Indian Biotechnology

The Roadmap to the Next Decade and Beyond

A Report by Association of Biotechnology Led Enterprises (ABLE) for the Department of Biotechnology, Government of India

May 2012

सत्यमेव जयते

Department of Biotechnology
Ministry of Science and Technology
Government of India

ABLE Association of Biotechnology Led Enterprises

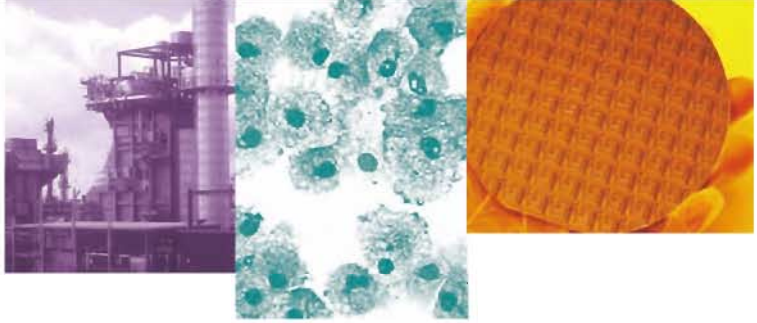
The collective face of the Indian Biotech Industry

Department of Biotechnology,
Ministry of Science and Technology
Government of India,
New Delhi, India

and

Association of Biotechnology Led Enterprises,
Bangalore, India

This report was prepared by ABLE and authored by
Dr. Satya Prakash Dash, Chief Operating Officer, ABLE.



contents

Foreword

India is at the threshold of a decade of innovation and Indian biotechnology is poised to provide solutions to myriad challenges that we as a country face be it in health, food or fuel security. The solutions that India can offer will have both national and global relevance.

The Government of India (GOI) through the Department of Biotechnology (DBT) has helped nurture the biotechnology field in India since its inception in 1986. India now has a large pool of outstanding people and infrastructure, created through several innovative schemes, which can serve as the capstone for the future growth of this sector and help India achieve its vision to become a bio-economy and to extend benefits of biotechnology to our people. With the right support from GOI, the combined revenues of the biotechnology and healthcare sectors could reach $100 billion by 2025. The components of this bio-economy will involve all aspects of the biotechnology sector, from new forms of vaccines, novel protein therapeutics, bio-similar manufacturing, improved plant hybrids and renewable energy from biological sources.

The frontier areas of biotechnology, such as stem cells, synthetic biology and systems biology will also play an increasingly important role in the emerging bio-economy in India and DBT is already focused on providing support to these emerging areas. DBT has established several innovative industry focused schemes such as SBIRI, BIPP and Ignition Grant. These programmes are helping the industry to proactively incorporate innovation as the driving force for R&D, enabling the industry to build capacity for future growth and are creating platforms for positive collaborations between industry and academia for translational biotechnology.

This report captures the emerging global and Indian scenarios in all aspects of biotechnology and recommends several policy interventions which have the potential to catalyse the transformation of the Indian biotechnology sector.

DBT is committed to building and fostering an enabling environment for biotechnology in India. This report, created by the premier biotechnology industry organisation ABLE, academics, the Department of Biotechnology and BIRAC is certain to focus stakeholders' efforts in distilling the path ahead to establish India as a global destination for innovation in biotechnology.

Dr. M. K. Bhan
Secretary
Department of Biotechnology,
Government of India,
New Delhi

With the right support from GOI, the combined revenues of the biotechnology and healthcare sectors could reach $100 billion by 2025.

Foreword

Biotechnology as a sector is growing steadily and has enormous potential to provide solution to several challenges in the health care, food, energy and related sectors.

It is important to create a road map which sets out the strategies and actions to accomplish the goal of exponentially expanding the growth of the sector. This report by ABLE would be very useful since it highlights the current status of the biotech sector in India, addresses the specific gaps and challenges and gives clear recommendations on the directions to accomplish the desired goals.

We hope that this would be useful to industry, academia and all other stakeholders including the policy and decision making bodies, and would help in creating a road map for the biotech sector for the next decade.

