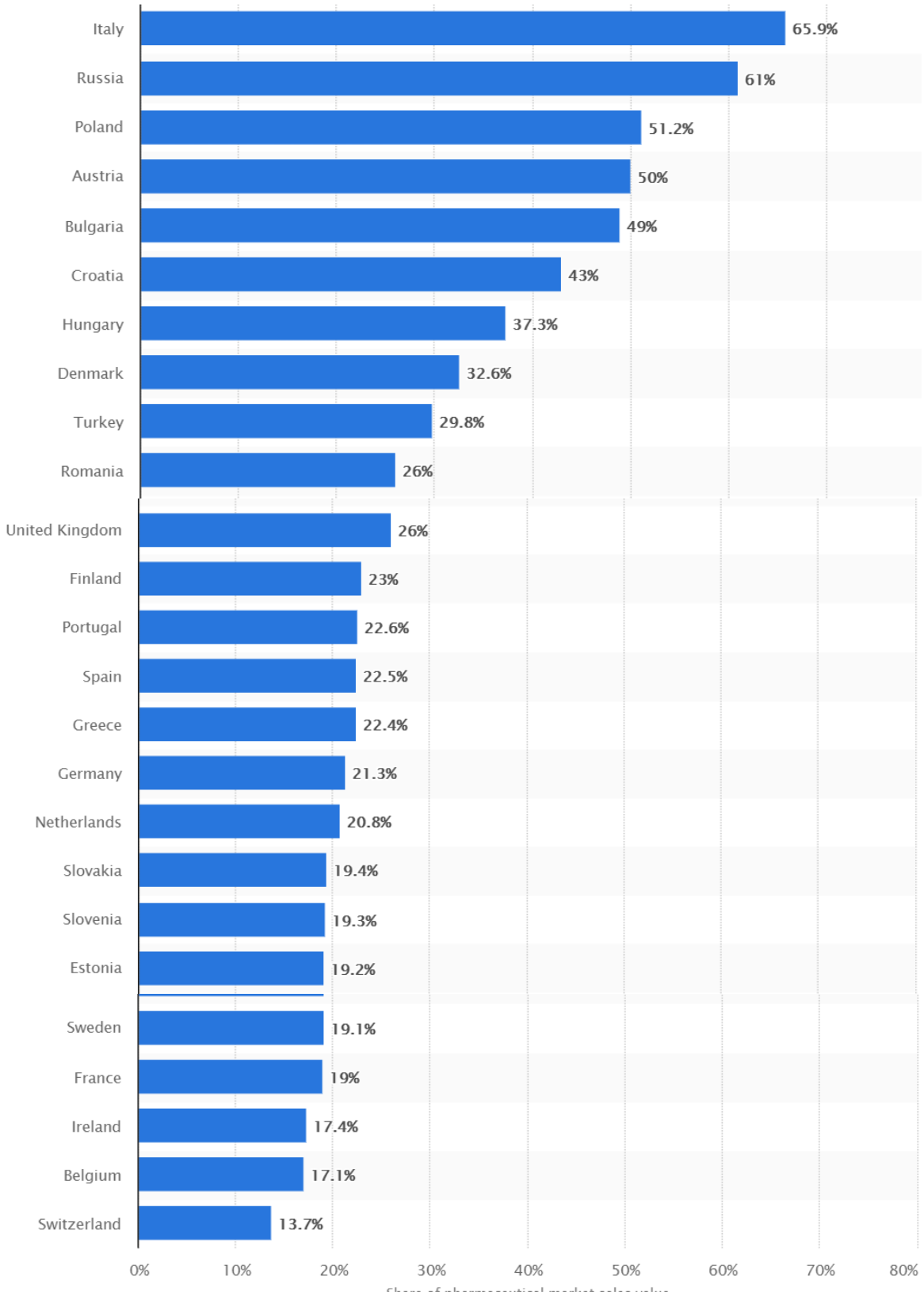
Market size

The size of the European Generic drugs market has been forecasted at USD 69.80 billion in 2020. It is expected to reach USD 98.36 billion by 2025, growing at a CAGR of 7.10% from 2020 to 2025.

The cost-effectiveness of generic drugs has given it a competitive lead over branded drugs in the market. The key driving factor for generic drugs is patent expiry for branded drugs. Patent for Branded drugs with sales of up to USD 135 billion expired in 2015. Nearly USD 150 billion worth of patents for branded drugs expired by 2020 which will give generic drugs a huge advantage.

One more trend which influences market growth is outsourcing. Importers are using outsourcing as a strategy to reduce their capital which will be an advantage to generic drugs. The only restraint for this market is rigid rules set up by the regulatory authorities for approval of these drugs and the threat of counterfeit drugs. This market will increase tremendously during the forecast period.

The is tremendous scope for increasing the penetration of generic drugs in Europe. The generic penetration of various countries is as follows:



Market share of generics in Europe (2018)[4]

There are only three countries, Poland, Russia and Italy where generic penetration is more than 50% and only Poland and Italy in the European Union. In major countries such as Germany (31%), UK (29%), Spain 22% and France 19%, the generic usage is low. Since, in most of these countries, state intervention in healthcare, especially supply of medicines is high, there is ample scope for Indian industry to work alongside with other stakeholders such as International Generic and Biosimilar Medicines Association to increase intake. We should note that the high penetration of Generics in the US has happened in spite of high incidence of grant of evergreening of patents in the US compared to Europe.

Since healthcare costs in most of the European countries are met by the state, there should be a strong lobby to convince the people and the governments, that quality of generic drugs is equivalent to their innovator counterpart and second the obvious cost advantage. Any savings in drug costs can go towards providing higher access to innovative or medicines with active patents. During Covid, most government had to increase their healthcare costs manifold, and this is the right moment to push for generic drugs to bring down the overall cost of state healthcare support.

India not being a member of either ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) nor PIC/S (Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme) weakens its case of providing a strong and effective regulatory environment in the country and thus acceptance of its medical products in many countries. These matters are discussed in detail in Chapter 6 on Regulatory issues.

The Indian government has often stated its commitment to global harmonization systems, but preparatory work has not yet begun.

4.1b Pharmaceutical Hub in the "Emerging Europe"

For various reasons ranging from strong control over quality, fear of the availability in quantity during covid type situations and rising automation in pharmaceutical formulations production, pharmaceutical production in the European Union is becoming a more viable proposition.

Since many former communist countries in Central Europe have joined European Union, much of industrial production has shifted from high-cost countries such as Germany to low-cost countries such as Poland, Hungary etc. A large part of automotive production has already shifted. For companies in Germany, these "emerging Europe" countries provide lower costs and are located close to the markets. These 12 countries from "Emerging Europe" present numerous opportunities for Indian manufacturers looking to establish and expand in Europe.

India should learn from German automotive manufacturers and attempt to establish an Indian Pharmaceutical Hub for production and distribution of generic formulations, not only within EU but also Eastern European countries such as Ukraine, Russia etc. This hub could be on the lines of recently announced Indian pharmaceutical zone in Mexico by six Indian companies. This will provide a long-term market for export of APIs from India.

These countries are recipients of EU funds for modernisation of industries and Indian manufacturers can explore the possibility of such funds. Higher production within EU would also dampen the enthusiasm for countries like France and Germany which are exploring higher generic production within their boundaries. The European Union will announce a definite policy on incentives for indigenisation by 2022. Therefore, there is a small window of opportunity for Indian pharma companies to enter or expand within Europe.

The pharma market in Emerging Europe itself is quite dynamic. Poland is the largest pharmaceutical market in Central and Eastern Europe. As of 2020, Poland is the largest country in Central and Eastern Europe. It has 38.5 million inhabitants as well as a GDP of $1.35 trillion. Over the years following 1989 and the reinstatement of a free market system, Poland has been the most stable and prosperous economy in this region. In 2020, the Polish pharma market is valued at over $2 billion. As it is in a very convenient geographic location, Poland is a major transport hub and is a great spot for international trade. Long-term market stability, transparency and lots of R&D have led more and more investors from Europe and the rest of the world towards doing business with pharmaceutical companies in Poland. As the quality of life in Poland increases, the future of pharma companies will only get better. Tax incentives and subsidies from the EU have made pharmaceutical companies in Poland competitive in the European and global market. Hungary, The Czech Republic and Romania also display similar trends, though on a smaller scale.

Some Indian companies, most notably Sun Pharma and Aurobindo Pharma have made strong entry in this region with an eye towards, not only EU but Eastern Europe too. There is room for more Indian companies to move into Europe through Central European countries.

4.2 Gain higher market share in Biogenerics

Biopharmaceuticals consist of Monoclonal Antibody, Recombinant Growth Factors, Purified Proteins, Recombinant Proteins, Recombinant Hormones, Synthetic Immunomodulators, Vaccines, Recombinant Enzymes etc., and these are largely used in the treatment of Oncology, Autoimmune Disorders, Metabolic Disorders, Hormonal Disorders, Disease Prevention, Cardiovascular Diseases and Neurological Diseases.

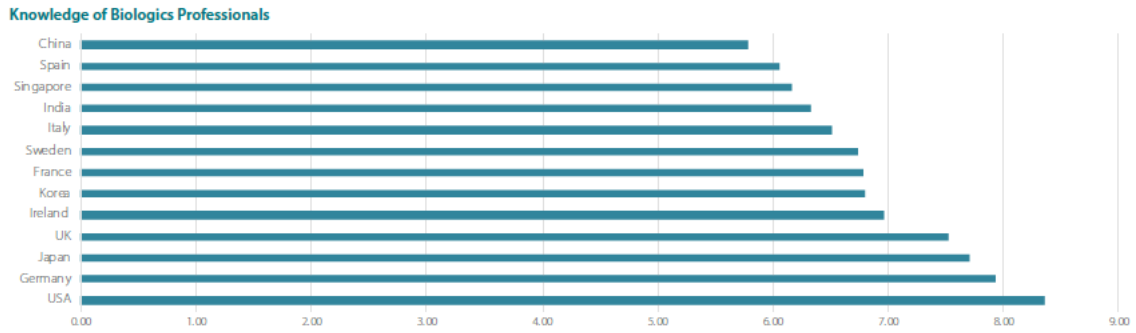
Today, one in very three drugs approved is a biotherapeutic. According to Mordor Intelligence, the global biopharmaceutical market is valued at approximately USD 325.17 billion in 2020 and is expected to witness a revenue of $496.71 billion in 2026, with a CAGR of 7.32% over the forecast period.[5]

In 2018, the sales of the top five selling recombinant proteins (Humira, Keytruda, Herceptin, Enbrel, Avastin), all antibody products, totalled just over $48 billion. The compound annual growth rate for antibody product revenue, which include naked monoclonal antibodies, Fc-fusion proteins, antibody fragments, bispecific antibodies, antibody conjugates, and other antibody related products, was approximately 20% from 2004 to 2014. However, this growth has slowed to the mid-teens in the recent years due to the maturation of many products and emerging alternative therapeutic modalities. Also, it is difficult to sustain such growth rates as the overall market size increases.

With the expiry of industrial property protection, over €90 billion of the first generation of blockbuster biologics has become open to biosimilar competition by 2020. These will become available for small number of countries, including India, where such capabilities exist to develop biogenerics (or biosimilars).

The Indian sector is growing at a rate of around 12% and its total output is valued at over $3.4bn. New products which need to be developed include Interferons, Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), Blood Factor VIII, Herceptin, Oral Insulin, New Monoclonal Antibodies (more than 200 molecules are available globally). The biosimilars market was valued at approximately USD 28.2 billion in 2020, and it is expected to grow to USD 103.6 billion in 2026, with a CAGR of 24.2% over the forecast period. Indian industry must grow at twice the present rate to take a significant share of the world's bio-generic market which will be approximately $250 billion by 2030.[6]

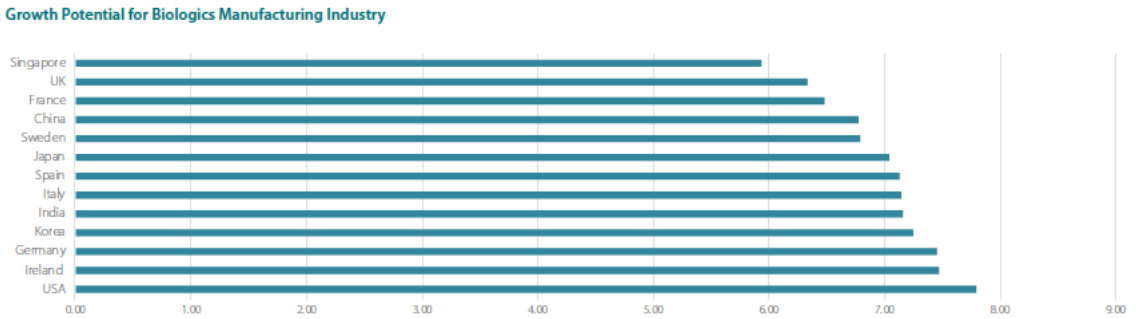
The strength of the Indian biotherapeutics sector is also due to the availability of a large number of knowledge professionals. According to CPhI Insights[7] 2019, U.S. (8.35), Germany (7.93) and Japan (7.69) remain the industry leaders for knowledge of their biologics professionals, with a second tier featuring the UK (7.52) and Ireland (6.96). Interestingly, Korea (6.80) has overtaken France (6.78) for knowledge of their biologics professionals, and this is perhaps reflected by the significant growth of manufacturers such as Samsung Biologics and Celltrion over the last few years. The industry's other key movers are India (6.46), overtaking both Singapore (6.15) and China (5.78), which is now perceived as Asia's second most knowledgeable biologics market.



4.2a Growth Potential of Biologics Manufacturing Industry

In the CPhI 2019 survey of industry professionals, U.S. (7.80) saw the highest score for growth potential of its biologics manufacturing industry. Ireland (7.48) consolidated its position as a first-tier market with the second largest growth, finishing ahead of Germany (7.45) and Korea (7.24). The confidence within the region is demonstrated by industry giants such as Pfizer, GSK, Allergan and MSD having prominent operations and investments in the country. The country has also significantly grown the number of biologics sites from 2 in 2003 to around 20 this year. Singapore (5.94) and the UK (6.33) were once again ranked the lowest by respondents in terms of their growth potential.

It should be noted that India's manufacturing ranking is much higher that China, France and UK and with the Covid epidemic entering the second year and with state support, this lead can be extended, especially in the field of vaccines. Though global vaccine supply from India has taken a backseat recently, this epidemic will also create more investment in expansion of current and greenfield manufacturing capacity.



There are fewer global competitors in biopharmaceuticals compared to generics due to complex manufacturing process as well as requirement of large investment. The government should enable to business environment to make it more attractive for innovator companies to invest in their own as well as JVs.

The ongoing pandemic of COVID-19 globally is expected to have a significant impact on the biopharmaceutical industry. Most of the biopharmaceutical companies are striving extensively for the development of the vaccine against the SARS-CoV2 virus. Some of the candidates are traditional-type vaccines such as inactivated and attenuated products, however, most of the vaccine candidates being developed are advanced DNA, RNA, and protein subunit vaccines. Thus, this factor is expected to boost the growth of the biopharmaceutical market over the pandemic. However, the clinical and regulatory procedures for drug

candidates of other indications can witness a slow pace due to the shifting priorities of the healthcare system, to reduce the infections to clinical trial patients.

The market is largely driven by the growing geriatric population, increasing burden of chronic diseases, and rising inclination toward targeted therapy. According to the Globocan 2020[8] report, a total of 19,292,789 new cancer cases were diagnosed, with 9,958,133 deaths due to cancers worldwide. Additionally, as per the data from United Nations World Population Prospects 2019 report, by 2050, one in six people in the world will be over age 65, which is an increase from one in 11 in 2019 and by 2050, one in four persons living in Europe and Northern America could be aged 65 or over. The number of persons aged 80 years or over globally is projected to triple, from 143 million in 2019 to 426 million in 2050. Also, the huge demand for biopharmaceutical is facilitated by an accelerating focus on research and related investment. The ability of biopharmaceutical products to address previously untreatable conditions has introduced innovative drugs in the market. Thus, given the aforementioned factors, the studied market is expected to bolster over the forecast period.

Also, the market demand for biopharmaceuticals is increasing with the rising desire to circumvent both the side-effects associated with some small-molecule therapeutics and invasive surgical treatments. However, stringent regulatory issues along with the requirement of high investment in the development of a biopharmaceutical drug, are the growth limiting factor for the future. If India wishes to make a significant presence in the world market, it must bring at least $2 billion in investment from diverse sources, FDI, PE etc. over the next 2-3 years.

Even in the field of vaccines, where India leads the world in supply, there are only a handful of firms and no new firm has entered the sector in the past few years. Only two companies possess BSL-3 production facility in India under which covid19 vaccines can be produced. Bharat Biotech has been producing Covaxin at its Biosafety Level-3 (BSL-3) facilities in Hyderabad and Bengaluru. Indian Immunologicals Ltd (IIL) and BIBCOL have entered into a technology transfer agreement with Bharat Biotech. In addition, one state government undertaking, Haffkine Institute, has also entered into a technology transfer agreement with Bharat Biotech.[10] With strong government and private sector investment, both IIL and Haffkine have the potential to grow into world-class biologic companies.

However, they cannot start production for another six months due to plant modification for BSL-3 production. Besides lack of production facilities, there is a large import of building blocks for vaccine production which are presently imported. The government has to take a call on the total manufacturing ecosystem if it desires global leadership in vaccine supply. We cannot assume that covid19 will be the last pandemic and the country must create capacity for the entire value-chain if a similar pandemic occurs.

According to The Economic Times, If the country plays its cards well, the industry could take off at an important moment, as part of a global shift from conventional small molecule drugs to biologicals. "The potential looks like several billions of dollars from a patent expiry point of view," says Anand Kumar, deputy managing director of Indian Immunologicals, "but the challenges are many".[9]

Though the global biogeneric market is very large at $200 billion, the investments in development & manufacturing infrastructure are also very high when compared to conventional generics. The development is itself lengthy and expensive and could cost more

than Rs.100 crore and take up to six or seven years. Manufacturing costs are much more. Biocon, for example, spent $200 million on its insulin plant in Malaysia. Compare this to just a few crores and two years needed for a generic drug.[10]

In addition, Indian companies have seen a long struggle in quality management of generics manufacturing as seen from rising number of FDA observations. How quality can be maintained for biogeneric, is in our opinion, the greatest obstacle in mirroring the global success of generic drugs. As the following table shows, no Indian bio-generic has yet been able to first-to-file.

Approval Count	FDA Approval Date	Biosimilar	Biosimilar Manufacturer	Reference Product	Reference Manufacturer	Molecule	Launch Status
1	March 2015	**Zarxio**	Sandoz Novartis	Neupogen	Amgen	filgrastim	2015
2	April 2016	**Inflectra**	Celltrion	Remicade	Janssen (J&J)	infliximab	2016
3	August 2016	**Erelzi**	Sandoz Novartis	Enbrel	Amgen	etanercept	2018
4	September 2016	**Amjevita**	Amgen	Humira	Abbvie	adalimumab	2023
5	May 2017	**Renflexis**	Merck & Co	Remicade	Janssen (J&J)	Infliximab	2017
6	August 2017	**Cyltezo**	Boehringer Ingelheim	Humira	Abbvie	adalimumab	
7	September 2017	**Mvasi**	Amgen	Avastin	Genentech	bevacizumab	2019
8	December 2017	**Ogivri**	Mylan	Herceptin	Genentech	trastuzumab	
9	December 2017	**Ixifi**	Pfizer	Remicade	Janssen (J&J)	Infliximab	
10	May 2018	**Retacrit**	Hospira (Pfizer)	Epogen	Amgen	epoetin alfa	2018
11	June 2018	**Fulphila**	Mylan	Neulasta	Amgen	pegfilgrastim	2018
12	July 2018	**Nivestym**	Hospira (Pfizer)	Neupogen	Amgen	filgrastim	2018
13	October 2018	**Hyrimoz**	Sandoz	Humira	Abbvie	adalimumab	2023
14	November 2018	**Udenyca**	Coherus BioSciences	Neulasta	Amgen	pegfilgrastim	2019
15	November 2018	**Truxima**	Celltrion	Rituxan	Genentech	rituximab	
16	December 2018	**Herzuma**	Celltrion	Herceptin	Genentech	trastuzumab	
17	January 2019	**Ontruzant**	Samsung Bioepis (Merck)	Herceptin	Genentech	trastuzumab	

Unlike conventional generics where launch is immediate after ANDA approval, there is a wide gap between approval and launch in the bio-generic space. It may be due to manufacturing difficulties. Although over 50 biosimilars are available in the domestic market, only when an Indian biosimilar is launched in the US, we can be confident that the quality issues in manufacturing have been sorted out.

Success in global markets is slowing coming to Indian companies. Intas Pharmaceuticals became the first Indian company to get a biosimilar registered of the biotech drug Filgratsim under the brand Accofil in the EU in February 2015. It is now getting ready for more products and for foray into the US.

In June 2020, a joint development between US-based drugmaker Mylan and partner Biocon was the first to receive USFDA approval for its insulin glargine biosimilar brand name Semglee, in both vial and pen variations. Semglee is biosimilar to Sanofi's Lantus which had a global sale of US$ 6.4 billion in 2015. The patent expired in 2014. Semglee is the third successful outcome of Mylan-Biocon partnership.

This event brings to focus two constraints for Indian biosimilar companies, high cost of development & approval and building manufacturing infrastructure. Therefore, partnerships are more crucial in bio-generics than in generic products.

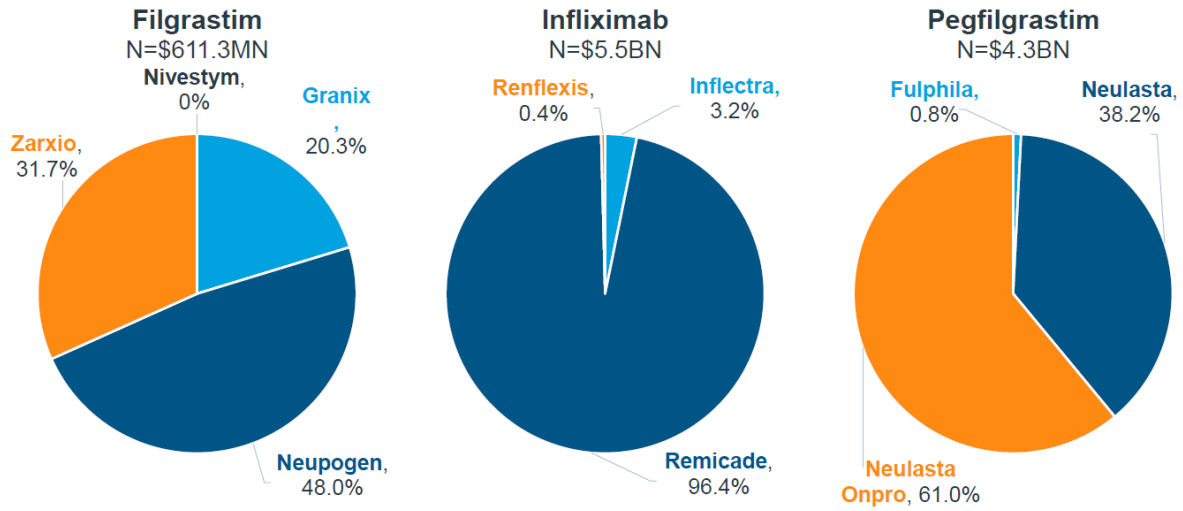
It goes without saying that the bio-generics will grow at a high rate in the foreseeable future. However, these drugs are very expensive due to high R&D expenditure and thus have fewer sources of supply. Even their generic form, bio-generics have fewer sources due to the limited expertise in developing biological procedures for manufacturing.

Therefore, the high cost of projects and the high-quality parameters required for their acceptance in the regulated markets would require a much larger investment in R&D than for conventional generic drugs. This requires a larger net of partners where Indian companies can collaborate with companies abroad to share costs and revenue. It also requires establishing a bio-generic institute on PPP model which can undertake development of drugs and their quality manufacturing. Such an institute has better chance of collaborating with universities and other non-profit institutions which operate in similar space.

The low level of competitiveness and higher profitability of bio-generics in the global markets should provide grounds for finding resources for their development from unconventional sources of finance. The companies should cast their net wider for financial support, especially Impact Investment.

If India has to create that advantage in biosimilars, it is not just enough to make the right regulations and conditions for industry. The country must expand the biology research ecosystem by greater state investment in education and fundamental research. How the country handles the research ecosystem could be a deciding factor in the long run. "China and Korea have nucleated the basic research ecosystem far better than India," says Cartikeya Reddy. No one should be surprised that Samsung has started building the world's largest biologics manufacturing plant in South Korea.[11]

Unlike conventional synthetic drugs where price erosion by up to 90% is normal within a year of launch of generics, the price erosion is much less in the biogenerics space and the innovator companies can manage high market share and profitability for years to come.



Market share of innovator brand remains high even after launch of biosimilars[12]

Biotherapeutic drugs are extensively used in areas where traditional synthetic molecules have not found success such as cancer treatment. It is likely that due their monopoly, duopoly or oligopoly supply constraints, there is possibility of them being out of reach of the vast Indian population.

As we have recently seen in case of Covid19 vaccine, it is only the large size of government procurement and public pressure on the two manufacturers, the prices were kept low. In fact, the same vaccine at private hospitals is priced at Rs.1200 for one dose, that is Rs.2400 for a complete course. The imported vaccines are priced still higher even after the government has waived at import duties.

Even in the United States, from where most novel biopharmaceuticals generate, the fear of cartelisation is high.

"The U.S. health-care industry keeps prices artificially high and competition low, operating by the dictionary definition of a cartel: 'An association of manufacturers or suppliers with the purpose of maintaining prices at a high level and restricting competition." West describes that the cartel operates by invading Washington with hordes of lobbyists with big budgets to preserve the status quo. "In 2017, this cartel unleashed 1,400 lobbyists and spent $277 million to defend its interests".[13]

For example, to cure hepatitis C two drugs launched by Gilead (Sovaldi) and followed by AbbVie (Viekira Pak) were priced at $84,000 for a course of therapy. Even when prices were brought down from $14,000 to $4,500 in certain cases, they still are too high for the Indian population.

According to National cancer registry, the projected incidence of patients with cancer in India among males was 679,421 (94.1 per 100,000) and among females 712,758 (103.6 per 100,000) for the year 2020. One in 68 males (lung cancer), 1 in 29 females (breast cancer), and 1 in 9 Indians will develop cancer during their lifetime.[14]

India also has 6.2 million cases of Hepatitis C cases. Under these circumstances what can India do to ensure that the benefit of these latest drugs for lifesaving treatments are not out of price for much of the population.

1. Price negotiations at the national level. The prices of newer drugs can be brought down by the government through negotiations at a national level, just like Covid19 vaccines while allowing private companies to import and distribute. A certain quantity can be channelled to major hospitals in the public sector such as AIIMS, Tata Cancer Centre and PGIs where cancer and other major treatments are available for the poor population.

2. Establishment of a National Biopharmaceutical Institute to develop biogenerics knowhow which can be licensed out to prospective entrepreneurs at a low license fee along with training & plant design. Government already has a scheme Common Facilities Centre (CFC) Scheme under which such an institute can be established on PPP model, where Central government provides seed money for building & equipment, state government provides land and utilities, and the members can provide funds for project research. However, the total amount of subsidy, that is Rs.20 crores is too little for such a facility to come up. The government should ease the requirements for R&D Centres and enhance subsidy for take-off to take place.

At present, only a handful of private companies develop these products for their own sales. A common facility can license drugs on royalty basis to ensure monopoly and cartelisation does not take place and prices are fairly governed by supply & demand.

4.2c How Korea Built a World-Class Biosimilars Industry

As has been shown in above rankings, South Koreas is fast developing its biopharmaceuticals industry, both bio-generics and novel drugs.

South Korea has overtaken many of its regional counterparts to boast a highly impressive biosimilars pipeline. Explaining how Korea specifically managed to rise to such a stature in the world of biologics, TH Kim (Samsung Biologics) recalls, “The western companies began five or six years earlier than the Korean companies. However, we have caught up and dramatically cut our approval times. People often ask me how this was possible. The answer is that we went “all in” – complete dedication to the market. Once we chose to specialise in biosimilars, there was no room to survive if we failed with the few projects we had”.

One of the main issues facing developers of biosimilars is the bottleneck surrounding global approvals. “In my opinion, many companies either fail to gain approvals, or the process is delayed because of their inadequate manufacturing facilities” hypothesizes TH Kim. He continues, “Although over 100 companies have products that have received approval by either the EMA or the FDA, most do not possess the capacity for production and have failed to improve their facilities and operation technologies in line with their R&D advancements”.

Soon Jae Park, CEO of Alteogen, a biotech developing bio-better products – derivative variants of the original biologic molecule which show improvement in one or more attributes over the original – concurs, “we have to understand that the drugs produced, although being called biosimilars, are essentially new biological entities. This means that there is no standard program for drug manufacturing, so clearly production capabilities affect the progress of the product”.

While global players like Samsung Biologics have overcome these challenges, smaller biotech companies must take a shrewder approach to making it in the biologic’s world – “Alteogen needs to be smart in order to survive,” asserts Soon Jae Park. “Consequently, Alteogen is looking for partners that have the manufacturing capabilities and are able to help us in the further steps of the product development” he adds.

For Korea to truly entrench itself as a biologic’s leader, the challenge is not only to innovate within manufacturing, but to develop the most innovative products. Despite recent manufacturing successes, some have voiced the concern that fast followers will emerge with which Korea cannot compete on costs. “I do not think that biosimilars will be very attractive for Korean companies in ten years. Costs in Korea will further increase and developing countries will catch up. Even today, countries like China and India can produce biosimilars, obviously at a lower price,” declares Soon Jae Park.

The next stage for the industry is to leverage its strengths in biosimilars as a launchpad for new biologics and, like Alteogen, Biobetters. “Korean companies will need capabilities to develop their own biological drugs based on new chemical entities in order to compete,” proposes Park.

“To illustrate this point with an example, Alteogen has developed NexP™ Fusion Technology, a next-generation long-acting bio-bettter technology. This shows excellent long-acting properties without causing any loss of activity as medicines, so they can stay longer in the body,” reveals Park. Making this innovation the norm will help entrench Korea as the leading player in the biologics game.[15]

Therefore, this is a golden opportunity for Indian companies to collaborate with smaller South Korean companies so that Korean R&D and Indian low-cost manufacturing can be a win-win outcome for both nations. This collaboration with other countries such as Taiwan, Iran, Brazil, Russia etc. can be a game changer for future growth.

4.2d CDMO opportunities in biogenerics

The low cost of research and development has promoted the increased development of biologics in the country. For instance, while the development of a biosimilar takes approximately eight years in the European Union, the development of a similar biologic takes only three to five years in India. The cost to develop a biosimilar in the EU or U.S. is estimated between $100 and $200 million, while in India it costs $10 to $20 million. This lower cost of development is attributed to several factors, including the lower cost of recruiting patients, fewer labour and service fees, as well as less stringent regulatory approval criteria.

Despite the local regulatory framework, there have been international successes for Indian companies such as Biocon, which successfully entered the U.S. market with two biosimilars — a pegfilgrastim and a trastuzumab — through its Mylan partnership. Most Indian companies that are engaged in biosimilar manufacturing do not attempt to enter the U.S. market due to the litigation and regulatory costs.

Therefore, for smaller biogenerics companies, an attractive route should be to collaborate with larger global companies who develop the products and transfer manufacturing to Indian affiliates. There are several emerging opportunities in CDMO sector due to the pressure on reducing cost and time for bringing product to the market and to be competitively priced in the marketplace.

4.2e Process Control in Biopharmaceutic Manufacturing

The methodology & tools developed for quality processing of synthetic molecules cannot be applied biopharma products. There are some fundamental, basic differences between the two paradigms. Instead of a controlled synthetic organic reaction in a chemical reactor, the manufacturing of biologics (monoclonal antibodies, recombinant proteins and DNA, vaccines, etc.) relies on complex cellular biosystems with high sensitivity to their environment and feeding regiment in an aqueous matrix, not simply controlled by well-established principles of organic chemistry.

The production of large molecules by microbes and mammalian cells requires the control of numerous processing parameters which are not present in synthetic molecule manufacturing. All impurities in APIs are critical, but with biological impurities (often proteins, not seen previously), the stakes are potentially higher. Not only are there potential long-term carcinogenicity and mutagenicity dangers, but, with unknown proteins, there are also

potential immediate allergic reactions. For drugs such as insulin, which are used life-long, even the smallest impurity over time can do much harm to the patient.[16]

In the last decade alone, the annual number of approvals of biopharmaceuticals, by the US FDA, have steadily risen. In fact, in 2019, a total of 28 biopharmaceutical products (including monoclonal antibodies, recombinant proteins and gene therapies) were approved in the US. Further, over 8,000 biological pharmaceutical products are currently under clinical investigation, across the world. Given the evident benefits (including high efficacy, target specificity and favourable safety profiles) of biologics over small molecule drugs, the biopharma market is poised to witness continued and consistent growth over the next several years.

However, biologics production is a complex and capital-intensive process fraught with a wide range of challenges. Some of key concerns of contemporary innovators include the rate of attrition of pipeline drugs / therapies, prolonged development timelines, complex molecular structure (which demand niche and specialized expertise), current facility limitations and capacity constraints, and safety and efficacy-related issues.

Already biotherapeutics have reached 50% of total global medicine sales and therefore, it is as important in biosimilar production as in novel biotherapeutics production for develop knowledge & skills need for their high and consistent quality production. This requires the establishment of a biotherapeutics institute in PPP space to develop manufacturing knowledge for the entire industry and encourage more companies to enter the space. This is also important for biosimilar companies producing the “same” active molecule, but from a different synthesis/bio-expression route. While the major active ingredient may be identical to the patented one, any biological process expresses numerous proteins, each particular to the mode of expression and the most problematic feature of any biosimilar will be the exotic side products and potential side effects. Again, excluding copyright infringement possibilities, several Guidance and policies of the USFDA also add to the complexity of making and selling biosimilars.[16] Therefore, our quality programs will need to become many times more stringent and carefully designed.

Bio-manufacturers in China are orienting themselves to be major players in GMP manufacturing. China now has over 50% more facilities than India, and has over 8% of global capacity, although the average facility size is significantly smaller than in India or Western markets.

4.3 Contract Development & Manufacturing Organisations (CDMO)

CDMOs take over parts of the drug product development and manufacturing activities on behalf of sponsoring pharmaceutical companies. The entire value-chain is as follows:

Contract Research	Development	API Production@	Formulation	Packaging
Target identification	Drug development	Extraction	Solids	Injectables
Lead discovery	Sourcing	Synthesis	Semi-solids	Controlled-release
Medicinal chemistry	Cell-line dev.	Fermentation-small molecules	Non-sterile liquids	Others
Pre-clinical (in-vivo & in-vitro)	Scale-up	Fermentation large molecules	Sterile liquids	
Clinical trials Phase I-IV*	Tech. transfer	Other methods	Other finished doses	
Formulation development	Process analytics dev.			

It is our opinion based on global market analysis that CDMO is the dark horse of Indian pharmaceutical industry. With limelight on generics and vaccines, the huge market which will open up for Indian CDMO is not fully appreciated by policy makers. Growth in CDMO, besides bringing much needed revenue has several additional advantages.

1. CDMOs operate at high-end of the global pharma value-chain where profitability is higher than generic exports.
2. These are high technology-oriented operations and can provide many knowledge personnel who can seed other enterprises.
3. India is one of the few countries which top level infrastructure in information technology, the workhorse for modern technology development.
4. Relatively free from competition from countries which only export on price such as Bangladesh.

Therefore, with full support for CDMO sector, it is possible to scale up this business to $80-100 billion within a decade. We will give below the reasoning.

As we have seen in the API production trends, more MNC are shedding captive manufacturing which is 60% of total API production in favour of CMOs and in cases like AstraZeneca, 90% of API outsourcing has gone to CMOs in China. This trend will flow in the biotherapeutics sector too, due to several advantages as outlined by a report from Root Analysis.[18]

Some Chinese CMO companies are already racing towards finding their place in the top 10 bio-manufacturing.

2019 Rank	2023 Rank	Company	Company Type
1	1	F. Hoffmann-La Roche	Product
2	4	Samsung Biologics	CMO
3	2	Lonza Group	CMO
4	3	Boehringer Ingelheim	Hybrid
5	7	Johnson & Johnson	Product
6	9	Amgen	Product
7	6	Sanofi	Product
8	10	Novartis	Hybrid
9	-	Merck KGaA	Hybrid
10	-	Pfizer	Product
-	5	Celltrion	Product
-	8	WuXi Biologics	CMO

Top 10 bio-manufacturing capacities (CPhI Insights 2019)

This is one area where the various stakeholders, such as government, biological companies and their associations must work together and partner with entities in South Korea, Iran, Israel and other countries.

4.3a CDMOs in India

India has already shown that it is the lowest cost producer for generic drugs and vaccines. The journey for global competitiveness in APIs has recently re-started. And hopefully, it will also show good results. We have a very competitive specialty chemicals industry and has skilled manpower & in-depth knowhow. Therefore, these is no reason why contract

manufacturing cannot take a larger share of the world market. The top 10 companies in the CDMO market own less than 30% of the market, with the largest players holding only 2-4% each. CDMO Market is growing at 6.9% per annum and outlook for 2030 is estimated as follows. Different segments are growing at different rates as discussed in following chapters.

CDMO Segment	**Global CDMO Market $ bn.**	**% Share achievable for India by 2030**	**Value $ bn.**
API	130	40	52
Formulation	44	40	18
Packaging	25	10	2.5
Repurposing	30 (Total market)	10	3
CRO	112	10	12
		Total	85

We estimate a CDMO market potential for India at $85 billion by 2030 as a conservative estimate.

According to Mantell Associates, The Indian market is expected to witness the highest growth in the CDMO space, largely due to the low cost of the R&D and manufacturing.

The biggest advantage in outsourcing to India is the cost benefit compared to the United States and Europe; it is estimated that the cost of outsourcing to India will be 37.5% lower than this competition. Another major advantage in outsourcing to India is the world class manufacturing facilities available. Usually, CDMO plants include state-of-the-art equipment from the likes of GE Healthcare and Sartorius Stedim Biotech. Sai Life Sciences, for example, has a 100% successful track record in regulatory inspections both from the FDA and PMDA, and work with 7 of the top 10 pharma companies.

There have been many companies that have enjoyed recent success; Biocon, Sai Life Sciences, GVK Bio and Piramal Pharma Solutions (to name a few) have a fantastic track record in terms of commercial delivery.

Finally, even if you look at profitability, the Indian CDMO's outperformed their counterparts having far higher EBITDA margins from 25-35% compared to 10-20% margins of their European and US competition. My own personal experience aligns with this – from networking day in day out with executive professionals in the CDMO space, a common theme that arises is the topic of outsourcing manufacturing, particularly to India.[19]

6.3b Repurposing Existing Drugs

Drug repurposing (DR) (also known as drug repositioning) is a process of identifying new therapeutic use(s) for old/existing/available drugs. It is an effective strategy in discovering or developing drug molecules with new pharmacological/therapeutic indications. In recent years, many pharmaceutical companies are developing new drugs with the discovery of novel biological targets by applying the drug repositioning strategy in drug discovery and development program. This strategy is highly efficient, time saving, low-cost and minimum risk of failure. It maximizes the therapeutic value of a drug and consequently increases the success rate. USFDA also encourages such application under newly introduced Section 505(b)(2).

Need of the low investment in terms of time and money is fuelling demand for the drug repurposing which is leading to increase number of pipeline products is propelling growth of the drug repurposing market. Additionally, some of the other factors propelling growth of the global drug repurposing market are low research cost and easy bioavailability is propelling its growth from past few years.

Some major successes for repurposing are sildenafil (Viagra), a phosphodiesterase-5 (PDE5) inhibitor initially developed for coronary artery disease (angina) by Pfizer (1985) has been repurposed for the treatment of erectile dysfunction. It potentially reduced the development cost at shorter development time. Metformin (Glucophage), an oral anti-diabetic medication used widely in type 2 diabetes mellitus has been developed as a cancer therapeutic which is currently under phase II/phase III clinical trials.

In recent years, the drug repositioning strategy has gained considerable momentum with about one-third of the new drug approvals correspond to repurposed drugs which currently generate around 25% of the annual revenue for the pharmaceutical industry. It has been accounted that approximately 30% of the US Food and Drug Administration (FDA) approved drugs and biologics (vaccines) are repositioned drugs. According to recent estimates, pharmaceutical industries have significantly placed the market for repurposed drugs at $24.4 billion in 2015 with projected growth up to $31.3 billion in 2020.[20]

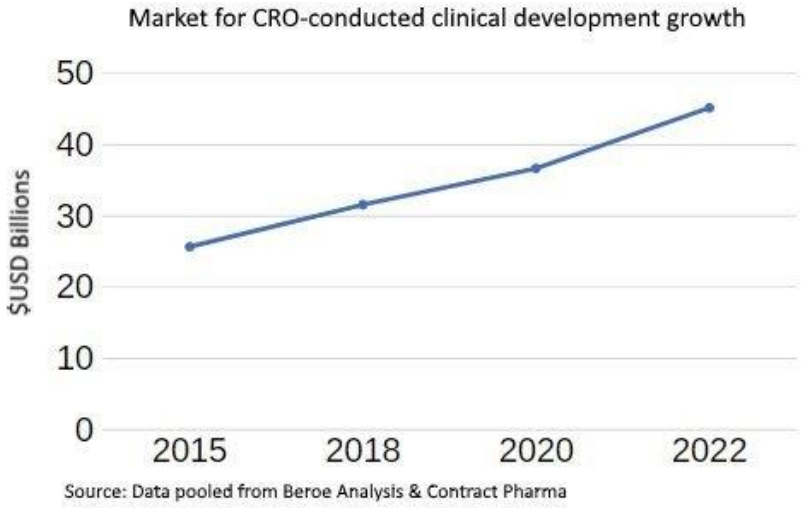
CDMOs are well placed to seize this opportunity and can tie up with innovative drug companies. According to MarketWatch, the global Drug Repurposing market size is projected to reach USD 30 billion by 2026, from USD 25,3 million in 2020, at a CAGR of 2.9% during 2021-2026. Indian companies should attempt to seize at least 10% of this opportunity which will bring in $2-2.5 billion revenue.

6.3c Clinical Research Organisation (CRO)

Typical CRO services include patient and site recruitment, clinical monitoring, analytics, biostatistics, medical writing and regulatory compliance etc.

There are large opportunities for Indian companies in the CRO space. In spite of the promise of this sector, the growth, till now has been disappointing.

As outsourcing rises unsurprisingly so does the demand for contract research organization (CRO)-conducted clinical trials. In 2016, the overall bio/pharmaceutical outsourced development spend was $26 billion and was expected to reach $31 billion in 2019. While the clinical research organization market size (CRO-conducted clinical development) in 2015 was $25.7 billion and is expected to increase to $36.7 billion by 2020,the Beroe Analysis fills some gaps and states $31.6 billion in 2018, and it is expected to grow at a (Compound annual growth rate (CAGR) of 12 % to reach $45.2 billion by 2022 as shown below.



With this growth, we can estimate global CTO market at $39 billion in 2020 rising to $112 billion by 2030. India's CTO market size was estimated to be $1.7 billion in 2017 growing at 8.7% to $2 billion in 2020. Thus, India's share is a low 5% of the global revenue.

India accounts for nearly 16.0% of the population worldwide and nearly 20% of the disease burden across the globe, yet less than around 1.4% of total global clinical trials are conducted in the country. This can be attributed to lack of proper regulations. However, the recent amendments in regulations by the Central Drugs Standard Control Organization (CDSCO), such as reduced approval period and online registry, are anticipated to drive the market growth.

The global CTO market is estimated to rise to India, looking at the major advantages for the country should aim for at least 15% of the revenue by 2030. We have the necessary foundation to scale up the business. Indian industry is growing at 3.3% less than the global growth and with an ambitious growth rate of 15%, India can take a market share of $8 billion by 2030.

There has been a continuous increase in sponsors outsourcing to vendors from 43% in 2016 to 65% in 2018. While the clinical research organization market size (CRO-conducted clinical development) in 2015 was $25.7 billion and is expected to increase $45.2 billion by 2022 at a CAGR of 12%. Therefore, we can estimate the outsourcing market which is showing no signs of slowing down to reach $112 billion by 2030. India should aim to capture at least 10% of this revenue.

No CRO company in India has the resources to become a full-service CRO, at least in the near future due to the investment involved and the global nature of the work. IQVIA, the world's largest CRO has a revenue of over $11 billion with 70,000 employees. However, there are many opportunities in Functional Service Provision (FSP), that is, specialising in one or more CRO functions and therefore, there is more scope for domain specialisation as a competitive advantage rather than just cost saving. This specialisation can range across therapeutic areas such as oncology (No.1 today) to functional areas such as biostatistics, clinical data management etc. This is one area where SMEs can carve out their niche.

According to an Avoca Group survey, 53% of CRO budget of sponsors go the FS and 43% to FSP. Even FS providers say that 57% of their revenue comes from FSP and 43% from full-service.

Artificial Intelligence (AI) and Machine Learning (ML) are emerging areas in the CRO space and Indian companies with their depth of knowledge & skills in I.T., can take a significant share of this sector.

Another significant area is increased demand for and pressure to ensure that each NDA/ANDA successfully passes at first submission.

4.3d New API opportunities in emerging therapies for CDMO

There is an emerging opportunity in providing APIs for emerging therapies through small-volume production. Small-volume continuous (SVC) manufacturing techniques have emerged in recent years to support targeted drug therapies.

One significant change in recent decades is the shift away from blockbuster therapies for a wide patient population toward more targeted precision medicines. The emergence of precision medicine has two important effects that substantially reduce the demand for a given API. First, the patient population is smaller. Second, precision medicines often have a low daily dose since the underlying biological target is clearly identified.[21]

The combination of these factors means that annual API requirements for a precision medicine can be as low as a few hundred kilograms per year. Some CDMOs in India already support global pre-clinical and Phase I studies. These facilities are small & compact, can be easily reconfigured and allows simplified scaleup.

This is another area where more CDMOs can enter and provide APIs in small quantities, a few hundred kilos a year. This is still an area where complete knowledge is not available and the cost of setting up of an experimental facility is beyond the capacity of any single CDMO in India. A body of knowledge is already available for SVC and further R&D within the country through a dedicated institute set up by a consortium of CDMO can further provide research insights. This facility will also create the workforce which can be deployed.

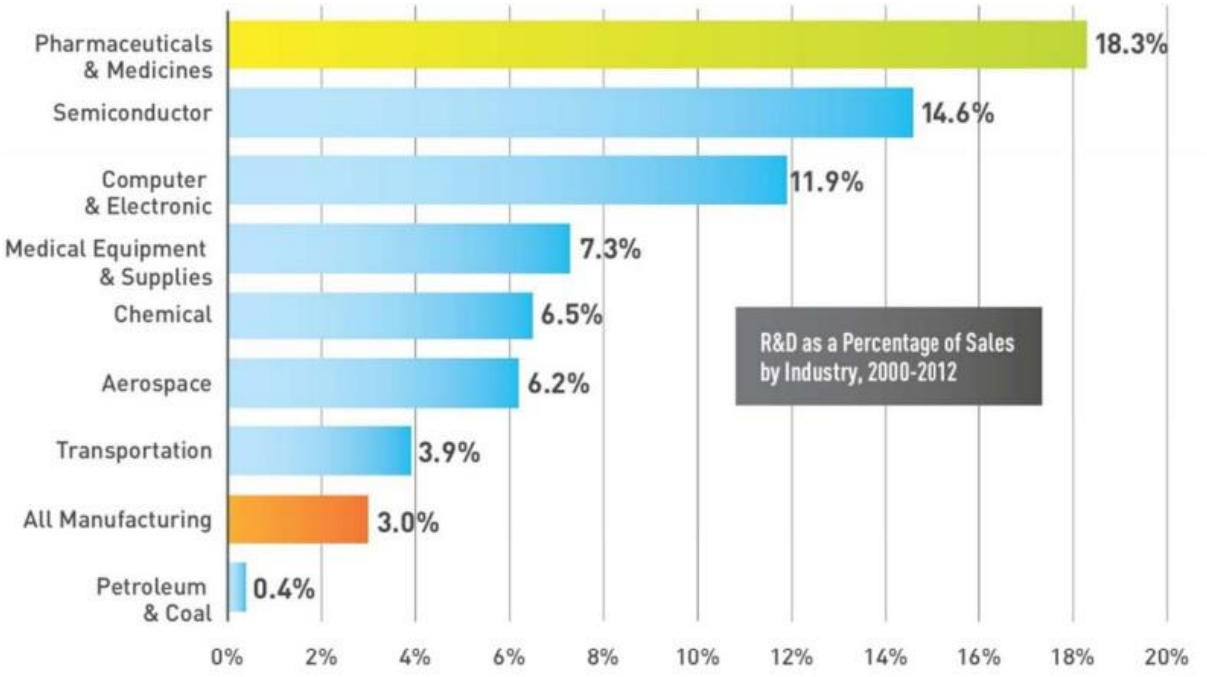
To address some of these issues, the USFDA issued a draft guidance in early 2019 titled Quality Considerations for Continuous Manufacturing. It shows the commitment of FDA to back new manufacturing technologies.

Very few countries beyond the developed ones can move into this area and India, with adequate funding, can take the lead over China.