Dr. Renu Swarup
Advisor
Department of Biotechnology
Government of India,
New Delhi

This report by ABLE would be very useful since it highlights the current status of the biotech sector in India

Foreword

Indian Biotechnology is at an interesting inflection point. While, the academic focus in biotechnology in India is about as old as the sector, i.e., about 25 years, the industry has also blossomed in the last decade. At the start of the new millennium, the then Prime Minister challenged us in his poetic style that if IT (information technology) stood for India Today, then BT (biotechnology) has to stand for Bharat Tomorrow.

The Department of Biotechnology (DBT) rose to the challenge and ten years later we have made enormous advances in capacity building in our academic and research laboratories. Large outlays for the sector were obtained in the XI plan and state of the art labs and translational centres have been created and generous funding of research projects has been disbursed to principal investigators and centres of excellence have been created across the nation.

The Biotech Industry leveraged the entrepreneurial surge and investor appetite for the life sciences to build a well rounded foundation. The industry self-organised in 2003 with ABLE becoming the collective voice of the sector with the Biospectrum magazine playing the role of the scribe. The industry registered a revenue figure of $4B in 2011, and is expected to reach the target of $5B soon, proving once again that stretch goals are effective in high technology sectors. The spectacular success of the BioPharma sector has given it about a 60% share of the top line, while Industrial Bio, Agri Bio, Bio Services, and BioInformatics have grown organically to provide a good foundation for the next phase.

The next decade and beyond is the focus of this roadmap. The national leaders have declared this to be the decade of innovation and biotechnology is synonymous with innovation. The Innovation Imperatives are clear enough - biosimilars and diagnostics for affordable healthcare, integrated traditional medicine, green biotech for less dependence on petroleum, bioremediation for environmental recovery, agricultural productivity and value addition, leapfrogging with genomics, synthetic biology and biomedical informatics. DBT and ABLE need to work together to stoke these engines of innovation.

As noted by the annual ABLE-Biospectrum surveys of the Indian Biotech Industry, the growth has been steady at around 20% CAGR for almost a decade now. With the excellent foundation, improved infrastructure, expanding regional markets receptive to home-grown innovation in biotechnology products and services, a public administration that is increasingly responsive to advocacy of the industry and a growing pool of skilled manpower, it does seem possible for the industry to step up its growth rate to around 30% CAGR. This would lead to a $100B annual revenue target by 2025 - the next stretch goal for the industry.

This roadmap prepared by ABLE for DBT began as an exercise in the XII Plan process in 2011. The Chief Operating Officer of ABLE, Dr Satya Dash, and his team are to be complimented for the extraordinary amount of care and effort that has gone into preparing this report. The nation stands to benefit from it. Jai Hind.

Dr. P M Murali
President ABLE 2012-2015

Dr. Vijay Chandru
President ABLE 2009-2012

The Innovation Imperatives are clear enough

Executive Summary

The Indian biotechnology industry has evolved over the last three decades to a mid maturity stage. Over the last decade the sector's revenues have rapidly increased from US $500 million in 2003 to US $4 billion in 2011, growing at an average rate of 20% year-on-year. If a favourable business environment is created, the biotechnology and healthcare sectors combined will be able to grow at a rate of 25-30% and have the potential to generate revenues of US $100 billion by 2025.

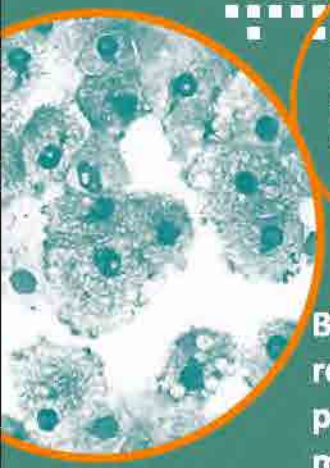
The importance of this high technology sector will become evident as its products catalyse the transformation of the Indian economy by offering solutions to the multitude of challenges that both India and the world will encounter in food security, fuel security and healthcare. Furthering these three foundational areas, on which a nation's economy and prosperity depend, represent the key opportunities for India to evolve into a bioeconomy.

In particular, the bioeconomy opportunities for India predominantly lie in biologics, especially biosimilar and vaccine manufacturing, stem cells, medical devices and diagnostics, contract research and manufacturing, integrating scientific evidence-based traditional knowledge into healthcare, agribiotechnology and green biotechnology, especially bioremediation and bioenergy. Technology enablers in the form of systems and synthetic biology will help advance the aforementioned areas.

India has the potential to become a global hub for R&D and manufacturing in all aspects of biotechnology. However, several gaps and challenges remain to be bridged and overcome. These challenges are in the domains of regulation, infrastructure, translational routes, skills and market pull.

A concerted and joined effort by the Government of India, industry and academia will help India reach its potential and become a true bioeconomy.

India has the potential to become a global hub ...in all aspects of biotechnology. However, several gaps and challenges remain to be bridged and overcome.



1 The Emergence of the Indian Bio-economy

Bioeconomy is defined by the OECD (2009) as "set of economic activities relating to invention, development, production and use of biological products and processes" [1]. In lay person terms, what the OECD definition means is creation of an economy where biotechnology and its applications help accrue economic and societal benefits for the region and the country at large. Bio-economy is a global phenomenon with several countries such as the USA, Canada, UK, Germany, Japan, Switzerland, Denmark and Israel as well as rising Asian and Latin American economies such as South Korea, India, and Brazil are at various stages of being a bio-economy. The leading countries that have already initiated plans for a bio-economy are the USA, Canada, Germany, UK and Japan.

1.1 Drivers of Bio-economy

Two main forces are driving the economies to be bio-based. They are science & technology as well as societal changes.

1.1.1 Science & Technology

The change in science and technology cycles has become rapid and new frontiers that were in realm of being very nascent a decade ago are gaining traction and influencing our daily lives as well as offering us solution to solve several challenges that we face- both global and local.

One of the foremost drivers for science and technology over the last two decades has been convergence of different scientific domains especially biology, engineering (IT & computational), chemistry and material sciences that earlier did not overlap. This convergence has allowed for engineering disciplines and principles to be integrated into biological science realm.

Our understanding of complexities especially at multiple levels such as at cellular, organ, tissue level and even at organismal level is rapidly growing as scientific tools become more sophisticated and enable analysis at nano-structural level such as studies involving single molecule and its interactions. This integration has also created ways that were hitherto difficult to study. Scientists and technologists are able to now look deeper into brain and other tissues, create artificial organ structures, model organ and disease to find better drug candidates and targets, improve plant varieties and extract oil from algal cultures. Coupled with this, information technology is impacting healthcare as well as agriculture in multitudes of ways by enabling remote disease detection, disease surveillance and in some cases healthcare delivery as well. New technologies such as RNA interference, companion diagnostics, synthetic biology and personalised medicine will continue to expand their domains of influence in human health and disease.

Agriculture, the mainstay of human civilization has gone through a couple of productivity revolutions and with new technologies such as molecular marker assisted breeding (MAS) and genetic engineering, another round of productivity leap is on the anvil. Scientists are regularly using genetic engineering techniques to elicit biofuels from plants, cyanobacteria and different species of algae thus reducing dependencies on fossil fuels.

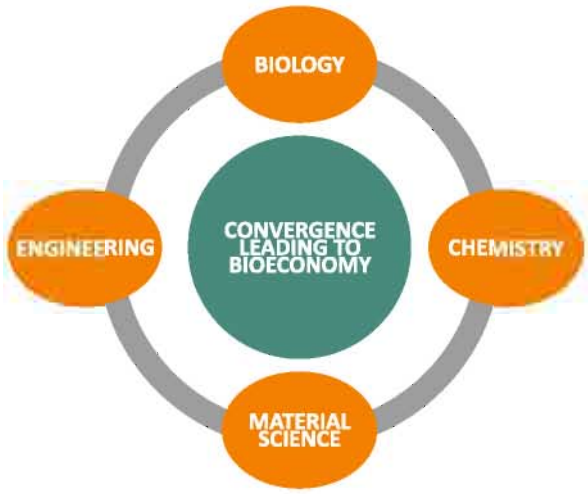


Figure 1.1 The convergence of several disciplines leading to a bio-based economy: Bio-economy.