4.3e Novel Drug Development

Since the development of penicillin to the success of biologics such Humira as well as the new classes of drugs such as statins, cardiovascular disease mortality rates have sharply reduced over the last 50 years. HIV/AIDS, which was once a fatal disease has been turned into a manageable disease with anti-retroviral drugs. into a now manageable (albeit chronic) disease. Drugs, no doubt have played a big role in shaping society and humanity.

In comparison with other industries, drug companies spend more on R&D than their counterparts shown in the following table[21]:

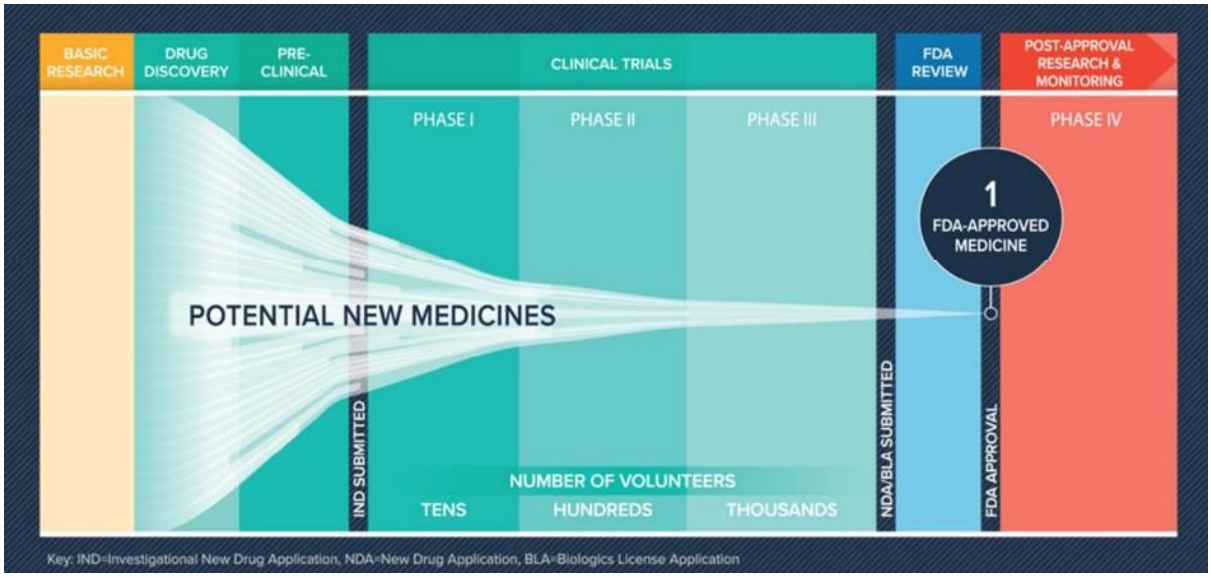


On average, the pharmaceutical industry spends 6 times more on R&D compared to all manufacturing sectors.

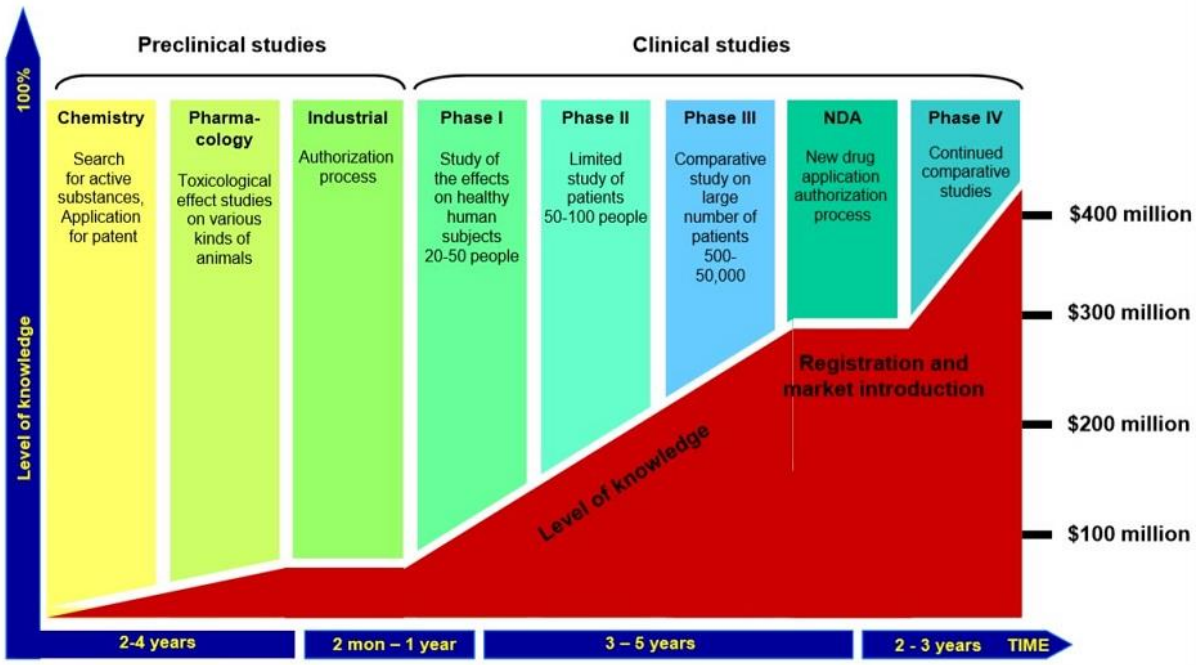
Many Indian companies claimed some years back that the cost of development of a drug in India can bring down the cost by up to 75%. However, in practice this did not happen. For a drug to be brough to market, the development of a drug discovery ecosystem must be in place for results to follow.

This drug discovery research ecosystem involves universities to conduct preliminary research with funding from drug companies, government and NGOs such as Foundations & Trusts. This is followed by outsourcing companies which conduct clinical research work on behalf of drug companies. In addition, there are standalone research organisation which conduct early phase research up to Phase I or II and sell or collaborate with drug companies to take the drug delivery phases to their conclusion. It is estimated that the cost of bringing a drug to market is over $ one billion and only one in a thousand targets reach commercial success. The R&D budget of the larger companies such as Pfizer is larger than the turnover of our largest drug companies.

This is another area where government can play its part to be a catalyst for growth of innovation in New Drugs.



According to CPhI Insights 2019, The USA (8.12) retains its top position in this year's report on innovation. It also boasts the largest growth increase (2.5%) out of all assessed markets, while Japan (7.51) and Germany (7.43) remain in second and third position respectively. 2019 has seen Korea take huge strides forward in innovation, scoring a reputable 6.54 and overtaking Spain (6.13) and India (6.01). Korea's reputation continues reaping the rewards of recent regulatory reforms and a growing biotech market, with an increasing number of companies highlighting Korea as the upcoming region for innovation (experiencing an 8% rise over the last two years). India, surprisingly, has fallen to the bottom of the table with the worst growth rate (-6.3%) of all the countries. However, according to a recent report , the Indian Pharmaceutical Alliance (IPA) is urging the government to set up a fund to provide a 'much-needed boost to innovation in the pharma and biopharma space'. If enacted, this may see an improved reputation for innovation in the next few years.



The above model[22] of R&D costs of bringing a new drug into the market is largely quoted from Tufts Centre Report[23] which was based on the costs provided by US multinationals. It is in the interest of multinationals to keep the illusion of high development costs to keep out new competitors in novel drug discovery and to lobby the government for financial concessions.

There are many critics of this costing and it is suggested that the actual cost would be significantly lower as discussed later in this chapter.

A recent news item has reported that the Government has in recent times has shown the inclination to address this glaring gap by launching a dedicated policy plan to address the R&D deficit in pharma sector. A series of reports last year had suggested that the Department of Pharmaceuticals was planning to create a separate department for R&D and was looking at having a dedicated R&D head in place to push for discovery of commercially viable new molecules. This policy push when comes to fruition will help channelize the scattered innovation efforts and give them better direction.

However, looking at the resource crunch which the government is passing through, due to Covid and other factors, it is unlikely that any major thrust is forthcoming in the immediate future.

More that setting up a separate department, more important is to facilitate the establishment of common R&D Centre through the Common Facilities Centre (CFC) scheme on PPP model. R&D CFC has not been a great success in any industry and the government should consult the industry and make the process easy to implement as well as fund it adequately. Such an independent institution can create collaboration with major universities and non-profit institutions abroad where a large part of R&D is carried out.

The government already provides tax benefits to build research infrastructure but that by itself is not adequate. The government can certainly do more in tax benefits, but it is also necessary to ensure that the money is being spent on exclusive R&D infrastructure. It is a

common practice to show Quality Control laboratories as R&D facility since most equipment largely have dual use and this provide an exaggerated state of R&D activity in the industry. For example, High Performance Liquid chromatograph is used in both research & quality control laboratories.

Therefore, without disturbing the tax benefits, we recommend that incentive should also include tax deduction for obtaining Indian, US and European patents. In China, corporate income tax can be cut from 25% to 15% for firms that file many patents. Considering that till 1985, China did not have a patent protection law to rise to world's top patent filer in 2018, its patent incentive system has played an important role.

Further, there should be incentive for first to file ANDA for synthetic & biosimilar drugs. Similarly, there can be an incentive to replace an imported API with Indian developed and manufactured API.

However, one thing is clear, without innovation, we cannot progress a great deal only on the foundation of an industry whose success is based on reverse engineering. Copying has done its bit to create a solid foundation for a profitable industry to develop. For the next stage of development, Indian industry must invest in innovation through research which should be supported by the government, not only through incentives but to build universities' research capabilities so that they can partner the industry and deepen the innovation well.

Indian space program is a sterling example of investment & consequent results in R&D. Indian government has made thousands of crores of investment in Indian Space Research Organisation (ISRO). In 2021-22 itself, the budgetary provision was over Rs.14000 crores. The results of our satellite programs is visible to all. 10% of this investment in the Indian pharmaceutical research for five years can bring equally impressive results.

This innovation ecosystem can also be built by supporting the CMO & CDMO industry to flourish in India. The spinoff in developing talent and bringing new knowledge is incalculable.

4.3f Outsourcing of Packaging

Due to an increase in biologic-based drug development and complexity of APIs, injectable delivery is becoming a preferred option. As a response to these emerging trends, CDMOs/CMO are investing in manufacturing expansions and acquiring advanced technology. Indian CDMOs are well-placed to take advantage of this market as they are also increasingly moving into aseptic injectable drugs API. It can be a forward integration or a standalone activity.

In 2019, as many as 38 (out of a total 105) injectable drugs were approved in 2019 in the US compared to 50 oral products and 15 products using other delivery methods. In EU and Japan too, similar trends were noticed.

4.3g India-Only Talent Surplus Country by 2030

According to an article from The Association of Clinical Research Professionals "The demand for clinical trials is growing as the pool of clinical research associates (CRAs) and other professionals is shrinking. It's a stubborn problem threatening the very quality of trials

and undermining the opportunity to bring more innovative drugs and devices to vulnerable patients".[24]

Any worthwhile expansion in this sector would open a vast revenue source for hospitals and CROs as well as produce an ever-expanding pool of skilled talent. This is a manpower intensive industry and by 2030, India will be the only talent surplus nation in the world. Therefore, there is need for easier and faster regulatory mechanism as well as a larger number of institutions for the induction of freshers in the sector.

According to another article, clinical research industry is faced with a talent access problem when more than 70% of life sciences CEOs say they are worried about key skill shortages, and more than two-thirds report difficulty recruiting talent with the skills they need, all of which contribute to organizational risk. Not only is there a shortage of seasoned clinical research individuals but also the realization that existing talent sometimes lack the needed experience and skillset required to maintain the necessary quality and compliance standards.[25]

Some courses ranging from certificate to post-graduation are being offered by private institutions. Since, the Indian clinical trials industry is very small, the government should facilitate Indian linkages with top Clinical research institutions in US and the EU for enabling students to work abroad and gain worthwhile experience and insights.

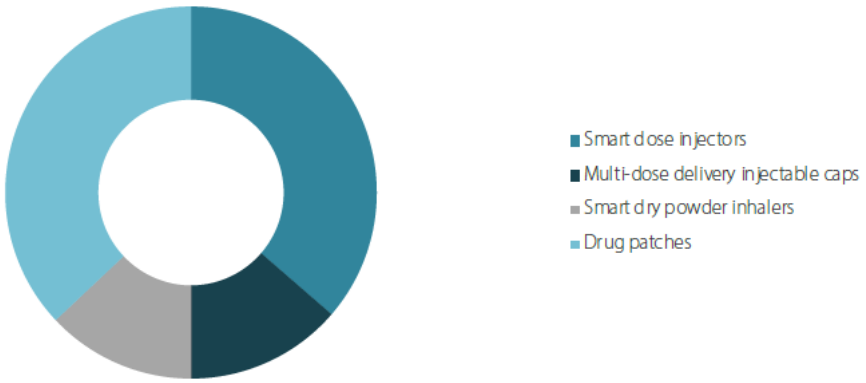
Clinical Trials is only one of a score of segments which support drug research and the overall availability of talent throughout the value-chain will be severely constrained in years to come. Indian talent can work in various functions throughout the world, just as in Information technology and bring rich knowledge and experience to seed the Indian industry.

Again, quoting CPhI Insights, The United States maintains its position as the world's preeminent drug delivery economy, with a score of 8.2. In the last year, it opened up a substantial lead over Germany and Japan – 2018's second and third placed economies – as both saw a year-on-year score decrease of around 5%. The positions of the United Kingdom and France have remained largely unchanged. However, the most significant result is Switzerland. The biggest year-on-year increase of around 6% has seen Switzerland move ahead of Germany and Japan to claim second place with a score of 7.7. As a result, we now see a four-strong, tier one market. The United Kingdom and France make up tier two, and Italy, Spain, and Korea a third tier amongst the most innovative nations.

India and China remain at the bottom, but the real insight is in how they have again made substantial gains. Respective scores are up by a remarkable 25% and an even more astounding 43%. Maintaining these rates of improvement could see both countries achieving parity with tier 3 markets in the next year.

This would represent a key milestone for the global industry and signal that these two vast nations are now entering a mature stage. Executives are increasingly regarding India and China as equals of many western markets. This could well signal competitive challenges ahead as the emerging nations compete on quality as well as cost.

Take the case of drug delivery device segment. The most promising recent drug delivery devices: 37% of our experts believe that drug patches are the most promising drug delivery device, which is closely followed by smart dose injectors, taking 36% of the votes. Multi-dose delivery injectable caps and smart dry powder inhalers receive 14% and 13% of the votes, respectively.



Since the number of new drugs from synthetic sources are decreasing, the emphasis is now on drug delivery to maintain competitive lead. In this regard the R&D conducted by Cipla is commendable as it has taken lead in inhalers for generics and for this reason, will derive the most benefit among Indian companies in the crowded Chinese market and elsewhere.

4.3h Cutting drug development costs

As earlier noted, a 2014 study by Tufts Center for the Study of Drug Development (CSDD) provided an estimate of the cost of developing and gaining marketing approval for a new prescription drug. It came to a figure of $2.9 billion for life cycle cost of a novel drug from laboratory to market.

This cost was taken as a benchmark and often quoted by multinational corporations to justify high prices. Now a new study has challenged the Tufts conclusion.

The new study was conducted by the non-profit Institute for Safe Medication Practices (ISMP). The team took data from 101 new drugs approved from 2015 to 2017 into a licensed clinical trial cost estimator created by IQVIA. For the 225 individual trials reviewed, the study concluded the median cost of each was $19 million, with an interquartile range (IQR) of $12 million to $33 million. The estimated median cost for a pivotal clinical trial came out

to $48 million, with an IQR of $20 million to $102 million. In the 2014 Tufts study, researchers estimated the average cost of a Phase III trial to be $255 million.

The ISMP study concludes by stating, "Overall, the estimated costs are modest for establishing the benefits that will guide the treatment of thousands to millions of future patients." Even if there are drawbacks in the study, as it does not take into account the cost of dropped candidates at every stage of the drug development, it shows that the cost of clinical trials is certainly lower than earlier estimates.[26]

Some Indian companies have been advocating the low-cost drug development in India to rope in more contract research and it should be possible to again redo the arithmetic to bring several elements of the entire value-chain of novel drug discovery to India.

4.3i Information Technology to Cut Drug Discovery & Development Costs

Another major development which will aid the lower cost of novel drugs is the deployment of information technology tools such as Big Data, Artificial Intelligence and Machine Learning. Indian I.T. landscape is much more developed than many countries.

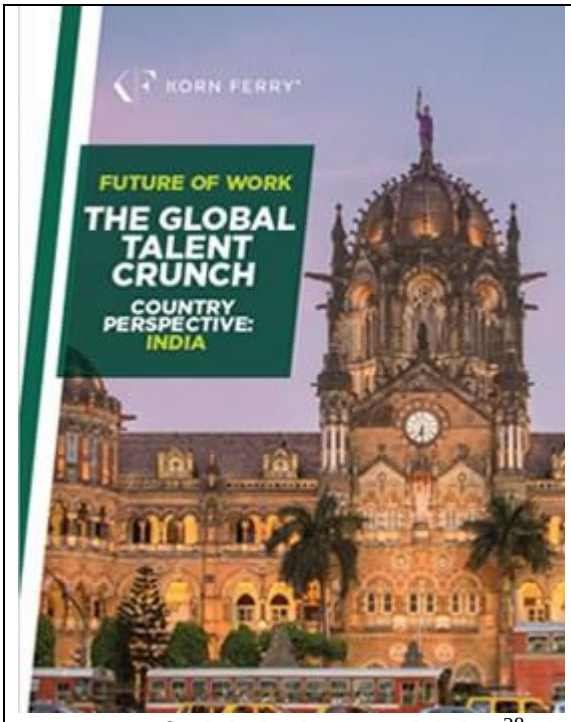
Once the lead compound has been identified via drug discovery, the process of bringing it to the market starts – this is drug development. The process from finding the lead compound to getting it to the market is expensive, both in time and costs with an approval rate of less than 12%.

In the past few years, AI supported by Big Data and Analytics, has made it possible for the use of automated algorithms to carry out tasks in drug discovery and development that once depended on scientists. Internet of Things (IoT) collects data at every stage of the drug development process. Medical researchers get actionable insights from stacks of unstructured data in good time. This makes drug discovery and development faster and accurate. For example, digital animal simulations bypass the need to test drugs on animals. To maximize the wealth of potential in AI, Big Pharma is going into partnerships with AI start-ups to help it make sense of the many data it is generating.

India has the third-largest ecosystem – India, in terms of number of technologies startups including hundreds in Big Data Analytics, AI and Machine Learning. However, according to the global innovation mapping and research company StartupBlink, which gathers local data of every country to rank their startup ecosystem based on the quality of startups, business environment coupled with the quantity, India has moved down from 17th position in 2019 to 23rd in 2020 out of 100 countries, below Estonia and Brazil. Its shows the poor infrastructural support including low internet speeds available to startups.[27]

If we can mobilise this talent and IT systems and combine this resource to pre-clinical and CRO industry, we can create a powerful CDMO industry which can match the strength in China and other countries. It requires setting up of an Indian Institute of Pharmaceutical Information Technology at Hyderabad under PPP mode which can capture the IT talent from Bangalore and pharmaceutical talent at Hyderabad and bring the two together. Along with, it can also conduct projects with multinationals such as IBM and Oracle which are active in pharmaceutical sector.

Cost is not the only factor for the CDMO shift. Availability of talent can play a more important role in persuading the drug companies to shift their CDMO activities to India. By 2030, India will be the only talent surplus country in the world, not even China.



A survey of Global talent availability[28] showed that the country may have a labour surplus, but it also has a lack of employable talent. The IT sector has been grappling with the lack of the desired level of those skills for years.

If India can align its education system to global requirements, it can reap big dividends

According to a study by Korn Ferry an internationally acknowledged staffing firm, in 12 years, demand for skilled talent will surpass supply with a global talent shortage of more than 85 million workers. This deficit is mainly due to the imbalance between technological advances and the talent needed to leverage those advances.

Developed economies will be hardest hit by the imminent talent shortage. Australia, France, Germany, Japan and the United States face the largest threat, losing $1.876 trillion in annual revenues by 2020.

India, the world's sixth largest economy is the only one in the study which will have a talent surplus by 2030, with 245 million more workers in the next 12 years.

The surplus of extra manpower is driven by a growing, younger working population with the country's median age expected to be just 31 years by 2030. This is a huge supply of talent compared to the aging population in China, Japan or the US.

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The present National Institute of Pharmaceutical Education and Research (NIPER) is situated in Punjab, neither close to the Pharmaceutical nor I.T. hubs and play a limited role in this area. However, a synergy can be built into the institute by widening its scope beyond pharmaceutical manufacturing.

Drug discovery services market is projected to witness strong growth prospects in the global market, reaching an estimation of US$ 16 billion revenue by 2026 end, according to a new study by Fact.MR. A few of the key influencing factors include:

- Increase in demand for outsourcing of clinical trial services & analytical testing.
- Inclination of key pharmaceutical companies toward outsourcing to avert hurdles.

- Rise in R&D expenditure.

According to Fact.MR, oncology therapeutic area is poised to come out as the biggest segment during the assessment period. By 2026 end, oncology is projected to surpass US$6.9 billion Mn revenue. The growth can be mainly attributed to growing number of patients suffering from cancer is ensuing in the higher demand for cancer therapies.

As per the report, medicinal chemistry is estimated to come out as the biggest type in the global drug discovery services market. The segment is estimated to attain around US$ 6,100 million in revenue terms by 2026 end. The large share of this segment is attributed to aspects such as the extensive application in several phases of preclinical drug discovery to offer robust candidates. Additionally, the widespread use of medicinal chemistry in academics, large pharmaceutical companies, and biotechnology companies are further supporting growth in the market. Several drug discovery services providers situated in Asia are enhancing their footprints in Europe and North America.

As per the research, Asia Pacific Excluding Japan (APEJ) is also projected to foresee notable growth amid 2017-2026. China and India are gradually becoming favoured locations for drug discovery outsourcing owing to the technological competences developed. Low manufacturing costs and fewer regulations are further impelling the growth in the region.[29]

4.3j Cooperative efforts with other countries

It is difficult to match the funding and risk appetite of drug MNC and one way out is to cooperate with other nations which have a similar aim of biotherapeutic development independent of MNCs. India has deep strengths in biotherapeutics, especially vaccines. India is going ahead with efficacy trials of 30 different vaccines for Coronavirus, which are at different stages of development. It also has strength in information technology which can be deployed in conjunction with other like-minded countries.

Patents continue to be the major bar to biosimilar market entry, particularly in the U.S., which is by far the largest single potential market for biosimilars. In fact, the majority of FDA-approved biosimilar products remain off the U.S. market. Their launch is delayed until after expiration of reference product company patents, increasingly after market entry dates are negotiated by biosimilar developers with patent holders (reference product manufacturers). Patents continue to fully determine U.S. marketability, with the 12-year exclusivity protection from biosimilar approvals, seven-year orphan, and other government-granted exclusivities granted to reference products having essentially no impact on U.S. market entry of biosimilars and other biopharmaceutical products. Patents generally protect U.S. reference products for >15 years, and this is increasing as even broader patent “thickets” are built around reference products, proving difficult for biosimilar developers to avoid.

To break the monopoly of Multinationals in thwarting the entry of biogenerics in their home countries, it is necessary to form a cooperative association of India and other like-minded countries which have a similar unstated aim of introducing biogenerics in their countries and in rest of the world.

There are several countries which are developing biotherapeutics such as bio-generics as well a novel entity such as South Korea, Taiwan, Iran, Jordan, Singapore, Brazil, Mexico, Israel, Russia, Argentina & Cuba. Since it is not possible to cooperate with China in any

meaningful way, such a cooperation in a body such as BRICS where China is a member is not possible, at least in the foreseeable future.

According to a new report, Biopharmaceutical products are being developed by an ever-increasing cross section of the pharmaceutical industry, including Big Pharma, generic drug, and foreign companies, with many of these new entrants entering the field by developing biosimilars. These newer types of entrants, along with smaller biotech business model-type biopharmaceutical developers are continuing to expand the global biologics pipeline and are bringing new facilities online.

This includes new entrants based in China, India and other developing countries increasingly entering biopharmaceutical R&D and manufacturing. For example, we are starting to see large commercial manufacturing facilities, with ≥50-100,000 L capacity, being constructed in China, where capacity is increasingly needed to satisfy domestic biopharmaceutical markets.

An increasing number and percentage of new pharmaceuticals entering the market will be biopharmaceuticals vs. small molecule drugs; and these will originate from more diverse sources. Combine this with biopharmaceuticals (vs. drugs) generally costing more and providing higher profit margins, and the pharmaceutical industry will increasingly be dependent on biopharmaceuticals for profits, innovation, and its basic survival.[30]

Even TIFAC has advocated a cooperative approach in its white paper "India also has the potential to become a net exporter of biosimilars of Insulin, Interferons, mAbs (Monoclonal Antibodies) , Enbrel, Humira, Rituxan, etc. The existing Indian manufacturers should be facilitated to increase their capacity and develop new products in association with Indian Institutions and R&D Centres. Even FDI may be invited from South Korea, Japan and Europe. India can be a big playing field for Clinical studies in the process of drug validation, trials and equivalence studies. India, with its large population and well-developed regulatory environment and infrastructure can provide an attractive destination for conducting clinical trials for such countries.[31]

As an example, we can view the development taking place in South Korea which is discussed earlier in this chapter.