There are several underlying technology enablers that are catalysing the current transformation of biotechnology. One that has made possibly the greatest impact in the last decade is the rapid progress in DNA nucleotide sequencing technology which presently makes it possible to sequence a whole genome in less than a week and at a cost of $10,000 or less. Such rapid sequencing techniques are helping to uncover DNA level complexities at a population, whole genome as well as organ and specific disease level. Tissue including cancerous tumour sequencing data is being used by scientists and clinicians to understand tumour biology in a greater detail. Techniques in microscopy especially single photon and con-focal microscopy have made it possible to look deeper into cellular level including movement of molecules.

The greatest impact in the last decade is the rapid progress in DNA nucleotide sequencing technology which presently makes it possible to sequence a whole genome in less than a week

These rapid evolutions of technology have brought about a sea change in the amount of data that scientists generate leading what many euphemistically call the 4th Paradigm (elaborated in Chapter 6). Analysis of the complexities of the data and deploying it for health and economic benefits will be the driving force of a bio-economy.

1.1.2 Societal and Global Shifts in the Economy

The world is rapidly globalising and the global economy is undergoing several changes over the last two decades especially with regards to flow of capital, integration of information flows, slow but steady shift in R&D for science and technology towards East and South.

The world population is rising and is predicted to touch 9 billion by 2050. Most of this growth will take place in developing countries. The world will face several challenges due to its rapidly expanding population. These challenges will be in healthcare, food and energy.

A growing population will have its own share of healthcare issues to deal with. Some countries have an inverse demographic pyramid with predicted shrinkage of their population (Italy, Japan, Germany to name a few); others such as Nigeria, India, Indonesia and Brazil will see their population growing over the next two decades. This will create unique sets of healthcare

challenges for each country. Countries such as Japan will have to deal with healthcare demands of a rapidly ageing population while countries such as India and China will have to deal with healthcare challenges of a young population and elderly as well. Developing countries will have to deal with both infectious as well as chronic diseases too.

The world is rapidly integrating with increasing mobility of people. This already has and will continue to pose healthcare challenges such as spread of epidemics such as H1N1, West Nile Disease among others.

With the growing world population food security will be an important agenda in the national policy setting especially as almost 4 billion of the world lives less than US $2 a day. The growing need for food will create a pressure to improve crop productivity, expand arable land area that would put pressure on forests and might lead to deforestation across the globe. Deforestation, besides impacting climate change will also create new healthcare challenges as several harmful microbes jump to new species including humans and livestock as hosts. This will lead to a concomitant increase in zoonosis (transfer of diseases amongst species) with implications for human health.

The global economy is truly a fossil fuel economy and the growth in world population will create prodigious demands on energy. Rapid technological progress over the last 120 years has depended on our ability to extract fossil fuels and derive energy from hydrocarbons. This dependence has created environmental problems such as increased pollution, destruction of natural habitats and climate change. New forms of renewable energy that have biological origins will be a key to global sustainable development.

Over the last decade... the Indian biotechnology sector has grown at a compounded growth rate of 20-22%

Many of the solutions to the global challenges (health, food and fuel) that humanity will encounter will come from biotechnology which in due course will contribute to several aspects of a country's economy.

1.2 The Indian Biotechnology the Vision, the Opportunity, and the Roadmap

The Indian biotechnology sector has evolved from being nascent to a mid-maturity stage. Over the last decade spurred by several positive changes in the ecosystem the Indian biotechnology sector has grown at a compounded growth rate of 20-22%. The revenue of the sector has grown from a mere US $530 million dollars in 2003 to over US $4 billion dollars in 2011. This sustained growth is no mean task. This sector consists of more than 300 firms that are spread all across India with almost half of them concentrated in and around Bangalore. The sector consists of firms from all aspects of Indian biotechnology viz. biopharmaceuticals (vaccines, biosimilars, medical device, stem cells), bio-services (CROs and clinical trial management firms), bio-agri and bioinformatics including systems biology firms.

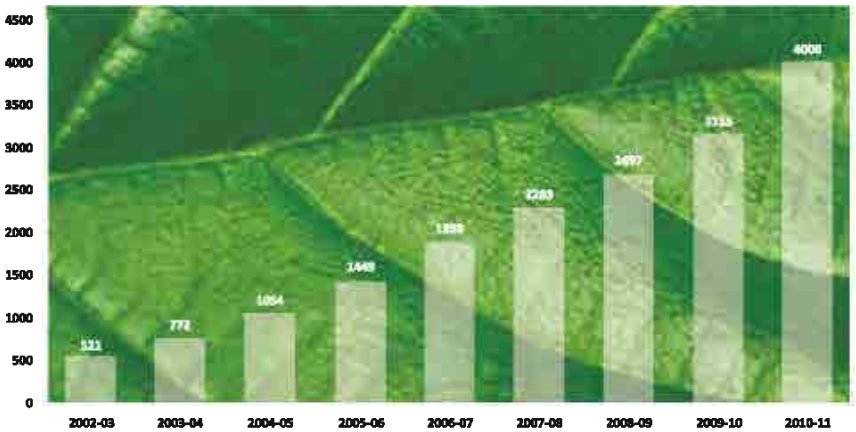


Figure 1.2 The growth of the Indian biotechnology sector from 2003-2011

From: Biospectrum ABLE Survey

The sector consists of both multinational such as Astra Zeneca, Novozymes, Monsanto) as well as indigenous firms such as Serum Institute, Biocon, Bharat Biotech, EcronAcunova, Metahelix and Strand Lifesciences to name a few. There are a few large firms however there is a long tail of small and medium size enterprises (SMEs).

India is now recognised as a global destination for vaccines, bio-services and increasingly for contract manufacturing especially biosimilars. Many firms are exploring exciting areas of stem cell biology, synthetic biology, agri-biotechnology systems biology and exploring evidence based traditional medicine.

1.2.1 The Vision and Opportunity for Indian Biotechnology: An $100 billion dollar industry by 2025?

In the next decade, India should aspire to be a leader in the global biotechnology arena such that it is home to bio-innovations that address challenges in healthcare, food and fuel security based on four paradigms- high quality, sustainability, affordability and accessibility.

The dynamic changes in the economy will make India a leading economic power in the world. The growth in GDP over the next decade will expand the domestic market and Indians will be able to afford healthcare products, demand for food commodities and energy will grow too. The population growth in India will impact its epidemiological profile. There will be increasing incidences of chronic, lifestyle and infectious diseases. It will also lead to growth of food and fuel demands in the next decade.

The growth in GDP over the next decade will expand the domestic market

In such a scenario there is an immense opportunity for the Indian biotechnology to play a positive and an important role in the Indian economy as well as contribute to the global economy. As mentioned before, the Indian biotechnology has multiplied six times from 2003 to reach more than US $4 billion. This pace of growth at 20% for over a decade is no mean task. However if the biotechnology industry operating landscape becomes more innovation friendly spurred by government's policies and nudge then the industry could possibly grow at 30% CAGR. This will make the combined total of the biotechnology and healthcare industry to touch US $100 billion by 2025.

A dynamic and vibrant biotechnology industry would be one of the main engines of innovation in India and will establish the country as a global destination for innovation with economic spillover effects such as creation of a large biotechnology manufacturing industry, high technology skilled jobs and supporting an ancillary industry that feeds the innovation engine.

1.3 India: Enabling a Biotech break-out Nation?

The potential of India to be a global innovation hub especially in biotechnology exists. The Indian biotech industry has also shown that when proper support systems exist they can deliver scaled up innovative products that are affordable and are of high quality. A few examples exist such as in vaccines wherein biotechnology firms such as Serum Institute, Bharat Biotech and Shantha Biotech have developed high quality and cheap vaccines especially and supply more than 50% of vaccines to transnational organizations such as WHO and UNICEF.

However to scale up and increase the frequency of such innovations from India and make it a top destination for biotechnology, GOI needs to formulate an implementable strategy for the future growth of Indian biotechnology for each of the segments as well as roadmap the evolving areas such as stem cell, synthetic biology, systems biology and molecular assisted breeding and genetically modified food. An agreed upon vision that takes into account the views of industry, scientists and other stakeholders should be formulated and implemented by the policy makers.