4.4 Plant-based health products

This sector present high-growth, high-value opportunity for India, both in the domestic as well as export markets. Due to hectic schedules and changing lifestyle patterns, there is a steady increase in the incidence of lifestyle diseases such as diabetes, obesity, and high blood pressure. Thus, consumers are taking preventive measures for reducing the effects of lifestyle diseases. The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care.

Various plants have shown a wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects. In traditional systems of Unani, Ayurveda and Siddha, almost 90% of prescriptions are based on drugs obtained from plants. Drugs from the plant sources are easily available, are less expensive, safe, and efficient and rarely

have side effects.

Owing to the inherent disease preventing properties such as slowing down digestion and absorption of carbohydrates, botanical supplements are a healthy alternative to prevent and reduce the effects of lifestyle diseases and this is supplementing revenue growth of the global botanical supplements market.

The coronavirus pandemic has reminded the world of the importance of good health and strong and resilient immune systems. While effective and curative medicines are indispensable in fighting such aggressive viruses, our best defence lies within our bodies. The World Economic Forum, too, has highlighted the importance of a strong immune system in fighting the virus and has recommended sleeping well, eating a balanced diet, moderately exercising regularly and reducing stress to lead a healthy lifestyle. Ayurveda has all the ingredients for living a healthy balanced life.

Since Covid19, The Indian market is looking up. Previously, Ayurveda-based products in the Indian market were restricted to hair oils, the local dietary supplement called the chyawanprash, and over-the-counter palliatives. Now, natural Ayurvedic ingredients are increasingly being integrated into a growing number of products, ranging from shampoos, skincare creams, oils, powders, toothpaste gels and soaps to cough syrups, teas, packaged juices and nutritional supplements, among other fast-moving consumer goods.

A survey by market research firm Nielsen found that the natural segment accounts for 41% of the total of Rs 44,790 crore personal care market share. Many MNCs, which were the leaders in the toothpaste category, lost their shine when home-grown Ayurveda companies found favour with consumers, forcing some companies to come out with herbal variants.[32]

Not only in India, but there is also renewed interest in most advanced countries to look at alternative medicines (a term for a variety of non-allopathic health sources). Traditional Chinese Medicine (TCM) has a world market of $10 billion while Ayurveda market is a tenth of this. India is sitting on a gold mine of well-recorded and traditionally well-practised knowledge of herbal medicine, and we have scratched only a small surface of its potential. To give an example, the market for Ashwagandha which was barley known in the US a few years ago grew at 90% in 2019 compared to previous year.

What is missing in gaining a larger market share is the lack of rigorous scientific validity for these products which lead to higher growth. India has not been able to capitalize on this herbal wealth by promoting its use in the developed world, despite their renewed interest in herbal medicines. This can be achieved by judicious product identification based on diseases prevalent in the developed world and provide clinical validation. Such herbal medicines will find speedy access into those countries.

An herb like Psyllium (Isabgol) where India has a near monopoly and which is its largest exported herb. It has many uses in digestive system, cholesterol control and weight loss. Internal Bowel Syndrome (IBS) is a very common disorder and scientific tests show that about 10% to 15% of people in the United States have it which comes to 32 million. A 2008 report by Achievers' Resources on behalf of the Gujarat government — the state is one of the largest cultivators of psyllium — shows that during 1996-2001, about 33 US patents were granted on various uses of psyllium husk, with US companies cornering 24 of them. Apart from the food innovations, patents were granted on the use of the husk in drug compositions

to reduce cholesterol, improve bowel movements and palatability, treat constipation and as a dietary supplement. Some scientists call it the hidden superfood.[33]

Out of 848 patents registered in the US Patents Registry USPTO during the last two decades, only four out of these are from India.

With clinical research and obtaining of international patents, we can rapidly increase the value-addition of herbs. Today, 60-70 of our exports consist of low-value dried herbs and crude extracts.

Example- India is the largest producer and exporter of turmeric. Indian turmeric has the highest concentration of its principal chemical curcumin. Its health benefits are immense. However, we need evidence-based studies to link turmeric to its benefits.

Turmgel lozenges - Turmeric's biggest challenge has always been its low bioavailability (meaning the degree of its absorption into the body's circulation system so as to have an active effect). Turmgel lozenges was formulated to be sucked on slowly, and not chewed or swallowed. It was developed using globally patented Quicksorb Hydrogel Technology that allows the bioactive turmeric extract in the lozenge to dissolve in the mouth and get instantly – and directly – absorbed into the bloodstream. This Indian SME has patented its technology in many countries and has launched the product in select international markets. According to the manufacturer's website, "Turmgel is the world's first and only supra-bioavailable mouth-dissolving turmeric lozenge that delivers 100% of turmeric benefits directly into the bloodstream – safely, and side effect-free".[34]

According to the National Center for Complementary and Integrative Health (NCCIH), over 30% of adult Americans prefer complementary and alternative medicines such as:

1. Medicinal Botanicals / Dietary Supplements -the whole plant or plant-part extracts used for maintenance of health by affecting a body structure and its function

2. Nutraceuticals-the food containing supplements from natural (botanical) sources, that deliver a specific health benefit, including prevention and treatment of disease

Such products are also known as food supplements, health supplements, dietary supplements and nutritional supplements. We will use all these terms interchangeably.

3. The cosmeceuticals-the cosmetic product that contains biologically active ingredients having an impact on the user.

The growing geriatric population and its increased awareness of nutritional values and preventive healthcare has further augmented the global herbal supplements market. It is expected to reach USD 8.5 billion (Bn) by 2025 and expand at a Compound Annual Growth Rate (CAGR) of 6.2 per cent.

Although there are no significant data on the effects of nutritional supplements—herbal or non-herbal—against the coronavirus that causes Covid-19, we know that at the minimum, these supplements increase overall immunity and provide much needed nutrition. Even as researchers closely evaluate the evidence of nutritional based interventions, with special

emphasis on respiratory infections, available evidence suggests that Ayurveda and Ayurvedic herbs are powerful in building immunity, strengthening, and repairing our body.

Factors such as mounting health concerns over the side-effects of modern medicine are also driving consumer adoption of Ayurvedic and natural products. These include personal care and health care which incorporate Ayurvedic nutraceuticals, Ayurvedic medicines and dietary supplements. Ayurvedic medicines developed as nutraceuticals provide the immunity and build body defences to live a healthy life.

Over the years, scientists have integrated essential Ayurvedic herbs like turmeric, emblic, ginger, garlic, curcuma, cumin, and Indian basil and other traditionally important dietary components within nutraceuticals, food supplements and functional foods to fulfil individual dietary needs. These products have natural bio-active compounds considered beneficial in preventing diseases. The consumer trends and preferences, traditional foods with health benefits are being packaged and promoted in smart and innovative ways to meet consumer demands that are increasingly moving from traditional diets to more sophisticated and healthy food types. Several such Ayurveda-influenced products include ready-to-drink juices, capsules and nutrition powders are gradually moving toward mainstream food and beverages segment.

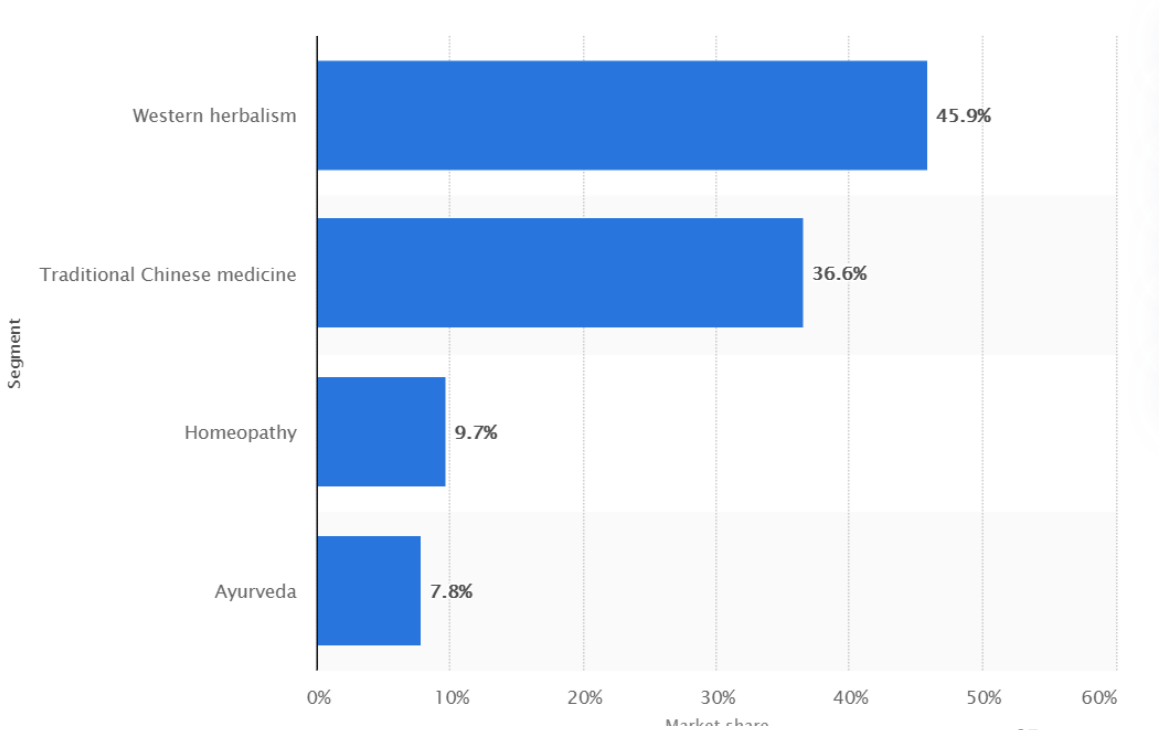
The global botanical supplements market is estimated to be valued at more than US$ 40 Bn in the year 2017. By 2025 end, the global botanical supplements market is expected to reach a market valuation more than US$ 65 Bn, by 2025, registering a CAGR of 6.9%. [35]

The Drugs segment is estimated to account for a value share of 47.0% and be valued at nearly US$ 19 Bn by the end of 2017. The Cosmetics segment is projected to witness a relatively high growth rate, registering a CAGR of 7.2% in terms of value and is expected to gain 46 BPS in 2025 over 2017.

Botanical supplements are preferred by the ageing population, thereby driving botanical supplements market growth. In 2014, according to a population survey in the U.S., about 65.2 million people have reached 65 years of age and are inclined towards using personal healthcare products. This offers lucrative opportunities to botanical supplements manufacturers to offer botanical extract-based products in the personal healthcare segment.

By another analysis, Herbal Medicine Market Value to Surpass USD 129 Billion Revenue Mark by 2023 at 5.88% CAGR. Herbal medicine comprises products derived from plants and consumed directly with little processing. The lack of extensive processing is probably the major difference between herbal medicine and conventional medicine, as the field of herbal medicine seeks to preserve the natural composition of the plant, while conventional medicine devotes considerable efforts to isolate the active ingredient and produce it on a large scale into medicinal products. This field of medicine has been the oldest field of medicine in human history, as all medicine originally started with the use of plant materials for remedial action against various natural ailments. The field has experienced a resurgence in recent years due to the growing demand among consumers for naturally oriented, process-free, chemical-free medicine. Preference for personal medication could also drive the global herbal medicine market at a strong rate over the forecast period.

Global Ayurvedic Market was value US$ 4.5Bn in 2017 and is expected to reach US$ 14.9Bn by 2026 at a CAGR of 16.14%. A 10% share for India would add at least $1.5 billion to exports, doubling the present export value. With targeted marketing and producing value-added products, we can increase the share to at least 25% by 2030, that is, $6-7 billion.



Distribution of the global herbal medicine market as of 2017, by segment[37]

Lack of stringent norms and regulations pertaining to the safety and efficacy of botanical health supplement products is a factor expected to affect the growth of this market globally. Owing to less emphasis on labelling and safety of these products, incidences of false health claims by manufacturers to market their products has increased significantly.

These factors have impacted consumer outlook towards botanical supplements, and this is expected to adversely affect the growth of the botanical supplements market to a certain extent. In December 2016, Patanjali Ayurved was fined US$ 18,000 for misleading product advertisements.[38]

4.4a Phytochemicals

Phytochemicals are natural chemical compounds, which are found in foods derived from plants. In these, phytochemical substances act as systems of natural defenses for their plants, protecting them from infections and microbial invasions as well as giving them color, aroma and flavour. The main sources of these compounds, over 2,000 identified, in foods are fruits, vegetables, legumes, whole grains, nuts, seeds, mushrooms, herbs and spices.

Plants may be regarded as vast libraries of organic compounds which have considerable medicinal value. There is an increasing demand for plant drugs throughout the world. They are widely used in human therapy, veterinary, agriculture, scientific research and countless other areas. If systematically developed and promoted, India can earn up to $10 billion for plant-based health products within a decade.

We ready possess an anecdotal knowledge resource of medicinal properties of plants which has been built up over hundreds, even thousands of years. Even nomadic hunter-gatherers had knowledge of medicinal plants. Screening & investigation of chemicals present in these plants can lead to discover of new and safe drugs.

Many compound families of phytochemicals like carotenoids, tocopherols, glucosinolates and phenolic compounds can be obtained through plant by-products coming from agroindustries and since these are high-value products, their wide exploitation would be a boon to the entire economy from farmers to entrepreneurs. We are giving some examples of plants where India is one of the top producing countries in the world.

Example – Develop world class cannabis derivatives industry

In a historic vote, supported by India, The UN Commission on Narcotic Drug, removed cannabis and cannabis resin from Schedule IV of the 1961 Single Convention on Narcotic Drugs, where it was listed alongside deadly, addictive opioids, including heroin.

In Ayurveda, cannabis, known as bhanga (Indian hemp) in Sanskrit has been long acclaimed for its therapeutic properties. Several startups have sprung up in India which are conducting research on medical cannabis as well as producing consumer products such as shower gels, soap bars, balms and lotions which are made from hemp seed oil. Research and commercial cultivation policies in already in place in Uttarakhand and UP.

A stigma has developed around the use of hemp as it is confused with marijuana (charas), both belonging to the cannabis family. Cannabis contains two psychoactive compounds tetrahydrocannabinol (THC) and cannabidiol (CBD). High percentage of THC in marijuana is responsible for its use in getting high. Legal hemp must contain 0.3% THC or less which is not adequate to get high. CBD is the cannabis derivative which is therapeutically important, and it is sold in the form of gels, gummies, oils, supplements, extracts, and more. In fact, hemp seeds are known to be a super-food that can boost our immunity.

CBD: A multipurpose therapeutic drug

According to a report by the market research firm Research and Data, the Cannabidiol market is projected to grow at a rate of 21.8% in terms of value, from US$ 5.49 billion in 2019 to reach US$ 26.25 billion by 2027. The market is primarily driven by the increase in the usage of CBD in medical applications, supplements, beverages and skincare. No doubt, immunity boosting products are witnessing a high growth due to COVID-19.[39]

As a pharmaceutical therapy with multiple applications, the cannabidiol marketplace is likely to witness significant R&D investment in the pharmaceutical industry. For its potential in the treatment of a number of diseases, multiple scientific studies have shown promising results of cannabidiol. The first cannabidiol drug Epidiolex[40] has been approved by US Federal Drug Agency, which has validated some of the cannabidiol's therapeutic benefits. It is also expected that the US Drug Enforcement Administration (DEA) will reschedule and change the cannabidiol compound classification in the near future.

In 2019, for the first time, CBD became one of the 40 top-selling ingredients in US mainstream retail outlets. In this channel, CBD sales totalled US$ 36 million, making it the 9th largest selling supplement ingredient. Sales of CBD increased by a remarkable 872.3% from 2018 to 2019 — the largest increase of any other top 40 ingredient in the mainstream channel after a 303% increase in sales from the previous year.[41]

CBD products have been promoted for a wide range of health issues, such as anxiety, insomnia, drug addiction, and acne, among many others. It is estimated that 64 million US adults had tried CBD in the previous two years. Among those surveyed, the most common reason for taking CBD was to relax and reduce stress/anxiety, and 64% rated CBD as "extremely or very effective" in doing so.

Cannabis oils exported by all countries totalled US$ 2.9 billion in 2019, according to World's Top Exports. This reflects a 23.3% increase for all cannabis oil exporters starting in 2015. India was the second largest exporter with US$ 320.8 million (11.1% share) in revenue, after China which exported US$ 964 million (33.4% share) in 2019. Although our growth of 12.8% is satisfactory, some smaller countries' export growth is many times higher. Examples include Vietnam (up 529.5%), Madagascar (up 232.2%), Morocco (up 218.1%) and Netherlands (up 124.5%).[42]

There is a large market potential for Indian to export CBD. If India has to compete with China as well as other rising countries, it must increase its production manifold. In addition, it must have a simpler regulation for the domestic market to grow. With growth in domestic market, India's value-added products can also find export markets.

The government should provide the right direction, policy & regulatory framework for the medicinal cannabis industry to flourish. The excessive regulatory stranglehold on the opium industry has steadily reduced the number of licensed cultivators which has considerably reduced our exports. For a high of 98 tonnes in 2016 (HS Code 130211), our exports have come down to 48 tonnes in 2018 and 14 tonnes in 2019 as per ITC Trade Map data. If one adds all the cost associated with production of opium derivatives such as monitoring and security, it is an essential but no longer a profitable crop for the farmers or the government. CBD is not a psychoactive compound and the government should come up with promotional policies which will make India the top producer and exporter.

The shortly expected hemp regulations from The Food Safety and Security Authority of India (FSSAI), a draft of which was circulated in 2020, will be crucial for the growth local hemp and cannabis sector, unlocking its potential for use in the food and beverage products and boost value-added exports.

Carom seeds (ajwain)

Trachyspermum ammi (Bishop's weed, carom seed, ajowan or ajwain) is a herb used as a spice in the Indian kitchen. This herb has many active compounds with pharmacological effects such as alkaloids, steroids, glycosides, tannins, saponin and flavonoids, thymene, amino acids, dietary fiber as well as essential oils like thymol, c-terpinene, p-cymene. It possesses various pharmacological properties such as antidiarrheal, antifungal antibacterial, antiviral, antispasmodic, antihypertensive and broncho-dilating, abortifacient, galactogogic, antioxidant, antiulcer, anti-aflatoxigenic, antifilarial, hepatoprotective and antihyperlipidemic effect. This has digestive stimulant actions. The seeds are highly useful in peptic ulcers. This also shows signs of blood pressure lowering potential. India is the third largest producer in the world.[43]

Cumin phytochemicals
India is one of the largest producers of cumin in the world. Cuminum cyminum contained: alkaloid , coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid. Pharmacological studies have shown that Cuminum cyminum has antimicrobial, insecticidal, anti-inflammatory, analgesic, antioxidant, anticancer, antidiabetic, antiplatelet aggregation, hypotensive, broncho dilatory, immunological, contraceptive, anti-amyloidogenic, anti-osteoporotic, aldose reductase , alpha-glucosidase and tyrosinase inhibitory effects properties.

White sesame seeds
India, Sudan and Myanmar are the leading producers, and it has one of the highest oil content.
Sesame seeds contain many phytochemically important chemicals like flavonoids, phenolic acids, alkaloids, tannins, saponins, steroids, terpenoids and various minerals. These compounds provide its medical properties such as antioxidant, antibacterial, cardio tonic, antidiabetic, hypo-cholesterolemic, antitumor, antiulcer, anti-inflammatory and
Analgesic.

We are only exporting low-value raw seeds & herbs or extraction with primary distillation. These are processed abroad which gives these companies much higher value addition. Even a product like isabgol (psyllium husk) which is monopoly product from India, there is hardly any research on its possible new medical properties. The government should encourage establishment of integrated contract farming to phytochemicals clusters. Intensive research can increase the yield and provide sustainable quality raw materials from which to isolate phytochemicals.

The time is approaching when, in the absence of clear scientific studies including clinical trials, we cannot market these products in major markets such as The European Union and thus lose the emerging opportunities.

In addition, the country should also use sustainable green technologies for the extraction of phytochemicals such as Ultrasound-assisted extraction (UAE), Microwave-assisted extraction (MAE), Enzymatic-assisted extraction (EAE), Supercritical fluid extraction (SFE) and Pressurized liquid extraction (PLE). Continuous R&D is required for technology application and upgradation. [44]

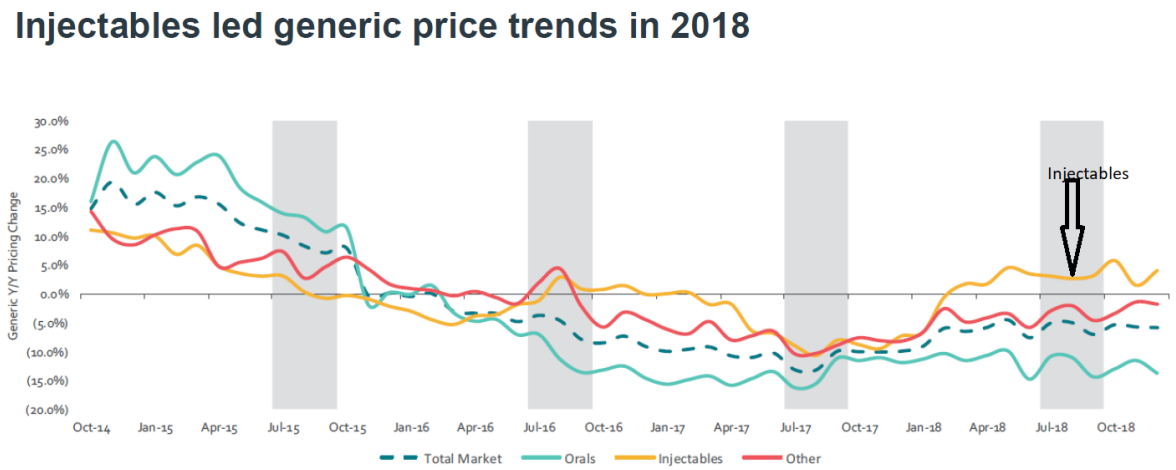
If the country invests in four integrated clusters as described above along with a phytochemicals research centre, at a total cost of approximately $200 million, it can derive revenues of upwards of $10 billion per annum within a decade.

4.5 Drugs off-patent but no generic in market
This is another area, where Indian expertise can create generic market for drugs which have gone off-patent, but no generic substitute has been approved. In such cases, most me-too exporting countries cannot compete and since the generic market will have limited or nil competition, higher prices can be charges.

The latest compilation has 452 such products in the FDA list[44] which is issued bi-annually. The list contains 307 products classified as Part I (drug products for which FDA could immediately accept an ANDA without prior discussion), 136 as Part II (drug products for which ANDA development or approval may raise potential legal, regulatory, or scientific issues that should be addressed with the Agency prior to considering submission of an ANDA) and 9 products being added to the Appendix which indicates one or more ANDAs referencing NDA drug products that have been approved since the publication of the previous list. As can be seen from above list, a majority of drugs fall in categories where a specific drug-release device or technology is used. This cannot be developed by most countries, but India has the capability which can also be enhanced through cooperation with other companies around the world.

Products that have been added include the commonly used anti-cancer drug Docetaxel as well as the peptic ulcer treatment Esomeprazole Magnesium suspension. In 2017, FDA had announced the Drug Competition Action Plan (DCAP) to encourage robust and timely market competition for generic drugs and help bring greater efficiency and transparency to the generic drug review process, without sacrificing the scientific rigor underlying their generic drug program.

Almost 45% of these drugs are injectables. It is not surprising since these are more difficult to develop as generics, but it is also to be noted that the price appreciation for injectables has been the highest in recent years.



IQVIA Global/US Generics & Biosimilars-Trends, Issues & Outlook

According to IMARC Group's latest report titled, "Generic Injectables Market: Global Industry Trends, Share, Size, Growth, Opportunity and Forecast 2021-2026", the global generic injectables market reached a value of US$ 33.82 Billion in 2020. Looking forward, IMARC Group expects the market to exhibit strong growth during 2021-2026.

Owing to the advantages offered by generic injectables, governments in various countries are supporting their manufacture. Additionally, an increase in drug shortages, especially in the US, along with patent expiry of a number of blockbuster drugs, aging population and rising prevalence of chronic as well as lifestyle diseases represent some of the other factors driving the growth of the market. North America represents the largest region, accounting for more than a half of the global market.[45]

The market for injectables is also growing fastest as compared to other formulation classes as shown below (from the IQVIA presentation).

Formulation	2013 Share	MAT OCT 2018 Share
OTHER	8.9%	10.8%
DERMATOLOGICALS	7.0%	7.1%
INHALANTS	3.1%	2.1%
INJECTABLES	13.5%	18.8%
ORAL SOLIDS	66.8%	60.1%
SYSTEMICS	0.8%	1.0%

The data presented makes a strong case for companies in India to develop capabilities for injectables drug-delivery.