An institutional and structural framework has to be built to help India achieve its potential as a break out nation for biotechnology innovation. The five guiding principles that GOI could follow to enable India to be a biotechnology break-out nation are:

1. Create a strong, streamlined and transparent regulatory foundation that fosters innovation.
2. Reshape and build Government infrastructure to build capacity for research and development and facilitate translation and commercialization potential.
3. Facilitate technology access as well as market access for innovative products to achieve scale through public procurement.
4. Promote biotech entrepreneurship and provide a channel to access risk capital for all stages of biotechnology product lifecycle.
5. Nucleate and foster networks and triple helix collaborations.

Each of these principles are touched upon in the following segments.

1.3.1 Create a Strong, Streamlined and Transparent Regulatory Foundation that Fosters Innovation

The process of biotech innovation is long, arduous and is non linear. Biotech by its very nature is a highly regulated industry with a burden of regulation that is intense. Regulation and regulatory landscape is closely tied with investor's confidence and hence affects funding and financing landscape for the sector too. India has a well established regulatory system in the world. However parts of this regulatory system needs urgent overhauling and strengthening.

GOI has to make a quick strategy on how to re-vamp the existing regulatory system and make it single window, efficient, transparent and scientific evidence based

India presently has a cumbersome regulatory process with multiple agencies that hinder innovation due to several cumulative procedural delays. This is the case for both biopharma (including bio-services and medical device) as well as agri-biotech segments. GOI has to make a quick strategy on how to re-vamp the existing system and make it a single window, efficient, transparent and scientific evidence based. It is imperative that India should quickly build a single regulatory authority that is equipped with trained permanent personnel who understand the "science of regulation" as well as other affects of regulation be it the "economic cost" as well as the "risk-benefit" analysis.

GOI should create "Centre for Biotechnology Policy and Regulatory Sciences" led by a Biotechnology Leadership Council (BLC) of five industry representatives and five strategic stakeholders which will take responsibility for implementing on the Planning Commission recommendations and will provide a forum for Government and Industry to work together to develop a successful Biotechnology industry. This Centre will have a mix of scientists, technologists, toxicologists, policy & regulatory researchers, economists, and social scientists, thus creating a space where policy and regulations pertaining to all aspects of biotechnology can be analyzed. A similar institution in University of Cambridge namely Institute for Manufacturing (IfM) brings together elements of regulation, policies, Industry-Government interactions, Academia-Industry interactions and business strategy. IfM model can be studied and adapted for India for biotechnology policy practice studies. This Centre can play a vital role during the process of informed decision making by the regulators. The cost of establishing such a centre will be US $4 million over a 5 year period.

The regulatory body should regularly engage with the industry through various discussion and interactive forums. GOI should actively promote platforms that provide interactive space for regulators, policymakers, industry and academia.

The sooner the regulatory landscape is streamlined the better it will be for the growth of the biotechnology industry. Regulatory changes, that need urgent attention, for individual biotechnology segments such as biopharma, medical devices, agri-biotech is discussed in thereport. GOI also has to quickly make its regulatory position clear in emerging areas of synthetic biology, stem cells, systems biology and personalized medicine. In areas such as synthetic biology

and personalized medicine India could stay ahead of the curve if a positive environment is established immediately.

1.3.2 Reshape and Build Government Infrastructure to Build Capacity for Research and Development and Facilitate Translation and Commercialization

A country with imperfect institutions and which lacks capacity (in terms of skills in research and technology as well as technology commercialization) will not be able to catch up. GOI should continue to build and foster institutions that are dynamic, whose mode of operation is translational and that work closely with the industry.

Several structural level changes need to happen for building capacity in S&T as well as translational biotechnology.

A. Revamp the University system in India

India has close to 400 universities and around 100 research institutes. Barring a few, most of these universities are just teaching institutions and are poorly funded, have fossilized curricula and academic staff who are unaware of the rapidly evolving technological changes. It is from these 400 universities that India produces most of its science and technology undergraduates and post graduates. They lack real life lab-bench experience as well as analytical training. At the heart of this issue is that many scientists do not wish to join universities especially state universities due to lack of research funding as well as bureaucratic administration. The University system in India needs a quick revamp. Ministry of Science and Technology as well as Ministry of Human Resources need to have a joint strategy to change the current university system.