By creating the first generic equivalent drug, the Indian company can reap good margins, even though the market itself may be small. It has been seen that even after such drugs lose exclusivity, they continue to be subjected to huge price increases by the innovator company.

"Off-patent drugs that are sole source (ie, those produced by only 1 manufacturer) seem to be particularly prone to price hikes compared with drugs with more than 1 manufacturer. Despite opportunities for generic manufacturer competition, barriers to generic market entry have created monopoly conditions, allowing manufacturers to charge high prices despite patents and other exclusivities having ended. Notable examples of this dysfunctional drug market include the 500% price increase of albendazole (Albenza), the greater than 5000% price increase of pyrimethamine (Daraprim), and the 600% price increase of the epinephrine auto-injector (EpiPen).[46]

For example, in December 2020, Amphastar, an US generic company specialising in injectable, intranasal and inhalation products is able to bring complex generic drugs to the market such as recent approval of glucagon for injection USP to treat severe hypoglycemia. Until now, glucagon had been included on the FDA's list of off-patent, off-exclusivity drug products without an improved generic.

4.5a New guidance on CGTs to improve generic competitiveness

In March 2020, FDA had issued the guidance on Competitive Generic Therapies (CGTs). This guidance describes the process that potential ANDA applicants should follow to request designation of a drug as a CGT. It also outlines the criteria for designating a drug as a CGT, provides information on the actions FDA may take to expedite the development and review of ANDAs for drugs designated as CGTs, and explains how FDA implements the statutory provisions providing for a 180-day exclusivity period for certain first approved applicants that submit ANDAs for CGTs.

An example of the FDA improving generic competitiveness through their various initiatives is the case of the suspension form of Pfizer's Revatio, which contains the same active ingredient as Viagra (sildenafil) and is indicated for the treatment of pulmonary arterial hypertension (PAH). The drug was first approved in 2012 and generated sales of US$ 227 million in 2018. Since the approval of the first generic in May 2019, there are now seven approved generics of the drug on the US market. As a result, Pfizer reported a 37 percent drop in sales to US$ 144 million in 2019.[47]

4.6 Overseas manufacturing in our export markets

Indian pharmaceutical sector has shown a stellar performance in the export markets till now. However, looking at the decade ahead, we visualise many headwinds which have the effect of reducing the growth of direct export of finished dosage forms, the mainstay of Indian exports.

Our caution arises of several changes taking place in the global markets which though, were happening for some years but accelerated by Covid19.

Some of these are listed below:

1. Large scale local manufacturing projects of finished generic pharmaceutical products
2. Lower profitability in US and EU generic markets due to increased competition
3. Regulatory pressures reducing markets for Indian products
4. Increased competition in both regulated and unregulated markets.

This would require strategic thinking at national level to develop a strategy which will ensure that India not only retains its traditional markets but also conquer new markets.

4.6a Business environment in the export markets

There is a limit to traditional generic exports which has been a success story for India till date. We will have to change our business model if we wish to survive this this price sensitive market. Even a decade back, very few countries had meaningful indigenous production but today many countries in Asia, Middle East, Easter Europe and Latin America are engaged in building up or expanding their generic pharmaceutical industry. In Middle East itself, from 30 plants in 2013 to 47 in 2016, and is expected to reach 75 in 2020.The new plants which are coming up are all in billion tablet/capsule size category. The Gulf Cooperation Council (GCC) countries will spend $12 billion on pharmaceutical production. In Oman itself, world-scale plants are operating and a new $365-mn pharma plant is getting ready which will manufacture 100 types of drugs and plans export to 20 countries in the region.48 At present, GCC imports 80 per cent and Oman 93 per cent of its requirements. It is these smaller countries which have ambitions beyond their shores which will give strong competition to Indian exports. Jordan and Turkey already have thriving pharmaceutical industries which export throughout the Middle East and African region.

In Africa too, a land of small fragmented markets made pharmaceutical production unattractive for local production. With the launch of giant African Continental Free Trade Area (AfCFTA) after signing by 52 out of 54 countries, the stage is set for large scale formulation production and export within the continent to take a larger share of the $60 billion market by 2030.

According to Goldstein Research, Africa is the only pharmaceutical market where genuinely high growth is still achievable, value of Africa's pharmaceutical industry jumped to USD 28.56 billion in 2017 from just USD 5.5 billion a decade earlier. That growth is continuing at a rapid pace: we predict the market will be worth USD 56 billion to USD 70 billion by 2030. It is opportunistic for multinationals and pharmaceutical companies seeking new sources of growth as developed markets stagnate while patients will also gain access to medicines previously unavailable on the continent.[49]

According to a McKinsey report, "Overall, our analysis convinced us that increased local drug production is feasible in about a half dozen sub-Saharan African countries at current and projected demand levels. While only South Africa is currently as attractive to private-sector pharmaceutical investors as Brazil and India, other countries are rapidly improving their investment climate".[50] However, our and Chinese studies show that, in the light of scaled up market due to AfCFTA, many more countries in the Sub-Sahara region would set up their own plants by 2030. A List is provided in annexure-1. China expects 21 countries to have domestic production in the next few years. This will be discussed later in this chapter.

AfCFTA Secretariat was commissioned in Accra as free trade is set to begin in January 2021. African manufacturers will now be able to compete against Asian giants through significant economies of scale and scope. The drug registration harmonisation initiative, already in operation in parts of Africa will also be accelerated with this development creating ease of marketing operations and reducing cost for pharmaceutical companies.

The impact of this will be the attraction of leading generic pharmaceutical manufacturers to either build plants locally, take over undercapitalised plants or to partner with local manufacturers and equip them to produce their products under licensed manufactures or in Joint-Ventures.

In June 2020, The African Union launched the Africa Medical Supplies Platform which promotes the procurement of medical supplies from local manufacturers and taps into the harmonized regulatory systems created in the context of the Pharmaceutical Manufacturing Plan for Africa (PMPA). To give local manufacturing it a push, some countries such as Kenya and Ethiopia are also contemplating banning or restrict import of certain common drugs. This decision was deferred due to Corona pandemic but would again revert.

PMPA is a decade old plan but Covid has infused new life in it and countries are eager to accelerate its progress. The countries are realising that reliance of up to 80% of demand on imported drugs is not sustainable.

In April 2021, recognising that Africa was the last to obtain Covid19 vaccine supplies, The African Union and Africa CDC(Africa Centre for Disease Control) launched Partnerships for African Vaccine Manufacturing (PAVM), framework to achieve it and signed 2 MoUs. The aim is to create capability to manufacture up to 60% of demand within the continent by 2040. For example, no licenced vaccine for Lassa fever exists, despite the fact that this haemorrhagic fever affects 300,000 people and kills an estimated 5000 people a year in West Africa. With its expertise in vaccines, India can involve itself in combating this and other initiatives.

There are challenges the industry is confronted with that include the following, and are not limited to: 1) access to affordable financing, 2) access to technology and technical know-how, 3) inadequate human resource capacity, 4) small fragmented markets and poor market intelligence, 5) fragmented and weak regulatory systems, 6) fragmented and poor procurement and supply chain systems, 7) policy incoherencies across trade, industry, health, and finance, 8) poor business to business linkages and collaboration, 9) low investments in research and development as well as intellectual property. No single sector, government department, or organisation on its own can achieve these goals.[51]

One area where India has a clear manufacturing lead is vaccine production and Africa is seeing a strong demand growth. According to the estimate of McKinsey & Co., the public market for vaccines in Africa could rise from $1.3 billion today to between $2.3 billion and $5.4 billion by 2030, depending on the scenario. While Africa's population is growing faster than that of most other regions, significant immunization coverage gaps remain, and new products, such as vaccines for Lassa fever or malaria, could be introduced and used widely on the continent.

More than 9.4 million African children each year don't receive the third and final recommended dose of the diphtheria, tetanus, and pertussis (DTP) vaccine. This is just one of the current gaps in the continent's vaccination programs. When delivered in full, DTP and other life-saving vaccine programs currently save two million to three million lives annually.

This is a market which India has the potential to capture through a combination of African manufacturing and supply from India. It is possible only if India is able to domestically produce a larger number of ingredients which are required for vaccine production.

One Indian company has already opened an animal vaccine plant in Tanzania which will supply throughout Africa. The company invested only 4 million out of 18 million investment and the balance 80 percent came from Impact Investment sources and the same model can be applied for human vaccines as well as the wider generic production on the continent. Africa has already seen that it was the last to get vaccine supplies during Corona pandemic and if India does not take lead, there are others waiting in the wings to meet the demand.

Many are concerned about Africa's production costs, which could indeed be higher than in today's vaccine powerhouse locations (such as India—which makes approximately 70 percent of Africa's vaccines today). But the fast pace of technology innovation that we have seen in recent years at every step of the vaccine-development and -manufacturing value chain may mean that production costs are no longer a showstopper. Small-scale disposable technologies, high-density bioreactors, and innovation in fill-and-finish steps are boosting yields and have the potential to change the business case for newer entrants.[52]

4.6b Chinese threat in Africa

China too has seen the advantages which the borderless African continent presents. It has already opened two large pharmaceutical plants in Ethiopia and has made progress in other sectors too. Chinese entrepreneurs have commissioned five ceramic tiles plants in Kenya, Tanzania, Uganda and Ghana, the first in these countries while our entrepreneurs in tile manufacturing (4th largest in the world) have yet to open their account. Therefore, China is poised to cash in the AfCFTA Agreement in a big way, beyond infrastructure development and this progress will only accelerate in the future. Neither our media has covered it in any detail nor the trade bodies or the government have shown any strategic direction on this big opportunity. China is the first to recognise that beyond South East Asia, there is another territory for low-cost manufacturing. Africa with its vast natural resources and abundant cheap labour force will continue to boost value-added industrial production over the next decade.

China is also developing free trade zones in Africa. One is in Egypt which grow into a total area of 7.23 km2 in Suez Canal Economic Zone (SCZone) and the other is at Djibouti, both on the East coast of Africa. In addition, it has built Kilantro Pharmaceutical Industrial Zone in Ethiopia which will spearhead the country's ambition to become Africa's pharma hub.

Greater industrialisation would boost GDP much faster than present agriculture-based economy which will further expand the market for goods and services. The next decade will see a transition of much of Sub-Sahara Africa through massive investment in infrastructure, industrialisation and housing resulting from mass migration from rural to urban areas. The income levels will go up (e.g., in Ethiopia from $780 today to $1200 in 2025), so will purchasing power resulting in substantially higher out of pocket healthcare expenditure.

Generic pharmaceutical export is one of the few areas where India has a vast lead over China. India is the world's largest producer of quality and affordable generic medicines. India has recently also emerged as the largest producer of affordable vaccines in the world.

Presently, India has a vast lead over China in Exports to Africa too.

Indian medicines are well accepted and enjoy good reputation for quality combined with affordability. Africa suffers from poverty, low purchasing power, overwhelming burden of disease, high counterfeit and poor delivery system of medicines.

The pharmaceutical growth reflects economic strength accompanied by increasing healthcare spending. Sub-Saharan Africa (SSA), excluding South Africa, is notable in this regard: According to the Economist Intelligence Unit, its economies are growing faster than anywhere else in the world and this trend is expected to continue. FDI in the continent rose to US$46 billion in 2018, an increase of 11% on the previous year. Most Sub-Saharan nations would reach middle income status by 2025. As we have already seen, the continent's pharma market can grow up to $60 billion by 2030.

African nations are placing higher emphasis on healthcare with policies and investment, at national, regional and continental level. African Union has placed healthcare as the third highest priority for Africa.

Alongside the increasing economic wealth is a notable rise in healthcare spending, which has grown at a CAGR of 9.6% since 2000 (across 49 African countries). Fuelled by government, non-government organizations (NGOs) and private sector investment, this has largely focused on strengthening health system infrastructure, capacity building, treatment provision and specialized services.

China's pharmaceutical industry accepts that it cannot catch up with India in the developed markets. In addition, due to new tender system being implemented by the Chinese government, the large profits which Chinese manufacturers were reaping in the domestic market has already started vanishing. It is now looking at this large African market of the future and preparing its strategy to displace India as the largest pharmaceutical presence in Africa. After Africa, it would look at Latin America.

The Chinese threat is real and probable, the signs would be apparent in 3-5 years from now. We have already seen the demise of Indian mobile phone makers after the advent of Chinese companies. However, pharma is in a much stronger position, not only to face the Chinese threat but also take substantial lead and the next chapter will provide some solutions, not only to counter Chinese threats to Indian industry but offers a roadmap for rising to leadership position in global generic pharmaceutical marketplace.

These developments and challenges in Africa present India with an unprecedented opportunity to leverage its strength in generics, vaccines and biologics as well as managerial & entrepreneurial skills and deny this led to China. We will present certain suggestions in Chapter 8.

Some other development at country level are as follows:

Egypt hopes to reduce import of generic drugs from $1.46 billion in 2018, to $700 million in 2020 and nil in 2030. North African countries such as Morocco, Tunisia and Algeria are all in the process of expanding their generic production to reach 60-80 per cent of their demand and increase export to French speaking West African countries.

In Sub-Sahara Africa too, there is a renewed effort to indigenise production of pharmaceutical products to ensure that the $45 billion African market stays within African hands. East African countries from Ethiopia to Kenya, Tanzania and Uganda all have

announced plans for large scale generic industry. Even Chad is building a pharmaceutical plant with Egyptian assistance. Kenya is building a greenfield billion tablet/capsule capacity HIV drugs plant. Tanzania has announced plans for five plants. Square Pharma of Bangladesh has announced its first investment in Africa with a billion capsule/tablet plant in Kenya.

Ethiopia has taken a big lead in being the first to launch a pharmaceutical plan for the country which is designed to turn the country into a pharmaceutical hub for Africa.[53] At present only 20% of the $600 million market is met with domestic production. The market will rise to $ one billion by 2022. Indigenous production will increasingly supply this demand as new projects are commissioned. China has built a pharmaceutical manufacturing Zone and already two Chinese companies have invested over $200 million. Sansheng plant has a capacity of 10 billion tablets, 5 billion capsules and 40 million parenteral.

The scenario is the same in Eastern Europe and Latin America. Russia's indigenous pharmaceutical products supplies 27 per cent of demand. The government aims to increase domestic share to 50 per cent by 2020 and 80% by 2030.

In Chile, the largest domestic pharmaceutical maker Tecnoquimicas has announced USD 200 million manufacturing investment in two new generic plants which will substitute for USD 110 million of imports and will create USD 70 million of exports.

Even tiny Qatar is pouring over $400 million in pharmaceutical production and it is also looking at the GCC markets first and others later.

This is just a fraction of the manufacturing activity taking place around the world. In addition, Bangladesh is scaling up its industry for large scale exports. From $118mn.in 2018, it aspires to export $1bn. in 2025. In formulations exports, we will continue to face increasing competition from Bangladesh, Turkey, Egypt, Jordan, China, Morocco, Tunisia and later from Ethiopia.

Every country with a sizable population is looking at Bangladesh model to grow their generic industry. It is our assessment that more than 30 countries will be major competitors to India, in regional and global markets by 2030 (see annexure I).

Most of these countries are also looking at export markets to scale up indigenous production viable and make the industry viable. Some of the countries which will give stiff competition to Indian exports in Middle East and Africa are:

China, Bangladesh, Turkey, Egypt, Ethiopia, Qatar, Morocco & Tunisia, Jordan, Saudi Arabia, Kenya. Annexure 1 provides details of national plans.

4.6c Generic Competition from China

Likelihood of major disruption from Chinese generic manufacturers has gone unnoticed in India. China has been steadily building its generic capacity to challenge India and recent events have accelerated this process. We foresee major competition from Chinese companies in our traditional markets, especially in Africa for the following reasons.

China understands that it cannot challenge India's domination of the US, UK and other regulated markets. The sheer number of Indian ANDA (Abbreviated New drugs Application)

approvals, number of US FDA approved plants and the scale of Indian industry precludes direct challenge in these markets.

During 2019, Indian companies won 44% of all ANDA approvals by USFDA, maintaining its lead as in earlier years while Chinese companies gained 7% approvals. Though Chinese presence in US is small but the numbers are steadily growing.[54]

From 22 approvals in 2016, it increased to 38 in 2018 and 57 in 2019. In is our thinking that China is increasing its ANDA filing not only to increase its share of US market, the world's largest but use it to hasten the domestic regulatory approval as well to showcase its rising quality manufacturing to grab international markets. It is our assessment that China will offer very strong competition to Indian domination in the African market, to start with. The primary cause is significant decrease in the profitability in domestic market.

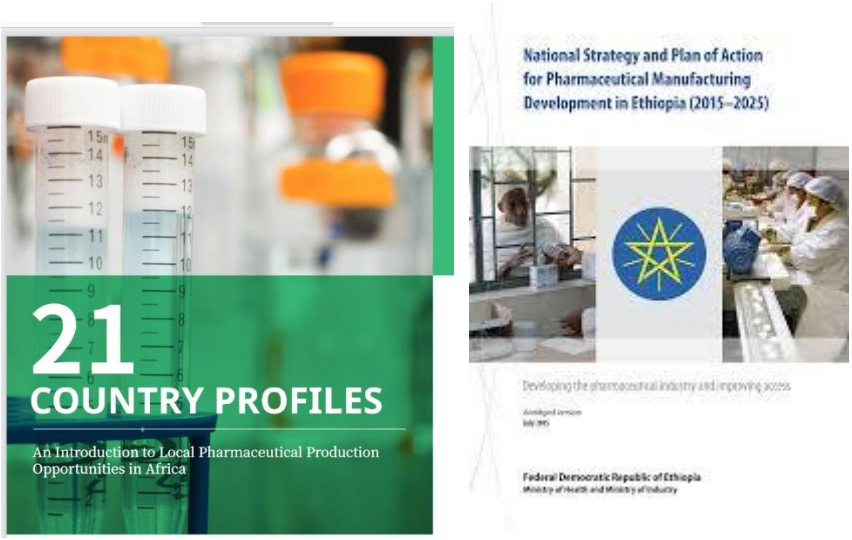
Profitability in domestic Chinese market has significantly decreased

The Chinese pharmaceutical market, which is dominated by domestic manufacturers, is the second largest in the world in terms of value after the US. In 2018, China launched a pilot project to drive down generic drug prices through a centralised bulk procurement program. Earlier, each province was independently floating tenders. Burdened with rising healthcare expenditure, growing cancer cases and ageing population, The Chinese government overhauled the drug procurement system. The Chinese Joint Procurement Office (JPO) listed 31 generic drugs for procurement in a pilot program across all public hospitals in 11 cities, accounting for around a third of the Chinese drug market. The result was a fierce price war resulting in the lowering of prices by an average of 52 per cent and in one case by as much as 90 per cent. The winner took 60-70% of all orders. The government plans to progressively take this program to other regions.[55]

For example, Sino Biopharmaceutical slashed the price of its hepatitis treatment entecavir by more than 90 per cent to beat out Bristol-Myers Squibb Co. and two local competitors. Acarbose price reduction was 78.5 per cent and Lipitor 75 per cent. At this rate, China's drugmakers can say goodbye to most of their profits.

Chinese entry into Africa

Alarmed with this scenario, Chinese industry decided to seek its fortunes elsewhere. Africa was the first destination. China Chamber of Commerce for Import and Export of Medicines and Health Products (CCCMHPIE) commissioned a study titled 21 Country Profiles[56] which identified 21 countries in Africa with pharma manufacturing potential and highlighted vast opportunities for Chinese pharma companies to expand and relocate their manufacturing to African countries.



Chinese move coincided with Ethiopia's ambition to turn itself into the pharma hub of Africa. It was the first African country to articulate a pharmaceutical manufacturing strategy & plan. To promote indigenisation of production, Ethiopian government has offered 25 per cent price preference and 15 per cent advance to local companies.

China has built an exclusive pharma industrial park in Kilintoro in Ethiopia on 240 hectares. Two Chinese companies have invested $200 million to build two large generic plants to cover markets in Ethiopia, Sudan, South Sudan and Eritrea, to start with. The Sansheng plant has a capacity for 5 billion solid preparations, 300 million ampoules and 10 million large volume parenteral. The size of plant, one of the largest in Africa itself is a signal that it does not restrict itself to Ethiopian market. This is only the first step and we will soon see more Chinese manufacturing both on East and West Coast as well as North Africa.

Next steps would be restrictions on import of drugs where sufficient local capacity is available. Kenya may soon ban the import of eight formulations for which adequate domestic capacity has been created. Other countries will soon follow. One only has to view Bangladesh pharma model to understand the direction which a number of African nations will follow.

The African Continental Free Trade Agreement has started being implemented in 22/54 countries where the respective parliaments have ratified the agreement. Other countries will follow suit creating a common market of 1.2 billion people. China is preparing its entry where, by 2030, the market may increase from present $27 billion to $65 billion as quoted earlier.

The Indian government should develop its own strategy for Indian companies to invest in world scale pharma plants. Not only it will ensure export of API but also equipment, consultancy and manpower. We would like to add that Chinese moves in Africa is not restricted to pharmaceuticals alone but a wide range of consumer-oriented projects to leverage the large common market envisaged in future.

4.6d Competition from Bangladesh

Bangladesh's pharmaceuticals zone will grow 15 per cent year-on-year to reach US$ 5.11 billion by 2023, propelled via high investments by local companies as they look for to grabbing a bigger share of the global market. As demographics move, the industry also

undergoes transformation to keep pace with the changing needs of the consumers. As a modern trade, pharmaceutical started its journey at the mid of 1980's. Pharmaceutical is one of the most prominent as well as flourishing sectors of Bangladesh. It started booming with the announcement of drug control ordinance (1982) and now it is 2nd largest industry in Bangladesh. However, it imports 97% of its API requirements, 60% from China and 30% from India at a cost of $600 million.

Bangladesh can produce specialized delivery products like inhalers, prefilled syringe injections, lyophilized injections, and dry-powder inhaler and sustained-release formulations. The country has already developed production facilities for tablets, capsules, liquid preparations, dry suspension, injections, ointment/cream, nasal spray and granules in sachets.

According to Bangladesh Association of Pharmaceutical Industries (BAPI), approximately 1,200 pharmaceutical products received registration for export over the last two years. According to Bangladesh Export Promotion Bureau, Bangladesh exported pharmaceuticals product to 147 countries in the fiscal year 2018-19. Among 147 exporting countries, top 7 countries (Myanmar, Sri Lanka, Philippines, Vietnam, Afghanistan, Kenya and Slovenia) constitute 60.32% of total pharma export. Rest 39.68% comes from other countries. Bangladesh has exported pharmaceutical products worth USD $130.0 million in 2018-19 as against USD 103.5 million in 2017-18 export has crossed $100-million mark for the 2nd time in the country's history. The exports are growing at 7% per annum. Bangladesh which is enjoying the continued extension of manufacturing of patented pharma formulations by WTO/TRIPs for the next 17 years which is expected to end in 2033, the country is undoubtedly emerging as one of the fastest emerging pharma-economy in the global markets.

This is the model most emerging nations in Africa are likely to follow for the growth of their industry.

1. Attract FDI for domestic production with Ethiopia like policies.
2. Ban or restrict import of specific drugs on reaching self-sufficiency as Bangladesh did.
3. Explore regional markets for exports to make projects viable

4.6e Move production of common drugs overseas

As we have already discussed, the export of most common, especially those found in WHO List of Model drugs will become more difficult with large scale local manufacturing and increased competition from other countries. Since the entire Africa is one market and more such markets will come up such as RCEP and larger regional Free Trade regions in South America, India should plan the establishment of regional pharmaceutical zones where Indian companies can set up manufacturing activities to cater to the regional requirements, these will be further discussed later in this report. This would create a long-term export market for Indian APIs, excipients, machinery & expertise. This topic is discussed in greater detail in Chapter 8.

4.7 Develop world's no.1 API industry

This is another $100 billion opportunity waiting to happen.

It very rarely happens that several events converge to show directions for a particular industry to seize opportunity for global leadership. That moment has come for the Indian API industry. Atmanirbhar Bharat has kickstarted the process to ensure that the country is largely self-sufficient in the production of APIs. Now, we have to seize the moment to create a vision where not only we supply a major quantity of APIs to Indian industry but also become no.1 in the world by 2030. What are the convergences of events which will make this vision possible?

a) Over dependence of Indian industry on Chinese supplies
b) Atmanirbhar Bharat led PLI scheme & API Parks
c) 30-50% rise in Chinese prices taking advantage of Covid induced demand
d) Many closures of Chinese chemical companies on tougher environmental laws
e) The global industry disruption of Chinese supply chain
f) The importers realising that they must develop China+1 strategy
g) The rising curve of domestic market and exports
h) Many countries undertaking generic formulations production without creating much indigenous supply of APIs
i) Many Multinational pharmaceutical companies exiting captive API business
j) PE investment flowing into API industry
k) India possesses all the ingredients of a specialty chemical industry ecosystem.