It is from these 400 universities that India produces most of its science and technology undergraduates and post graduates

Industry ready workforce is critical for the biotechnology industry to grow. Multi-disciplinary courses with a strong element of modern biological sciences as well as other analytical areas such as mathematics, statistics, modeling and design should be an integral part of curriculum. Industry participation during curriculum design and implementation would go a long way in re-vitalizing the educational system in India.

B. Encourage public funded scientists to translate their research

It is essential that publicly funded scientists and technologists are allowed to take their idea into the market and to have ownership of their patents. In India instances of academic faculty and staff starting enterprises is not so prevalent although it is gaining traction. There are only a few examples of successful transitions from academia to industry. One of the earliest examples in India of such a transition of an academic spin-off is Strand Life Sciences which was started by a group of professors from Indian Institute of Science (IISc) [9]. In the USA, academic scientists are encouraged to establish their own firms while maintaining their academic position. The Indian version of Bayh-Dole Act which has been mooted and presently is in the Parliament should be made into an act. The implication of such an act should be made aware to the research fraternity by DBT.

Indian academic staff wishing to start their ventures should be supported by GOI. A 3 year sabbatical scheme should be initiated for academic staff wishing to commercialize their ideas. Mentorship and soft training in management skills, financial subjects and market analysis tools should also be part of University programmes. The GOI should promote awareness about IP issues across the Indian academic and public funded institutions.

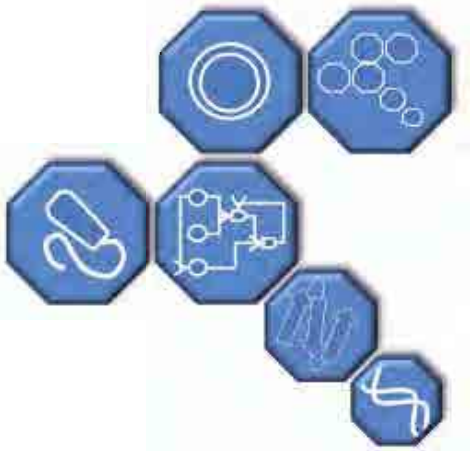
C. Establish Technology Transfer Offices and prepare a policy stand on technology transfer principles for public funded organizations

Academic institutions need efficient technology transfer offices that have retained staff who can scout and help scientists transfer their technologies to industry through various modalities. They can also serve as one of the industry facing bodies of a university. It is crucial to have a policy stand on technology transfer principles across public funding institutions and universities.

GOI should organize relevant training for the staff of TTOs and make them aware about the best practices in TTO offices from all across the world.

D. Build a live, dynamic, continuously updated repository of all technologies being developed in the public funded arena with a validated list of contact persons

Industry opines that there is a dearth of information regarding the various technologies being developed across Indian public funded institutes as well as academia. Many a times the information is not updated and the industry is unable to contact a relevant person.



Fostering and incentivizing mobility between industry and academia will go a long way in bridging the gap

GOI should build a repository of all biotech related technologies being built across India. This repository should be constantly validated as well as provide useful information as simple as whom the industry contact if it becomes interested to partner for a technology.

E. Incentivize Industry-Academia interface through multifarious tools such as fostering research mobility

Industry and academia interface in India remains weak and is discrete. Fostering and incentivizing mobility between industry and academia will go a long way in bridging the gap between industry and academia. One of the reasons for lack of mobility is because the two systems are different and there is no incentivization for mobility. In the US and UK such schemes have helped bridge the gap between industry and academia and mobility schemes foster long term academia and industry relationship building.