We will discuss all the above in greater detail.

4.7a Over dependence of Indian industry on Chinese supplies

Covid exposed our dependence for import of 60-70% of our requirement of APIs. It increased by a CAGR of 8.3% between 2012 and 2019. In 2018-19, over $3.5 billion worth of ingredients were imported by India, of which China supplied around 68 per cent. This means that a disruption in the supply chain from China could disrupt the availability of formulations in India, both for domestic supply and exports.

It is not only India, but this overdependence on Chinese manufactured goods to power the world's industrial output has alarmed even the US security establishment. According to a recent article in a major Indian defence magazine reporting on a recent hearing of the US Senate Armed Services subcommittee*, "Intended to optimize supply chains, reduce costs and thereby maintain competitive price points, these trade agreements have landed U.S. supply chains in a precarious position. Sourcing materials, managing inventories and maintaining stockpiles are fallen priorities behind greater financial returns*." A committee member noted that "*the vulnerabilities and gaps in our supply chains, particularly as it relates to national security, have taken on a new urgency*." The alarm bells are ringing on the reliance on Chinese origin electronic chips and other material to power America's defence systems.[57]

Therefore, Indian government has taken the right decision to encourage higher indigenous production of APIs and reduce reliance on China to a minimum.

We had a flourishing API industry which largely shutdown in the last decade due to unrestricted cheap imports from China. In the 90s, China provided incentives to its API industry to build large scale plants and dominate global supply by exporting low-cost APIs. The Indian manufacturers could not compete and moved away from API to formulations. API was not an isolated case. Many industries could not compete against Chinese imports in their formative years, such as electronics and had to fold up.

We must not forget that Dr. Anji Reddy started his illustrious career by developing and manufacturing an API which was not only cheaper but superior to its imports. In 1973, the pharmaceutical industry in India was dominated by American and European multinationals such as Pfizer, Glaxo etc. as the API industry in India is dominated by Chinese companies today. The global companies produced bulk drugs called API (active pharmaceutical ingredient) in their home countries and imported these to India. Dr. Anji Reddy synthesised the formula for the manufacture of metronidazole API an antibiotic, which was the first of its kind in India after overcoming several process obstacles. The quality was even better than the Italian ingredient being imported till then.[58] Dr. Reddy was the first Indian company to export Norfloxacin and Ciprofloxacin to Europe and East Asia.

Similarly, as late Dr. Hamied founder of Cipla recounted: "When I joined the pharma industry in 1960, the label 'Made in India' was not acceptable internationally." He then went on to outline how the API industry took shape in India: "In 1960 itself, I was influenced by a publication in 1959 of Prof RN Chakravorthy, who discovered the existence of Diascoria species in Northern India, which yielded Diosgenin, the precursor to steroids. As some of these, such as testosterone and progesterone, were not covered under existing patents, they could be produced within the country. Thus, started the synthetic API manufacture in my company".[59]

We must follow the Chinese route to build up a world scale API industry, that is government support for the next decade and build world-scale plants.

API industry today

API industry in 2030

We have that talent and ecosystem to make it possible. It may not be possible to decouple from Chinese stranglehold in the short run but possible in the medium run, that is by 2025.

4.7b Atmanirbhar Bharat led PLI scheme & API Parks

Self-reliance in the Indian pharma industry is nothing new. As narrated earlier, we had a flourishing API industry till the 90s, till its growth was stunted. For some years, Indian government has been pursuing a policy of creating a self-sufficient industrial base, first with "Made in India" and more recently with Productivity Linked Incentives (PLI). In March 2020, the Indian government announced a ₹6,940-crore scheme to reduce dependency on China and boost domestic manufacturing of APIs over the next eight years. The scheme will cover 53 crucial APIs and KSMs for which India is now critically dependent on imports. Another ₹3,000 crore was allocated to set up three bulk drug parks over the next five years.

The government has also decided to fast-track environmental clearance process for projects proposing production of bulk drugs in the country.

As we go ahead with the development of API industry in India, we should also be aware of the likelihood of dumping by Chinese companies to stunt the growth of Indian competitors. Recent claims that Chinese manufacturers are dumping active pharmaceutical ingredients (API) for antibiotics into the Indian market have sparked a probe by the country's Directorate General of Foreign Trade (DGFT).

However, a major omission in the planning of API Parks is establishing an R&D Centre which can cater to the product developmental needs of SMEs.

However, as we will argue in following chapters, we must raise our sights higher and seize this opportunity to become the supplier of choice to formulations manufacturers throughout the world. This would require a wide range of support ranging from R&D, logistics, power supply, cost of project & working capital loans, quality & size of industrial parks, rules & regulations etc. which are government domain, both Central & State. As many reports have already highlighted these constraints, we will not repeat these in this report, but we must look at China's development model for APIs and adapt it to our conditions.

i. 30-50% rise in Chinese prices taking advantage of Covid induced demand

Chinese API process have been rising for past two years but since Covid erupted, Chinese manufacturers have increased prices of APIs by 30-100%. For example, the price of heparin (a blood thinner – a critical drug in the treatment of cardiovascular disease) has risen by 211% since September 2018.[60]

Since this is a controlled price drug (the cheapest one in its class), frequent rise in prices and consequently delayed revision of prices by NPPA makes manufacturing unviable and

leads to shortages in the market. The heparin sodium API for the injections made in India is largely imported from China. Experts say that there are not many alternative manufacturers for the API, especially in India. This just one example of the stranglehold of China on Indian manufacturers.

ii. Many closures of Chinese chemical companies on tougher environmental laws

With the closure of many Chinese specialty chemical plants which include API plants, because of safety & environmental reasons, a market has opened for Indian manufacturers to tap Chinese market as well as other markets vacated by China. This is also one of the causes of price rise. The opportunity for specialty chemical largely stems from three causes:

Tightening of financing availability

The Chinese government's policy to tighten credit across the country's economy has been a particular handicap for the capital-intensive chemical industry that has in the past benefited from low-cost capital to expand capacity. Banks have shifted over the past year to demand more collateral, terminate loans prematurely, and refuse to renew loans, putting chemical companies at a further disadvantage for borrowing. Chemical enterprises also get charged an above-market average interest rate.

New environmental regulations

China's chemical build-up over the past two decades had prioritized growth over environmental quality. The 13th Five-Year Plan for environmental protection published in 2016 enshrining "clear waters and lush mountains" as a national policy has marked a sharp shift, as China's authorities have started to address environmental degradation.

Consequent of strict enforcement of environmental compliance, over 150 API plants have closed down. This closure had a cascading effect on the supply of pharmaceuticals throughout the world. In addition, capital expenditure for meeting compliance as well as payment of environment tax from January 2018 added to the final price of APIs. Total tax collected from all chemical industries can go up to US$ 8 billion per year.

Higher Labour Costs

The labour cost in China was lower than that of India till 2007. However, over 2005-2015, the average worker cost in China increased nearly 19-20% CAGR, against 4- 5% CAGR in India. In fact, over the last five years, this cost has more than doubled compared with India, rendering Chinese manufacturers' uncompetitive vis-à-vis India in terms of labour cost.

According to PWC, higher environmental standards around the world are increasing pressure on the production of some chemical inputs. This has led to a severe shortage of critical raw materials for specialty chemicals Multinational chemicals companies being unable to source supplies and declaring force majeure on unfulfilled orders and they are looking at alternative sourcing locations, including India, the Middle East, and even high-cost countries. Price increases of as much as 500 percent for certain specialty chemicals used in everyday products such as printer's ink, pesticides, and food and drink packaging.

The rise in costs for some APIs is as follows (pre-covid prices):

API	Rise in price
Paracetamol	45%
propylene glycol I.P.	30%
azithromycin	36%
ciprofloxacin	28%
ofloxacin	30%

Other APIs such as, esomeprazole magnesium, losartan potassium, , montelukast, methylcobalamine , pantoprazole sodium, rabeorazole , sildnafil citrate, telmisartan, cefixime, cefpodoxime proxetil, and cefuroxime axetil have also seen appreciable rise in prices.

China supplies over 90% of the world's vitamin C, which is one of the most polluting industries. Restricting production has pushed up the price. The global vitamin C market is growing at 2.2% per annum.[61]

One executive at a global specialty chemicals company put it this way: *"There has been a heavy impact because several of our products are single-sourced. The suppliers that are able to deliver have increased their prices continuously, leading to a 200 percent rise over the past 12 months."*

4.7c Global industry disruption of Chinese supply chain

Rising production costs, plant shutdowns, and uncertainty in supply are likely to accelerate global buyers' shift away from China. Companies are lining up alternate raw material sources. For advanced intermediates, the companies are looking for alternatives in India, Europe, and the U.S. Moreover, some multinational companies that have capacities and knowhow have started exploring recommissioning API facilities. If India could accelerate its API program, it could pre-empt the opening of mothballed plants.

4.7d Importers realising that they must develop China+1 strategy

Formulations companies throughout the world are either producing API in captive units or buy from merchant API producers which are largely located in China. If India has to rival China as a source of supplies, it must be able to show that not only it can match China in prices but also in quantity. Our recent experience with vaccine production has shown that India is very much dependent on imported ingredients to produce final doses and is subject to disruptions.

Even many Chinese manufacturers appreciate the capabilities of the Indian industry. They routinely send their API to India for further processing and then selling in third countries. As noted by a Chinese manufacturer, " **…**in that no other country can compete with India in terms of production cost and technology levels for API production. "It's not like producing a table or chair. Other countries do not have such advanced and complete production lines like those in India at the moment,[62]

Therefore, the plants in India should be built to global scale to provide cost advantage to India and it has the domestic capability to produce API from Key Starting Materials (KSM).

According to a KPMG study[63], Indian API costs are 20% higher than China. This is a result of China's cost efficiency, large scale manufacturing capacities, technical capabilities and supportive government policies. India has to act on all these fronts before it can be a rival to China.

The Government should support the establishment of globally competitive industry from end to end, from KSM to final dosage of which PLI is a small element. PLI is a starting line and not the finishing line. Since Indian manufacturing for the domestic market are exports are interlinked, the advantage for one will also spill over as advantage to the other.

India can make progress in API global competitiveness provided it also provides a substantial base for the manufacturing of KSMs. India has some backward integrated pure API companies, and these should be encouraged to take a larger share of the global business. If we only concentrate on API, China will increase the price of KSMs and reduce the price of APIs to drive Indian companies out of the world markets. Therefore, the production of entire value chain is essential, at least 70-80% of requirements.

India possesses one of the largest specialty chemical industry in the world which manufactures upwards of over 70,000 products. It has the necessary knowhow but cost of doing business is high.

India has made spectacular growth in World Bank's "Doing Business" Ranking. Within a few years, it has jumped from 100 to 63 in 2020. Still China ranking is 31. India must continue to make efforts to bring ease of doing business ranking still further. This will allow more FDI to flow into the entire pharmaceutical value-chain along with technology and expertise.

4.7e The rising curve of domestic market and exports

The domestic consumption market for APIs is expected to reach a size of US$18.8 billion by FY2022 with a CAGR of 10% according to market research firm RNCOS. In 2016, India's global generic API merchant market share was 7.2%, the third largest when the last record was taken, according to the IBEF. Since then, India's share has significantly increased as a result of the country becoming a major exporter to all key markets, including China.

The global API market is also rising. Throughout the world, historically captive API market is around 70% while merchant API takes balance 30%. This was the case when multinationals were large manufacturers of pharmaceuticals and used and integrated supply chain model to sell throughout the world.

The market is now changing. Following India's example, more and more countries are encouraging establishment of generic formulation industry, at least to the level of WHO Model List of Drugs. This will increase the size and growth of merchant small molecule API exports. As more drugs come out of patent protection, a further market for new API products will become apparent.

According to a patent watch firm 163 drugs are facing patent expirations and generic entry by 2025 and more will follow in years to come. In 2020 alone drug companies lost patent protection for USD17 billion worth of sales.[64]

Pfizer alone is set to lose up to $20 billion in sales due to patent expirations starting in 2026. In 2026 and 2027, the U.S. basic product patents on Prevnar 13, Eliquis and Xtandi are set to expire, potentially exposing products that generated sales of $6.3 billion in Pfizer's home market last year to off-patent competition.[65]

A by-product of the rise in API manufacturing is the rising size of excipient industry. Excipients are those products that do not possess any activity of drugs but facilitates the drug delivery process. This industry generally functions below the radar but as API indigenisation rise, there is an opportunity for excipient industry also to grow. India's excipients market is currently growing at 10% to 12%, according to Beroe, twice as fast as the global average.

The problems associated with instability, poor solubility and absorption, and other issues related to the active pharmaceutical ingredients are driving the demand for pharmaceutical excipients. The global Pharmaceutical Excipients Market was valued at USD 6.53 billion in 2019 and is expected to reach USD 10.15 billion by the year 2027, at a CAGR of 5.7%.[66]

India should create facilities to take at least 20% of this market. Organic chemicals have obtained the largest market of 42.5% as it is widely used in oral formulations, controlled release and superior delivery of drugs. India has vast experience in organic chemistry and possess large talent pool and research laboratories.

The reasons for both Indian and global excipient market growth include the advancement of functional excipients, increasing uptake of biologics and the rising adoption of orphan drugs. Many companies are focusing more on excipients to address issues such as segregation, low dissolution and poor bioavailability. Although the small global excipient market is dominated by the United States, Europe and Japan – contributing a combined 85% to the global market – India continues to be increasingly attractive destination. Buoyed by the lower costs of raw materials and labour, domestic and global players have increased their footprint within the country through joint ventures and organic growth.

Price remains an important factor in choosing a supplier of excipients and India's high excipient market growth rate can be put down to the fact that products are 5% to 7% cheaper than in the developed world.[67]

4.7f Many countries undertaking generic formulations production

Many countries around the globe have pushed local pharmaceutical production to the top of their health agenda in recent years and covid has only accelerated the process. Developing nations likely to follow India's example and resort to manufacturing drugs locally and importing APIs. This would create a regular demand for APIs and India must be the importer of choice. Chapter 8 provides more insights in rising indigenous manufacturing around the world.

A 2005 study by WHO proposed that local manufacturing was possible only in countries with a local market of $ one billion or more such as Russia, Egypt and Brazil. However, we find that many smaller countries are putting up brownfield and greenfield projects where there is insufficient local demand such as Qatar, Jordan and Chile which see larger markets which have opened up due to signing of Regional Free Trade Agreements such as East African Community comprising 6 countries and its larger avatar The African Continental Free Trade Area comprising 54 countries and thus find merit in economies of scale.

As far back as 2007, the New Partnership for Africa's Development (now the African Union Development Agency, AUDA-NEPAD) sought to address Africa's overreliance on imports of pharmaceutical products when it developed the Pharmaceutical Manufacturing Plan for Africa (PMPA), as mandated in the Assembly of AU heads of state decision of 2005.[68]

Africa has long been plagued by small fragmented markets which could not provide economies of scale of Indian or Chinese plants and this undercapitalised. However, this is about to change. AfCFTA will provide a single market for 1.2 billion population and spur the growth of indigenous manufacturing.

A pooled procurement mechanism which is under implementation and discussed earlier in this chapter will encourage leading global generic pharmaceutical manufacturers to build plants in Africa or partner with African pharmaceutical companies to manufacture generic products. There is a need for this form of strategic support for Local Pharmaceutical Production (LPP). Russia and Bangladesh are examples of countries that have deliberately and successfully supported the development of LPP. As a result, these countries have experienced an increase in foreign direct investments in the sector. They have also benefited from training and skills development, accelerated technology transfer and job creation.[69]

In recent years, domestic manufacturing has taken roots in several countries. Ethiopia wants to become the pharmaceutical hub of Africa and has set up an exclusive pharma industrial zone. Many countries from Tanzania, Kenya, Nigeria, Morocco, Tunisia and Egypt are ramping up production to take advantage of African single market from 2022 onwards and are looking at the size & growth of African market in future. Even Chad is building its first plant. Tanzania wants to set up five generic manufacturing projects and Kenya is planning a billion tablet/capsule plant for HIV drugs.

Egypt will not import generics from 2030 onwards, Morocco & Tunisia want to increase domestic supply from 50 to 80% and so is Russia. Tunisia is setting up a Pharma City. Tiny Qatar is building a USD375 million plant which will manufacture over 100 types of drugs to be exported throughout Middle East and Africa. Kenya may soon ban the import of some common drugs such as paracetamol to encourage domestic manufacturing. Other countries such as Egypt and Ethiopia may follow suit. The Chinese organisation identified at least 20 countries in Africa when pharmaceutical production is possible. Are Indian companies taking note?

The global generic pharmaceuticals market was valued at about $216.94 billion in 2018 and is expected to grow to around $309 billion at an annual growth rate of more than 9% through 2022. A significant amount will come through greenfield and brownfield formulations projects in emerging nations.

The question we should be asking is from where they will source their APIs? None, except Bangladesh and Egypt has shown any initiative & planning to set up a significant API industry.

API manufacturing is a much more complex process than setting up generic formulations industry. It requires the existence or development of a chemical synthesis ecosystem which includes Universities & research institutions, skilled manpower including PhDs, government support, mature industry and adequate domestic market. Many of the products may move to

continuous manufacturing, industry 4.0 as well as green chemistry processes and smaller countries may not be able invest in the same.

Global Small Molecule API Market is expected to rise from its initial estimated value of USD 151.30 billion to an estimated value of USD 254.38 billion by 2026, registering a CAGR of 6.71% in the forecast period of 2019-2026.[70]

It should be possible increase our present share of world market from 8% (USD 5 bn.) to 20% (USD66 bn), and even 30% (USD 99 bn) share of the $330 billion small molecule API market by 2030. It would require a minimum CAGR of 31% for next 10 years. A stretch target but not impossible.

4.7g Many Multinational pharmaceutical companies exiting captive API business

This is a recent phenomenon. Multinational heavyweights such as AstraZeneca and Pfizer are exiting API manufacturing to concentrate their resources on novel drugs development. The API space thus vacated will be going to contract manufacturing Organisations (CMO). So far, China has taken up the bulk of this CMO business.

AstraZeneca, which manufacture 85 per cent of its APIs is currently in the process of withdrawing from all API production in favour of outsourcing. This journey started in 2008 and it will outsource up to 90% of its API requirements to Chinese companies. Same year Pfizer CentreSource decided to outsource the manufacture of some of its APIs to two Asian contract manufacturers, enlisting the firms, ScinoPharm of Taiwan and Shanghai Pharmaceutical of China to "enable more cost-efficient API production" and the two firms added manufacturing capacity to deal with the new contracts. Pfizer said it would transfer the late-stage processing of 18 steroid API and intermediate products to the new manufacturing partners in three phases over the next four years, beginning with the commodity APIs that involve the less sophisticated chemistry first. [71]

We should be asking why, with all necessary infrastructure, abundant knowledge workers, multinationals have bypassed India in outsourcing APIs.? The answer should provide the roadmap for attracting outsourced API manufacturing.

With post Covid supply chain disruptions and other causes for China no longer a favoured destination explained earlier, companies in India should seize this opportunity for transfer of technology from AstraZeneca and later from other multinational companies to become their dedicated supply-chain partners. This would increase the body of knowledge and skilled manpower which can enhance the knowledge pool of the country.

According to Maximize Market research, worldwide rising outsourcing of API/drug molecule formulation from drug manufacturers will take place in order to eliminate the need for heavy investment in manufacturing processes.

India possesses all the ingredients of a specialty chemical industry value ecosystem.

India already has one of the world’s largest specialty chemical industries and produce over 70,000 products. According to IBEF, India is the sixth largest producer of chemicals globally and third largest producer in Asia in terms of output. The country ranks third globally in the production of agro-chemicals and contributes around 16 per cent to the global dyestuff and dye intermediates production. The chemical sector is expected to double to US$ 300 billion

by 2025, clocking an annual growth rate of 15-20 per cent with exports also rising at the same rate. No other country outside of advanced countries, besides China, can build such a diverse industry. Now that we have decide to build a world-scale API manufacturing industry, we are confident that merchant API export can not only rival formulations exports but can overtake generic exports and prove to much more profitable in the long run.

If India is able to attract 20% of captive API production and 40% of merchant production, with a viable excipient market by 2030, we have an opportunity to create a global market of $60 billion.

4.7h PE increase their investment in API producers

Private equity firms have rightly identified Indian API sector as a high growth area due to India's capability to increasingly meet global demands. Since the Covid19 outbreak in early 2020, about $5 billion is being earmarked by international PE firms into this lucrative business rather than formulation companies. More than 15 PE firms have shown inclination to invest in this segment. Unlike formulations business, API has relatively fewer competitors and outlook is very bright. No doubt, the government's PLI push have put new life into this segment.[72]

4.7i Take a larger slice of CDMO Market

According to Fortune Business Insights, the global contract development and manufacturing organization (CDMO) market size stood at USD 130.8 billion in 2018 and is projected to reach USD 278.98 billion by 2026, exhibiting a CAGR of 10.0% during the forecast period.[73]

Typical CRO services include patient and site recruitment, clinical monitoring, analytics, biostatistics, medical writing and regulatory affairs consulting. CDMOs, on the other hand, take over parts of the drug product development and manufacturing activities of pharmaceutical companies. They offer drug product development and manufacturing services, and active pharmaceutical ingredient (API) production and packaging services.

As we have seen, AstraZeneca completely discontinued in-house production of APIs and outsourced these products to contract manufacturers, almost 90% in China. To channel its investment in novel drug discovery and to cut down costs in downstream activities were the main factors in outsourcing.

There is a greater willingness to outsource among pharmaceutical companies, which increasingly use outsourcing services to decrease time to market, save costs, reduce complexity and reallocate internal resources.

China and India both possess facilities to provide cost-effective CDMO services. However, India has an additional resource which will become a more apparent reason for attractiveness in site location. It is its large number of educated & skilled manpower, especially chemistry & biotechnology. By 2030, all advanced countries as well as China will start experiencing shortages in scientific and technology fields which will critically affect their technological leadership and industrial production. Japan is already facing a huge challenge in software manpower and is looking at India to alleviate it. Many I.T. multinationals such as Microsoft, Google, Samsung, IBM etc. have set up large R&D Centres in India and they will reap greater dividends in the future from these facilities.

Therefore, Indian government should provide a conducive business environment to enable these foreign entities to collaborate with India companies for a win-win partnership. In this context, several Indian companies' standout such as Suven, Sai Life Sciences, Laurus Labs and Syngene.

To enable Contract Drug Development, chosen Indian Universities such as IICT, Hyderabad, IISC, Bangalore as well Niper should be developed, both infrastructure and manpower so that Industry-Academia consortium can jointly bid for outsourcing services.

According to PWC's report Current trends and strategic options in the pharma CDMO market "sterile liquids are currently enjoying the strongest growth, taking up an increasingly large share of the pharmaceutical development and manufacturing outsourcing market. The high growth in the sterile liquids segment is mainly due to the increasing importance of biologics".[74]

A majority of drugs in the FDA list of off-patent but no generics are also injectables. Therefore, this is an area, where Indian outsourcing can be developed. This will have lower competition due to inherent difficult nature of technology.

Since the new drug developments are taking place increasingly in complex and high-potency compounds, these require higher investment, both in quality manpower and infrastructure. We should aim at $80-100bn. CDMO market by 2030. Large scale CRO/CDMO in the country would have a spinoff effect on the entire pharmaceutical value chain by developing a large pool of manpower similar to what are witnessing in the I.T. R&D. This would lead to increasing startups in the sector.

A scheme like Productivity Linked Incentives which is designed for manufacturing units should be brought out for the research oriented outsourcing industry to compete for and get a larger share of the market.

Law of Unintended Consequences

The law of unintended consequences is that actions of people, and especially of governments, always have effects that are unanticipated or "unintended." The siting of Indian Drugs & Pharmaceuticals Limited at Hyderabad had an unintended consequence of providing a training ground of future entrepreneurs in the pharmaceutical industry. If the government can open institutions like NIPER at Hyderabad and Ahmedabad, the multiplying effect of these institutions in attracting CDMO industries to the region would be immense.

Another way could be to extend financial incentives to CDMO industry. Not only, it creates custom-synthesized drug ingredients but most important provides skilled manpower which is working at the state-of-art sector and working in close collaboration with innovator drug companies. Our drug manufacturing has evolved over the past 20 years beyond just producing basic APIs. and today we have companies which are collaborating with innovator drug companies in custom-synthesis of APIs in areas such as oncology. The innovator companies have realised that the Indian companies are as good as their US and European counterparts but at a much lower cost. These activities are outside the purview of PLI scheme though their contribution is creating a more innovative API industry. With government help, India can be in a strong position to help Western drugmakers and governments secure API supply away from China and also discourage reshoring US and European API production base.

One way is to facilitate the establishment of Life Science Technology Park in close proximity of a major University such as University of Madras or Hyderabad. This could be a SEZ on the lines of Software Technology Parks which would provide plug & play facility be open to CDMOs within India and also attract overseas CDMOs. There could be common facilities such as reactors, chemistry, biological & analytical laboratories

Illinois Science+Technology Park (ISTP) could be a model for such a facility. A nodal agency could organise conferences and other events which would bring Indian and foreign CDMOs in close contact to exchange knowledge and open avenues for collaboration. ISTP is dedicated to the cultivation of a multi-cultural environment that will create and sustain businesses from basic research through commercialization. This environment includes world class laboratories, office space and key support amenities. ISTP works closely with North-western University.[75]

The Indian cluster, by working in close collaboration with corporate, not-for-profit, and education partners can create an environment which will propel India into the big league of innovation.[75]

According to a statement by European Fine Chemicals Group (EFCG) in context of response to the draft of The Pharmaceutical Strategy for Europe, a document being circulated by The EC notes that "Whilst the APIs for innovative drugs are mainly sourced from Europe, more than two-thirds of APIs for generic drugs are sourced from Asia. However, for both innovative and generic drugs, most starting materials or critical process chemicals are sourced from Asia. Over recent years, structural shortages of medicines have been building up, because of weaknesses in the supply chain. [76] The recent COVID pandemic only exacerbated this existing problem, highlighting the urgent need to significantly improve the robustness of the pharmaceutical supply chain and allowing the identification of its vulnerabilities. Bringing back to Europe essential processes and key building blocks and leveraging the existing EU manufacturing capabilities can go a long way towards achieving this goal."

Not all European pharmaceutical companies agree with this statement and it is in the interest of Indian government to create conditions which will expand the CDMO industry and give confidence to European manufacturers that not India should be a favoured destination for innovation drug APIs both in technology, price and quantity. This would weaken the forces of reshoring as European companies are looking at millions of dollars in financial assistance in this regard.

Along with API Parks, India should also plan to build technology parks where varied R&D and support services can be located. We must learn from Europe where R&D companies are situated close to universities for greater academia-industry interaction. Such technology parks can be built around IICT Hyderabad and UDCT, Mumbai, for instance.

CDMO sector has been overshadowed by formulations and vaccine sectors within the pharmaceutical industry and by the government. It is the most technologically advanced sector of the industry and can support its entire R&D. It has the potential to develop into a $100 billion industry within a decade provided it gets the support for the government.

The government should look at the various segments of the pharmaceutical industry such as pharmaceutical, biogenerics & vaccine manufacturing and CDMOs as having different expectations from the government and policies should be designed for each segment to grow to its fullest potential.

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Chapter 5 The VUCA Scenarios for Global Leadership

Our pharmaceutical industry has reached a take-off stage where it can strive for global leadership in the generic, vaccine, CDMO and API sectors.

Today, we have an opportunity to take Indian industry to global leadership in generic pharmaceuticals, nutraceuticals and APIs, in spite of threats as described in previous chapters. It requires a strategic change in the direction in which we do business at present. The strategic direction has following elements, which essentially means taking control over end-to-end supply chain:

1. Take common generic (WHO List of Essential Medicines) export manufacturing overseas
2. Synergy of manufacturing & service
3. Build Common Pharmaceutical Manufacturing Zones in overseas Hubs
4. Integration with international regulatory Systems.
5. Complex generic & biopharmaceuticals manufacturing within the country
6. Multiply the business of CDMOs
7. Strive to be No.1 in API manufacturing
8. R&D based pharmaceutical development

5.1 Take common generic manufacturing overseas

As we have shown, simply manufacturing in India and exporting output will progressively bring smaller returns due to the me-too manufacturing in many countries and export from there.

Therefore, we must over the next decade form strong partnerships with local manufacturers and distributors either through Joint ventures with stronger companies or taking over the weaker, undercapitalised companies which today run outdated plants in countries such as Uganda, Tanzania & Kenya on the East Coast and Nigeria, Ghana & Ivory Coast on the West Coast of Africa.

The government should, through its export financing institutions provide concessional loans to entrepreneurs seeking such investments overseas. Overseas investment should be supported in the same was as direct exports as these will provide sustained business for the export of APIs, machinery and knowhow for a long time to come and over a period provide greater revenue as well as protect Indian exports from competition.

One Indian company Hester Biosciences has commissioned an animal vaccine plant in Tanzania and shared its technology with an Egyptian partner to jointly produce and sell throughout the world. The company was generously supported by Gates Foundation which provided $10 million in loan and $4 million in grant out of a total project cost of $18 million. This is a model which other companies should emulate.

Not only generic drugs but Indian manufacturers should follow this example to build strong partnerships in vaccine, medical device and nutraceutical sectors.

Any losses in export earnings from generics will be covered by export of APIs, excipients etc. manifold.

5.1a Investment in African pharma sector highlights growing trend

Today, many sources of funding have become available for seeding pharmaceutical manufacturing in Africa as some of the following examples show. A new trend is ***Impact Investment*** which channels philanthropy funds into socially beneficial businesses which can improve the condition of poor population (Hestor Biosciences' Tanzania project was a recent example).

1. **Impact Investment Consortium**

Three large European investors are teaming up to form a $750 million company to create biopharmaceuticals businesses in Africa aiming to broaden the range of therapeutics available in the underserved markets there. Development Partners International ("DPI") through its ADP III fund, CDC Group, the UK's publicly owned impact investor, and the European Bank for Reconstruction and Development ("EBRD") have joined forces in creating a funding platform with an initial $750 million to fund development of pharmaceutical industry in Africa. Their aim is to increase the availability and affordability of quality drugs and by developing local production and reducing reliance on imported drugs across Africa and reduce the incidences of counterfeit products in the market. It will also look to invest in broad-based and high-growth specialty generics assets across Africa, in high-demand areas such as oncology, autoimmune diseases, diabetes, respiratory issues, and critical care.

Their first investment deal is to create a major new player in the pan-African pharmaceuticals industry. The three founding investors have committed an initial $250 million of capital that have been used to fund the acquisition and combination of Adwia Pharmaceuticals, an Egyptian generic drugs manufacturer, and Celon Laboratories Pvt, an Indian oncology and critical care specialist. The platform will leverage its manufacturing and R&D Center of excellence in India to strengthen its local manufacturing operations in Africa, while capturing synergies from centralized supply chain management and business development. [1]

This first of its kind Pan-African platform is designed to compete in large, fast-growing markets as well as high-demand, differentiated therapeutic areas such as oncology through innovation and cost leadership. The newly created platform will improve the delivery of essential and affordable specialty generic pharmaceuticals across the African continent. This will be supported by up to an additional $500 million fund raise, to fund a strong pipeline of acquisitions, assist in new drug development, and establishment of new distribution channels.

Affordability and counterfeit and two major problems facing drug supply in Africa and India should build its business strategy aimed at these two issues. This is the type of financial model, the government through its EXIM Bank should explore to fund Indian pharmaceutical investment in the African continent. As we have mentioned, with the formation of 52 member African Continental Free Trade Agreement, the entire continent of 1.2 billion people has become on border-less common market paving the way for the establishment of pan-African business entities. This will allow setting up of large-scale pharmaceutical manufacturing plants which can supply medicines throughout the continent and beyond.

2. **International Finance Corporation**

IFC, a member of the World Bank Group is the world's largest multilateral investor in private healthcare, managing an active portfolio of about $1.3 billion worth of health investments. IFC investments in service providers, pharmaceuticals and medical technology are aimed at promoting greater access to affordable, high-quality healthcare.

It is investing $45 million in MS Pharma, a leading Jordanian-based pharmaceutical company, to support its expansion to new markets and promote access to affordable generic pharmaceuticals and healthcare products across the Middle East, Turkey, and Africa.

Another recent investment is a Ugandan pharmaceutical distribution company. The International Finance Corporation plans to invest US$12.6 million in the form of a loan in AK Life, a top pharmaceutical manufacturer, and distributor based in Uganda. The medical company operates under the brand name 'Abacus Pharma' in Uganda, Rwanda, Tanzania, Kenya, and Burundi. Abacus Pharma's primary business is the distribution of generic medicine, imported from China and India, throughout the East African region. The company has a 4,000 m2 warehouse in Uganda and two smaller warehouses in Tanzania and Burundi. Abacus Pharma also manufactures IV fluids, eye, ear, and nose drops from its Ugandan factory.

The investment by IFC will go toward growing its distribution network in East Africa through leasing of new warehouses and increasing its manufacturing capacity by adding production lines for the generic drugs.

Earlier too, IFC had financed a distribution company by investing $3 million in Goodlife Pharmacy Limited, to help the company expand to more than 100 stores within four years to create a Pan-East African retail pharmacy chain.

The East African region has been experiencing a rapid increase in investments in the healthcare industry with many private equity firms and institutional investors putting their funds in the sector. AK Life, which owns Abacus Pharma, has been in operation for 25 years and is majority owned by Carlyle Group, an international private equity company.

3. Africa Healthcare Fund

IFC is helping to provide health services and save lives in Sub-Saharan Africa by creating a new private equity fund that will invest in Africa's health sector. It is a key component of IFC's $1 billion Africa health strategy, which includes improving the operating environment for companies in addition to providing financing. The closing of the fund was preceded by a health roundtable attended by more than 30 major investors and donors including African health ministers and senior officials from Ghana, Kenya, and Mali. The event was an opportunity for IFC to raise the profile of the overall initiative. Potential new partners expressed a strong interest in coming in as investors while other donors were more focused on policy work.

IFC's Partners

IFC's partners in the Health in Africa Fund are the African Development Bank, the Bill & Melinda Gates Foundation, and the German development finance institution DEG. The fund will target commitments between $100 to 120 million over two closings. The first closing of $57 million includes investments from:

1. IFC ($20 million)
2. AfDB ($20 million)
3. Gates Foundation ($7 million)
4. DEG ($10 million)

Managed by Aureos Capital, the fund will invest in health SMEs, such as health clinics and diagnostic centers, with the goal of helping low-income Africans gain access to affordable, high-quality health services. The fund will make about 30 long-term equity and quasi-equity investments, ranging from $250,000 to $5 million, in socially responsible and financially sustainable private health companies. It will invest in a wide range of companies that deliver:

- Health services (clinics, hospitals, diagnostic centers, labs)
- Risk pooling and financing vehicles (health management organizations, insurance companies)
- Distribution and retail organizations (eye clinics, pharmaceutical chains, logistics companies)
- Pharmaceutical and medical-related manufacturing companies
- Medical education
- Providers of medical education

The Health in Africa Fund is part of the IFC-World Bank Health in Africa Initiative under which IFC intends to mobilize up to $1 billion in investment and advisory services over five years, following publication of its 2007 Business of Health in Africa report, which focused on how to improve people's lives by partnering with the private sector.

Besides the equity vehicle, IFC is improving access to long-term financing for smaller companies involved in health care through local financial intermediaries.

Bill & Melinda Gates Foundation

This is one of the major charitable institutions which has invested in building Africa's healthcare assets, both through loans and equity participation. Very recently, the Foundation invested $14 million through equity & loans in India's Hester Biosciences Limited to enter the African animal vaccine market through a manufacturing plant in Tanzania. It has also invested in a Ghanian drug distribution company.

Private Equity

Actis is a leading investor in growth markets across Africa, Asia and Latin America. It has invested in Medic, a Tunisian pharma company with ambition of growth in francophone countries. It acquired a Senegalese pharma company from Sanofi.

Africinvest-Investment in Polymedic which is a Moroccan pharmaceutical company. Polymedic has developed own label generics and products and manufactures originator drugs and other generic drugs for renowned pharmaceutical companies (Aventis, Leo, Bayer, Schering...). Today it boasts a portfolio of 130 Market Authorizations (MAs) involving several dosage forms: tablets, capsules, syrups, ointments and injectables drugs.

It has also invested in Lagray Chemical, a Ghanaian pharmaceutical company and Inpha-Medis , an Algerian pharmaceutical company.

Rx Healthcare is a joint venture between EFG Hermes Private Equity, one of the region's leading private equity players, Dr. Hatem El Gabaly, former Egyptian Minister of Health and Dr. Hesham El Kholy a veteran of the healthcare industry in Egypt and the MENA Region.

Global Healthcare Investment Fund (GHIF) - The Global Health Investment Fund (GHIF) is a $108 million social impact investment fund designed to provide financing to advance the development of drugs, vaccines, diagnostics and other interventions against diseases that disproportionately burden low- and middle-income countries.

These are only some of the funds operating in Africa and the number of funds as well as the size of funds will increase substantially after the launch of AfCFTA.

Indian firms with a successful track record should seize the opportunity for JV and buyouts of pharmaceutical assets in Africa through access to impact funding.

5.1b Government of India's initiative

At the third India-Africa Forum Summit in New Delhi in October 2015, where 41 heads of state and government were present, as were officials from 54 African countries, Prime Minister Narendra Modi announced that in addition to the on-going credit programme, India will offer concessional credit of $10 billion over the next five years and increased grant assistance of $600 million. This will include a $100 million India-Africa Development Fund and a $10 million India-Africa Health Fund.[2] A part of this fund can be utilized for establishment of greenfield and brownfield pharmaceutical manufacturing projects in Africa supported by investment in distribution and retail.

India can play a major part in two of the major drugs distribution problems in Africa, that is affordable medicines and counterfeit.

According to an article in The Sunday Guardian on China's Belt & road Initiative (BRI) in Africa " As for the future, China, blinded by a bloated sense of self-importance, cannot see that the type of infrastructure that will be welcomed post-virus is "soft infrastructure"—institutions that rely on human capital and services, including healthcare, financial systems, education systems, law enforcement and government services delivered direct to the public. China knows nothing about them".[3] This is where India excels.

India is providing about $1 billion in aid to Africa annually. Much of it is in the form of building "invisible" infrastructure assets such as hydropower plants and transmission lines etc. Our aid is not visible to the African people. On the other hand, thousands of Kenyans travel between Nairobi & Mombasa every day on Chinese built railway line. Indian government should channel a large part of its aid to Africa through "visible projects" such as hospitals, vocational education such as pharmacy schools, pharma logistic supply chain and building the African entrepreneurial class through funding of pharma retail chains. One 500 bed tertiary care super-specialty affordable hospital in a central location can provide referral service to thousands of patients every year throughout the entire East African Community (EAC) for at least 25 years at a cost of $10 million. 10 such hospitals at a cost of $100 million over 10 years can create thousands of jobs for the locals and create immeasurable goodwill and business opportunities.

India has a strong service sector which can be deployed in Africa. It can be a leader in providing " soft infrastructure" in Africa which will provide s strong base for countering

Chinese influence which is now being increasingly seen as predatory in nature. It is the typical behaviour of the moneylender in rural India. India's "visible aid" will touch the lives of millions of African people directly and counter the Chinese influence through BRI. Among the top Goals & Priority Areas of Agenda 2063 of The African Union[4] are:

1. Healthy and well-nourished citizens
2. Manufacturing / Industrialization and Value Addition

Indian "soft infrastructure" development should also be aligned with the aspirations and goals of the African people. Africa has:

- 17% of the world's population
- 30% of the world's disease burden
- 3% of the world's total health expenditure

India can play an important part in both these sectors by promoting healthcare infrastructure such as affordable hospitals, medical and allied skill development and manufacturing & distribution of low-cost quality drugs. India should play a bigger role in supplying vaccines to the poor African nations. According to an article in The Diplomat [34]"African states already have some level of pharmaceutical production and Egypt, Morocco, and South Africa are in the process of signing deals to manufacture COVID-19 vaccines. Many African countries want to develop their pharmaceutical sectors – not just get handouts. Doing so will also induce positive spill-over effects such as creating jobs and facilitating technology transfer. China is a key partner for Africa's pharmaceutical sectors, alongside others such as India. As well as already shifting its surplus manufacturing capabilities abroad, China wants to become a lead player in the global pharmaceutical market within 10 years. Making Africa a key area of relocation for pharmaceutical production, while speeding up and initiating more deals to manufacture COVID-19 vaccines in African countries that have pharmaceutical production capabilities must be a top priority".[5]

The Indian private sector is already present in African healthcare & pharmaceutical sectors and these should be further expanded to other territories where not present at present. The private sector should be encouraged to move boldly into Africa's healthcare sector and government agencies such as EXIM Bank can play a major role to make it happen. However, it requires a national strategic plan for African healthcare development. Healthcare, being a service sector can also create more jobs and entrepreneurs for local population than investment in other forms of infrastructure.

Affordable Medicines-There is little state control over the prices of drugs. Since most of the distributors and retailers are undercapitalised, they are unable to stock a large quantity or variety of drugs. This allows volatility in prices from 200-500%. One study has shown that the price of a paracetamol tablet in Africa costs more than the same in UK.

Counterfeit Drugs – Studies have shown that almost 40% of all drugs sold on the African continent are counterfeits. This is a big loss both financially and poor efficacy of medicines. Much of the counterfeiting takes place at distribution stage where counterfeit drugs are mixed with quality drugs.

Any initiative of the government of India in collaboration with the pharmaceutical industry which reduces the profiteering as well as introduction of counterfeit drugs will be welcomed by all stakeholders in Africa's healthcare, that is the governments, patients and the NGOs.

Our suggestions follow:

The government already has a template to solve these problems in Africa, its "Pradhan Mantri Bhartiya Janaushadhi Kendras." It makes available quality medicines at affordable prices for all, particularly the poor and disadvantaged, through over 5,000 exclusive outlets so as to reduce out of pocket expenses in healthcare. This will also create exclusive outlets for Indian medicines, both imported and produced locally.

5.2 An integrated Manufacturing & Service Strategy

We propose that the government, in partnership with African governments should formulate an integrated strategy to provide quality but low-priced Indian medicines and medical consumable through distribution & retail outlets managed by African entrepreneurs. Our outline for this scheme is as follows:

1. The Indian government should facilitate the establishment of common warehouse & distribution centre for medicines in Free Trade Zones located within East as well as the West Coasts. The government already has a Market Access Scheme which can be used for the establishment of common warehouses. These schemes should be extended to logistics companies which are ideally suited to undertake this activity rather than Export Promotion Councils which can oversee such an arrangement.

   These warehouses should provide value-added services retail packing & printing and also stock common medical & surgical consumables on behalf of exporters from India.

   Importers can take supplies from these warehouses institutional and retail sales. Since availability of common drugs (WHO List of Model Drugs) can be assured, this will provide a disincentive for frequent price rises and profiteering.

2. The government in collaboration with UN agencies such as UNIDO and African governments should establish Schools of Pharmacy at 3-4 select locations for imparting a limited curriculum consisting of pharmaceutical, management and I.T. syllabus. The aim is to provide a training ground for African entrepreneurs to enter retail pharmaceutical trade. This will provide an excellent avenue for self-employment.

3. The government should create a revolving fund for the establishment of People's Pharmacies (Jana Aushidhi Stores) which will allow the graduates of these schools to establish their retail outlets. The Indian government can provide the initial seeding of these shops with Indian products of a certain value as a loan. Local governments, NGOs and international agencies of UN such as UNIDO can provide other financial & locational assistance. To start with, such pharmacies can open within the premises of Government and non-governmental hospitals & healthcare centres.

If Indian government or Indian private sector is financially involved in establishment of these pharmacies, it can ensure signing of agreements exclusively stock & sell Indian Medicines and Indian consumables as well as home diagnostics etc. This integrated approach would make the outlets more financially secure as well as deny space to rival countries such as China.

The scheme should be tested in one or two of the smaller countries such as Malawi (among the poorest countries in East Africa) or Rwanda as a showcase to other African nations.

This scheme can result in the following advantages for India at a much lower cost that the aid provided by India in infrastructure development.

1. This will be visible aid in public view designed to solve the basic problems of the African people and create immense positive goodwill for India. We can counter the Chinese built Nairobi-Mombasa railway line which is the visible side of Chinese influence through opening of hundreds of People's Pharmacies.
2. An exclusive chain of outlets for Indian products where other countries, especially China cannot enter.
3. Provide quality medicines at low prices to most of the population with fool-proof supply chain to avoid entry of counterfeit drugs.
4. Provide self-employment generation facility for African youths, a key African developmental objective.
5. Help in solving some of the most pressing developmental problems in Africa.
6. Facilitate Indian exporters to sell more in Africa
7. Chinese and other exporters such as Bangladesh sell on price alone which in future will bring diminishing returns while integrated approach which create a value-added route will be able to retain remunerative prices for Indian exports. China is good at manufacturing but does not have the depth of capability to move into service sectors.

One company already follows this model successfully as depicted below. It manufactures drugs at its plant in India. These are delivered to strategically located warehouses in seven countries which provide the drugs for sale through its exclusive retail stores which number 14 at present in different countries. The success of this model is visible in running retail outlets even in countries ravaged by civil war such as Democratic Republic of Congo.

This integrated model provides a strong moat against incursions by Chinese and other exporting countries into India's export share. Indian companies should follow the **Co-Co** principle of Cooperative Competition. Compete in the marketplace but cooperate at the backend. This will allow even smaller companies to sell drugs profitably.

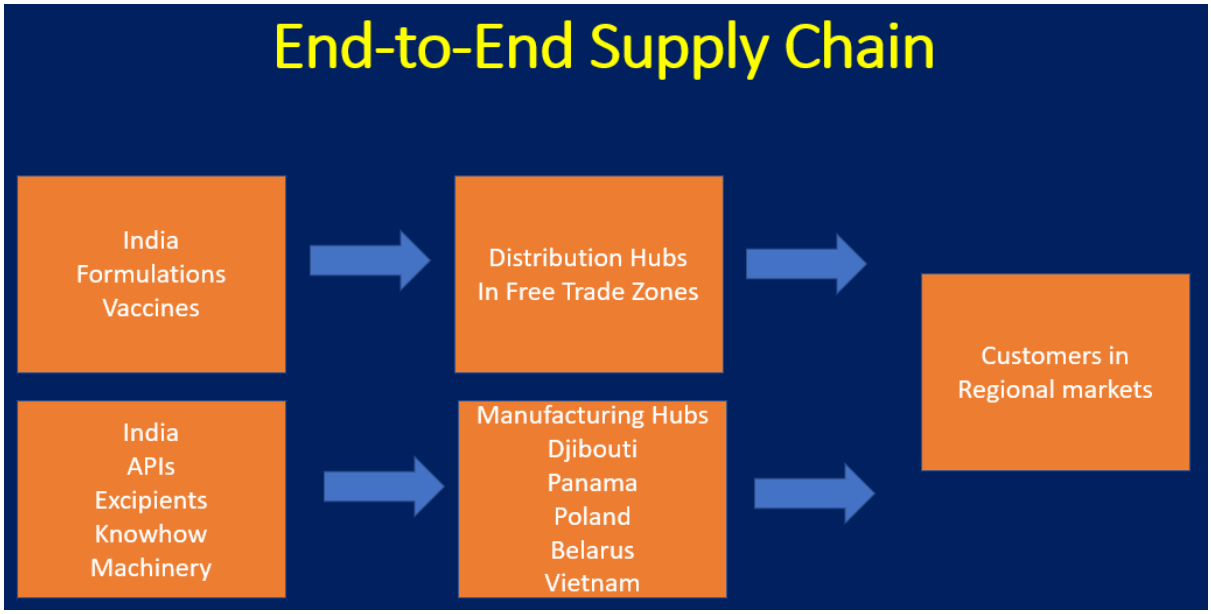
The system can be undertaken by one company or a network of drug companies, logistics companies and local business community at the distribution and retail end. Pharmexcil can facilitate its introduction and bring diverse interests together.

Indian entities can easily obtain international funds, especially Impact Investment as described above due to their proven successful operations and since the outcome will be felt directly by the poor.

We suggest that at least 50% of the aid should be spent on healthcare, building hospitals & pharmacy schools and providing concessional loans through EXIM Bank for construction of pharmaceutical assets in Africa, not only manufacturing facilities but also India-centric supply chain. From export point of view too, this makes sense in the long term as our supplies for APIs, excipients, machinery & spares and knowhow can more than make up for the loss of direct formulations exports. In API exports alone, we can create an African market for $10 billion by 2030. As we have shown earlier, more international funding is being channelled to African nations and if we don't take the lead, someone else will, such as China.

5.3 Build manufacturing Zones in select global hubs.

The time has come for India to take centre stage in the manufacturing sectors where we have displayed global competitiveness. For long term sustainability of this lead, Indian government should facilitate the establishment of several exclusive pharmaceutical and allied products manufacturing & distribution zones in strategic locations such as Panama, West & East Coasts of Africa, Poland, Belarus and Vietnam. The aim is to provide a strong control over the supply chain and prevent competitive countries from encroaching on India's markets.



As more and more countries sign regional trade agreements, they will practice protectionism as well as join pharmaceutical harmonisation programs such as PIC/S, it will be become more difficult to break into existing and new markets through direct exports.

China has already made a big start by building a pharmaceutical manufacturing zone in Ethiopia and three companies have already opened large-scale formulation plants.

Indian companies, in Africa, had largely concentrated their activities in South Africa which was the most attractive country till a decade back. Today, the centre of gravity is shifting towards countries like Nigeria, Ethiopia, Morocco and Kenya and with AfCFTA more manufacturing will take roots in countries north of South Africa.

Elsewhere too, larger regional markets are taking shape and Indian manufacturers should enter as a community rather than piecemeal to jointly undertake backend and liaison functions in those regions.

Therefore, we propose establishment of common manufacturing & distribution zones to take advantage of these developments. In such cases, we should not only consider the national business opportunities but how to leverage the local manufacturing to take greater share of the regional common markets

A beginning has already been made in this regard by a group of companies which have jointly negotiated for a manufacturing zone in Mexico. Six generic drug makers, namely Dr Reddy's, Zydus Cadila, Glenmark, Torrent, Hetero and Ackerman have signed a deal with the state of Hidalgo, Mexico, to establish a pharma hub for manufacturing and logistics amid the country's push to establish a major foot hold in one of the largest and fastest growing pharmaceutical markets in the world. Not only, will these companies have access to a $10.6 billion Mexican drug market but Mexico being a member of two major Regional Trading Blocs, The Pacific Alliance(210mn.pop.) and United States–Mexico–Canada Agreement (USMCA-POP.500MN.), this cluster can reach out to larger regional markets.

We propose more such clusters of Indian pharmaceutical companies to be established. We are giving below the rationale for such an exclusive zone on both coasts of Africa.

Today, it more important to site industrial clusters at locations from where distribution and supply-chain can be cost-effective, both for incoming material as well as output and the places chosen should provide secure environment for assets and manpower.

In Africa, small countries such as Rwanda and Botswana have shown they are capable of fast growth and leverage their geographical position in the regional economies.

Both Djibouti and Togo fulfil these conditions. They look small with very little to provide in the size of national markets, but their markets should be seen within a borderless smaller Common Market for Eastern and Southern Africa (COMESA) & ECOWAS economic communities respectively as well as the larger AfCFTA trading bloc.

Comesa is a common market of 21 African countries with a total population of 390 million of which Djibouti is a member. Likewise, Ecowas is a common market 14 countries of 387 million population of which Togo is a member. Both the countries have enjoyed peace for several decades. Now, with the African Continental Free Trade Agreement (AfCFTA a population of 1.2 billion can be reached.

Both Djibouti and Togo are deep water ports, and these countries are looking at their strategic location and investing heavily in logistics infrastructure to turn themselves into the “Dubai” of Africa. They have launched integrated logistics and Free Trade Zones to take advantage of the future industrialisation of Africa.

Djibouti is the port for the landlocked Ethiopia, the second most populated country with a railway line to Addis Ababa. On the other hand, Togo is sandwiched between two of the largest markets on the West coast, Nigeria and Ghana.

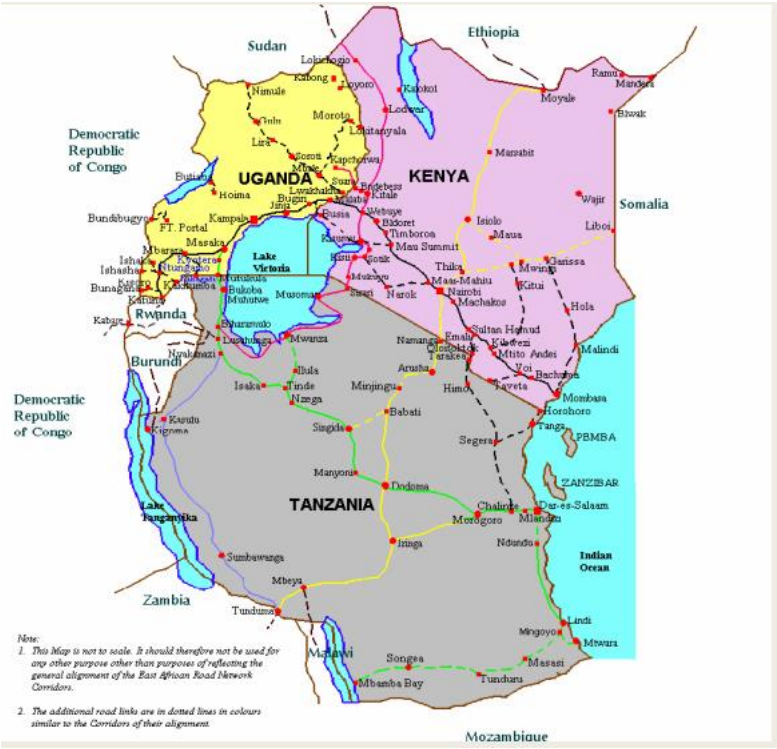
These are only two examples to show that smaller countries can also give big dividends in an inter-connected world.

5.3a East African community (EAC) as a manufacturing hub

Another possible location is within East African Community.

In sub-Saharan Africa (SSA), where the overall pharmaceutical market size is worth US$ 20 billion annually, the production of life-saving medicines is furthermore concentrated in very few countries: 50 per cent of pharmaceutical manufacturing takes place in South Africa and an additional 40 per cent in Nigeria, Ghana, Kenya and Uganda combined. The growth is estimated at 12% per annum.

EAC is a regional trade bloc consisting of Tanzania, Kenya, Uganda, Burundi, Rwanda and South Sudan, which is not only the most peaceful region in Sub-Sahara Africa but has also experienced one of the fastest GDP growth in Africa. This is also a region with the highest concentration of expatriate Indian population, deeply integrated in trade & commerce.



East African Community (South Sudan joined in 2016)

EAC has a population of 177 million (2019) which will rise to 270 million in 2030. The growth rate is averaging 6%+ for past 10 years. Out of 35 manufacturers (33 in Kenya), only 2 have WHO-GMP accreditation.

The combined pharmaceutical market size of the East African Community (EAC) in 2017 was about US$ 4 billion with a big volume spent on essential medicines, particularly Antibiotics, Antimalarials, Anthelmintics, Disinfectants, Analgesics and Anti-Retroviral medicines. The East African Community also has the advantage of harmonised registration and inspection guidelines. With a 12% growth rate, the market will grow to $10 billion by 2030.

In 2012, the EAC designed a Regional Pharmaceutical Manufacturing Plan of Action (EACRPMPoA) to guide partner states of the EAC towards collective and synergistic evolution of an efficient and effective pharmaceutical production sector, capable of making significant contributions to meeting national, regional and international demand for medicinal products until 2027 and beyond. The action plan is closely aligned to the short, medium and

long-term goals and policies of the EAC and individual member states and serves to complement past and present regional economic community and pan-African strategies.

The plan has set out the following primary strategic objectives:

1. Promotion of competitive and efficient pharmaceutical production regionally; Through usage of incentives such as preferences of up to 15 per cent on tenders for locally manufactured products

2. Facilitation of increased investment in pharmaceutical production regionally; this is through restricting certain imported products that can be locally (regionally) manufactured

3. Strengthening of pharmaceutical regulatory capacity in the region;

4. Development of appropriate skills and knowledge on pharmaceutical production in the region;

5. Utilisation of TRIPS flexibilities towards improved local production of pharmaceuticals, and

6. Mainstreaming innovation, research and development within regional pharmaceutical industry.[6]

The blueprint for the development of the pharmaceutical manufacturing sector in the EAC have the following four targets to be achieved by 2027 (may be delayed due to Covid).

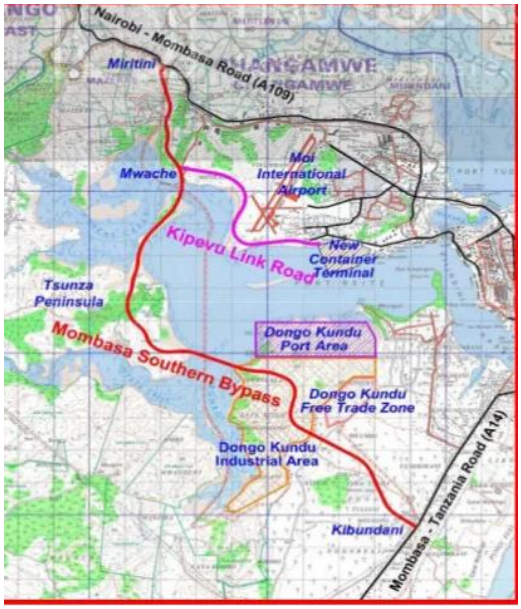
1. Reduce imports from 70% to less than 50%

2. Support expansion of product portfolio to cater for 90% of disease burden.

3. Governments to procure at least 50% from local manufacturers.

4. At least five companies to produce more advanced formulations such as delayed release formulations, small volume injectables, vaccines, etc

Looking at the growing market in EAC and its neighbourhood, Indian government should look at establishing a pharmaceutical zone at one of the upcoming Special Economic Zones such as Mombasa (including Dongo Kundu Free Port) or Lamu Port which is being developed to decongest Mombasa. Such an infrastructure can supply medicines to both North & South coast of East Africa as well as landlocked countries of DRC (Eastern side), Zambia etc.



Dongo Kundu SEZ is being constructed with assistance from Japan and India should examine the construction of a Pharma zone in this area.

African pharmaceutical market will grow to $45 billion by 2030 as a conservative estimate and $65 billion as optimistic estimate. India should aim for 60 percent of this market either through direct exports (30%) and through manufacturing on the Continent (70%). This local production should consist of WHO List of Essential Medicines which has approximately 500 drugs.

Pharmaceuticals alleviating chronic conditions such as hypertension and diabetes represent lucrative growth opportunities in the Sub-Sahara region, as do those for the therapeutic segments including anti-infectives, cardiovascular, diabetes, respiratory, oncology and central nervous system medicines. The anti-infective pharmaceutical market, which comprises antiretrovirals, antimalarials and antibiotics, is expected to represent close to 45 per cent of sales, remaining the primary market due to the high malaria burden. The cardiovascular segment represents 11.8 per cent of sales, and the central nervous system and oncology 4.3 per cent and 3.3 per cent respectively. However, oncology medicine is forecast to generate growth of 12.9 per cent per annum, driven primarily by an expanding middle class and underlying strong economic growth. The market will grow sharply after the signing of African Continental free Trade Agreement (AfCFTA).

7.3b Ghana as Manufacturing hub on the West Coast

Ghana not only is the most peaceful country on the West coast of Sub-Sahara Africa, it had the highest GDP growth rate in the world in 2019, prior to Covid pandemic. Although Nigeria is the largest market in Africa, its political, security and economic prognosis is fluid, to say the least. After, AfCFTA implementation, the size of the country does not matter so much as the entire African market will be open to all manufacturers, wherever they are located. Taking advantage of the changes in the business environment, Indian cashew processors have also focused on Ghana as a manufacturing hub where raw cashew from the entire West Africa can be brought for processing.

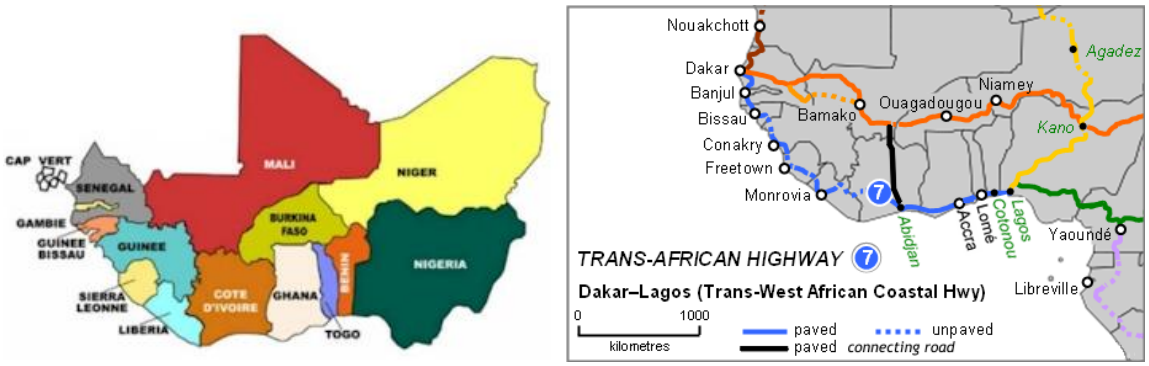
Ghana itself, is an attractive market of $606 million with a growth rate of 9.1% and is expected to reach $941mn. by 2024 (pre-covid data). Out of this 60% market is generics, innovator drugs 9% and balance OTC.

Across the region, generic drug makers will increase production to meet the rising demand and will be further helped by cost-containment measures encouraged by governments. Per capita spending on medicines will increase from USD20 in 2019 to USD41 by 2029, though remaining low by global standards.

Ghana has the ambition of being the ECOWAS hub for pharmaceutical production. The government has taken several policy decisions to encourage local production.

- Expanding of the list of raw materials exempt from VAT to accommodate inputs to support the local pharmaceutical manufacturing industry
- Providing additional funding to some local pharmaceutical companies to build new production plants and raise their standard of production towards international quality standards. The provisions will be made by Exim Bank Ghana.
- Rules are being implemented that ensures Ghana's Ministry of Health procures more locally manufactured medicines
- The government is looking to allocate a designated pharmaceutical manufacturing zone
- Reforming the national health insurance scheme

A small export market is also developing with exports are forecast to increase from $3.8mn in 2019 to $5.8mn by 2024, at a CAGR of 8.8%.[7]



Ghana is situated in the midst of a growing market

Ghana is a member of The Economic Community of West African States, also known as ECOWAS, is a regional political and economic union of fifteen countries located in West Africa with a population of over 387 million. Ghana is situated in the midst of this fast-growing region. Although Nigeria is the biggest market in this region, its political and economic see-saw condition makes is a poorer location. However, the entire region is well connected with Trans-Africa Highway. Out of 166 manufacturers in the region, a majority 120 are in Nigeria and 36 in Ghana. The large number of manufacturers in Nigeria give the impression of a healthy & vibrant industry but ground realities are different. The capacity utilization is below 40%, the plants are old, and companies undercapitalised.

Fitch Solutions estimates the ECOWAS market to grow from USD2.8bn in 2017 to USD5.3bn.in 2027.[8]

With the possibility of supplying to the larger regional market, harmonised registration process and appearance of new sources of funds especially through Impact Investing, there is a viable case of locating pharmaceutical plants in the region, especially for producing WHO List of Essential Drugs. Ghana has started a feasibility study to manufacture its own vaccine for covid-19 and to reduce Ghana's and Africa's reliance on foreign vaccines in the long-term.

Some companies have already started consolidating their positions looking at the overall future of integrated African Market. For the first time, a plant in East Africa, Cipla's manufacturing company in Uganda has received ECOWAS regulatory authority to market antiretrovirals and malaria medicines throughout the ECOWAS region. It has also received approval from The ZAZIBONA process which is a collaboration between national medicines regulatory. authorities (NMRAs) in Botswana, Namibia, Zambia, Malawi, Mozambique, Zimbabwe and South Africa.[9]

5.3c Africa counterfeit Problem

In addition to the low pharmaceutical production capacity, the African continent is confronted to an even bigger problem – counterfeits. Counterfeited medicines represent a US$ 1 billion (conservative estimate) industry worldwide where over 40 per cent of those medicines are sold in parts of Africa. According to the World Health Organization (WHO), substandard and counterfeited anti-malarial medicines cause about 120,000 deaths every year in Africa.

African governments have become increasingly aware of the problems posed by counterfeiting and several initiatives have come to exist including the Anti-counterfeit Network Africa, which was launched in Uganda in February 2016.

A larger Indian role in African manufacturing would also address this major problem.

5.3d A fresh look at Africa

Looking at the projection of demand for drugs in this continent, it is imperative that the government and the pharmaceutical stakeholders look at Africa afresh and take lead in pharmaceutical production & distribution in Africa.

India enjoys an excellent reputation in Africa, especially after the overbearing and opaque transactional experience with China which have led to debt trap in several countries. Now poor countries are trying to finance their recovery from the covid-19 pandemic without deepening their debt or their dependence on China. India's forays are tiny in comparison—around 7% of China's total stock in FDI in developing economies (excluding investment in Hong Kong which is sometimes included). But its approach has lessons for foreign investors trying to go about their business without raising alarm bells, though the FDI has topped $13 billion.

India's entry into Africa is seen as less threatening compared to China is that India's influence which is sprinkled throughout Africa is led by the private sector rather than the predatory & opaque giant state companies of China. Companies such as Tata & Mahindra

Group, Airtel, Cipla, Sun Pharma and many others have laid strong foundations in Africa and they will enjoy the fruits of the unified market of 1.3 billion people in years to come.

Similarly, in healthcare Apollo Hospitals and Dr. Agarwal's Clinics have done pioneering work. Indian businesses are purely commercial rather than an extension of foreign policy as in China. The implication—that, unlike Chinese firms, Indian companies do not take orders from their home government—makes them less threatening and more welcoming.

They have a reputation for doing a better job than the Chinese at hiring and buying locally. There is some truth to that. In 2006 the World Bank surveyed almost 450 businesses in Africa. On average, Chinese firms employed almost a fifth of their workers from China and other East Asian countries, whereas Indian firms brought less than 10% of their workers from India. The Chinese businesses imported 60% of new machinery from China; their Indian peers bought just 22% from India. That trend continues today, says Harry Broadman, the economist who led the research.

The resentment against India which had its peak in the 70s has been replaced by pragmatic attitudinal changes both in African and expatriate Indian minds. The government in Kenya has gone as far as recognising Asians as the country's 44th official tribe.[10]

Therefore, India must build on its goodwill in Africa to be the towering collaborator with the African governments and the emerging private sector in the overall healthcare space, from hospitals, medical colleges & pharmacy schools to affordable pharmaceutical & medical device manufacturing & distribution. This will prove to be a win-win proposition for both India and African nations. The overarching Indian strategy should be to deny space to our No.1 competitor China to gain a foothold in this $100 billion healthcare market by 2030.

Similar clusters can be created in Central Europe such as Poland or Hungary in the European Union; Belarus in the Eurasian Economic community and Vietnam in the newly formed RCEP Free Trade Area.

These assets will create a long-term market for our APIs, excipients, know-how and machinery. They will also put India in a commanding position to take on the rising competition to its exports and increase market share. If India can partner with the respective countries, we are confident that funding from international sources would be forthcoming. Especially in 2022, European Union is likely to announce financial incentives for on-shore production of medicines & API.

5.4 Integration with International Regulatory Systems.

It is imperative that the government should take action to enrol as members of ICH and PIC/S. This will give a strong message to the international community that the drugs produced in this country have the highest quality and at par with the reference drugs. This issue is discussed in detail in chapter 6. This is especially important in the light of China, which is a major competitor in the API business will also provide strong competition in the generic space is not a member of either and is not likely to apply soon. Thus, India can take a lead in the international markets.

This membership would make our drugs more accessible in the international markets and provide highest level of quality for the domestic market. The government can provide incentives and assistance for smaller companies to reach WHO-GMP level of compliance.

5.5 Complex Generic & Biogeneric Manufacturing Within the Country

As already discussed, there is lower level of competition in these segments of the pharma industry due to the high investment and knowledge required. We need to invest more in the biogenerics industry to derive substantial benefits, especially in the US market, the largest in the world. Since biosimilars are not precisely like originator drugs, patent holding companies have put in place IP related obstacles which should be overcome as a joint legal effort of various countries before the market opens up. The export outlook is not very positive at present but should open in about 4-5 years.

Indian biogeneric sector is growing AT 12% It requires both PLI as well as R&D support from the government. India needs to collaborate more with like-minded countries such as Korea, Taiwan, Brazil etc. even though India has the most advanced biogeneric pipeline among these countries. The government should facilitate this exchange through a nodal group such as the International Solar Alliance, which it pioneered. Such an organisation with affordability as a key theme would be supported by a wide range of international organisations. It should be possible to challenge innovator companies in the US through such an organisation. It should be possible to take 20% of the complex generics market of $142 billion and 10% of biogenerics market of $150billion by 2030.

5.5 CDMO-The big growth area

Contract Development & Manufacturing Organisations (CDMO) is an invisible & neglected sector of the pharmaceutical value-chain. However, India is ideally placed to derive the maximum advantage of outsourcing of various services. This is a high-tech area, and the Government should support this industry by making available a wide range of both entry level and middle level personnel. This sector will experience global shortage of skills within this decade and export of skilled personnel can be a major source of revenue. CDMO can reach a revenue $100 billion by 2030. The government can support this sector by creating at least one Pharmaceutical Technology Park on SEZ concept with integrated R&D, education and common facilities.

5.6 Strive to be No.1 in API manufacturing

Over 30 countries are engaged in major production of generic formulations. We estimate over 100 new plants will be established by 2030. Most of these countries have no plans for API industry. They will source either from India or China. Our PLI thrust should be taken to its logical conclusion by creating the world's largest API industry, not only in terms of scale but also the widest range of products on offer. Thousands of APIs are required in small quantities, that is kilos rather than tonnes, both for preclinical purposes and also generic manufacturing. The government should provide incentives to SMEs to produce such drugs which in aggregate have considerable import substitution value but also export.

The government should also protect this market not only in India but also our exports by ensuring that China does not derail this revival.

We estimate an opportunity of $100 billion worth of API for domestic industry & exports.

5.8 R&D based pharmaceutical development

Education, training, research & development are the only sectors where there is no depreciation of capital. In fact, with time the knowledge only accumulates and appreciates. These had been low-priority area of investment, both public and private. One billion dollar in investment can provide at least ten times the revenue in export of manpower itself by 2030, much more in application of this knowledge to the growth of our pharmaceutical manufacturing & service sectors, especially the SMEs.

It is our estimate that with proactive government policy and long-term investment in pharmaceutical assets as suggested, the country can see a global revenue of upwards of $300 billion from the entire pharmaceutical sector by 2030. It can be No.1 export segment of India.

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Annexure-I

Foresight Study of Top Generic Producers in the non-US/EU/Japan in 2030

These countries will reduce import of generic medicines as well as provide competition to India in regional or global export markets. The list has been made considering expanded markets due to Regional Free Trade Agreements.

None of them except China has any worthwhile API industry and are expected to import up to 90% of their requirements.

Country	**2019 market $ bn.**	**Growth**	**Generic Market**	**2030 market estimate $ bn.**	**Domestic generic production estimate % in 2030**	**Export Ambitions**	**Notes**
Africa							
Egypt	3.18	13%	33%	11	100%	Mena Sub-Sahara Africa	MENA's biggest pharma city
Algeria	3.33	13%	50%	12	90%	West Africa	New Ministry of Pharma Ind.to promote regional hub
Morocco	1.28	4%	45%	2	80%	West Africa	
Tunisia	0.80	9%	58%	1.9	80%	West Africa	
Kenya	1.0	10%	64%	2.5	70%	East Africa	3rd largest in Africa
South Africa	3.5	6.5%	71%	6.5	70%	Africa	Member PIC/S
Ethiopia	1.0	15%	NA-Est. over 50%	4.0	50%	Africa	Building African's largest pharma hub. Only country in Africa to implement pharma strategic plan
Tanzania	0.9	8%	NA Est. over 50%	2.0	40%	Regional	
Ghana	0.59	9.8%	64%	1.6	80%	West & Central Africa	West Africa pharma hub. Pharma Mfg. Zone
Nigeria	2.0	9.1%	80%	5.0	90%	Regional	14 drugs in import prohibition list
Uganda	0.47	4.7%	80%	0.75	90%	Regional	
Asia-Pacific							
Indonesia	9.9	10.2%	77	26	90%	Regional	Member PIC/S
Thailand	5.9	8.7%	57.2	12	80%	Regional	
Malaysia	1.0	9%	60	2.5	80%	Regional	Member PIC/S
Vietnam	5.2	12.2%	80	16	80%		
China	123	8.2%	84%	400	90%	Global	To challenge India by 2030

South Korea	24.3	7.1%	58.3	48	NA		
Middle East							
Saudi Arabia	8.2	11%	20	24	40%	Regional	Regional pharma hub
Turkey	5.47	17.7%	30	27	90	Global	
Jordan	0.58	6%		1.0		Global	
Qatar	0.6	14%	NA	6.0	90	Regional. GCC	
UAE	1.6	14%	NA Est. 50%	6.0		Regional GCC	
Iran	2.5	14%	NA Est.80%	6.0	90	MENA Central Asia.	US sanctions has reduced exports
South America							
Argentina	4.6	11.2	NA	12.5	70%	Regional	Discourages import from India
Brazil	34.5	8.5	25	80.9	80	Regional	Developing pharma production hub
Chile	2.4	12.4	43	9	80%	Pacific Alliance	
Colombia	4.2	7.3	44	4	80%	Pacific Alliance	
Mexico	17	7	30.8	35	50%	US, Canada, Pac. All.	Indian manufacturing hub
Europe							
Russia	27.6	9.5	59.8	66	90%	Central Europe, Central Asia	National Pharma 2030 Strategy

NOTE: This report is in series to our earlier one "**FUTURE OF TELECOM**" published in June 2020 https://bwmedia.s3-ap-southeast-1.amazonaws.com/Sectoral+Report-Future+of+Telecom_ver14.pdf