In the US and UK such schemes have helped bridge the gap between industry and academia and mobility schemes foster long term academia and industry relationship building. For example Rutgers University established "Rutgers Pharmaceutical Industry Fellowship Program" in 1984 in collaboration with industry [5]. This programme has now grown to include 12 pharmaceutical firms and over 500 industrial postdoctoral fellowships have been granted. The programme is structured to provide hands-on training in several diverse areas such as co-ordination of clinical trials, providing liaison skills to interact with regulatory agencies as well as with research organisations [5]. Similarly in the UK, the Medical Research Council (MRC) has established MRC Research Leader Fellowship Scheme worth £75,000 to promote pre-competitive industry-academia linkages [6]. This scheme has a wide mandate and there are no restrictions on the duration of the project or on maturity levels of project (projects could be pilot study, feasibility study or technical exchange of knowledge) [7]. MRC also promotes industrial postgraduate fellowships especially at PhD levels called "Industrial Case Studentships" that enable PhD students to spend part of their time in a industrial R&D laboratory [7].

Similarly GOI could fund PhD and postdoctoral fellowships of 3-5 years length wherein academic PhD and postdoctoral staff could spend time conducting research in an industry laboratory and can be supervised jointly by both an academic as well as an industry R&D head.

Further, GOI could incentivize academic faculty to spend time and energy to take an idea to the market. It should create a transparent career path framework for academics who wish to spend time in an industry while maintaining a position in academia. Promotion parameters and frameworks within the academia could be modified to accommodate faculty who have spent their time and energies in translating their work to the industry. Indian scientific academia should also be made aware of basic business principles of business models, strategy, finance and other management techniques. Involving reputed business schools such as IIMs into a research programme that has industrial application could enable scientists to see beyond the lab and appreciate the management talent needed to cross the commercialization valley.

F. Establish industry supported research institutions in a PPP model
Joint research institutes that are part public funded and part by industry should be established. One such PPP model institution in India is Ganit Lab at Bangalore which was established in partnership with Department of Information Technology (DIT), IBAB Karnataka and Strand Lifesciences as industrial partner. Many such institutions, supported by both industry and academia in different frontier areas and with a mandate to conduct industrially relevant scientific research, should be established. GOI can come out with a framework of metrics to measure the success of such PPP institutions.

GOI can come out with a framework of metrics to measure the success of PPP institutions

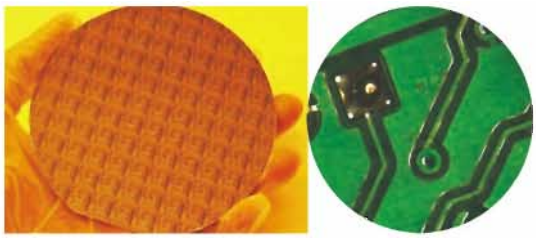
The USA and several other Western countries have many such institutions. For example,
i. The Fraunhofer Institutes in Germany in partnerships with industry conducts research into frontier areas of science.
ii. The Energy Biosciences Institute (EBI) in California is a partnership among University of California at Bereley (UCB), Lawrence Berkeley National Lab (LBNL) and British Petroleum.

New partnership models are emerging for drug development and commercialization between the academia and the industry. For example, the University of Dundee's School of Life Sciences has a well established partnership model with pharmaceutical companies for drug drug development [8]. The university has established a £20 million Dundee Kinase Consortium to develop drugs in partnership with industry [8]. This consortium focuses on developing new drugs for diabetes, arthritis and cancer [8].

The modalities, mandates, best practices and operational structures of such institutes should be studied and adapted to the Indian scenario.

G. Establish Incubators within research clusters
Several clusters are being formed in India especially in the metros such as Delhi, Mumbai, Bangalore, Hyderabad and Chennai however many more clusters with bio-incubators need to be created, funded and made sustainable especially in the Tier2 cities. Further, existing smaller bio-incubation facilities should be made sustainable. The long term plan should be to build a hub & spoke model of bio-incubators such that a "large bio-incubator" mentors smaller bio-incubators.

Several cities across India need to have incubating facilities for biotech enterprises. Atleast 10-11 more biotech focused incubation facilities need to be set up. These include Agartala (Tripura), Bhubaneswar (Orissa), Jadavpur (West Bengal), Ranchi (Jharkhand), Vishakhapatnam (Andhra Pradesh), Madurai (Tamil Nadu), Vellore (Tamil Nadu), Pondicherry, Nagpur (Maharashtra), Baroda (Gujarat), Dehradun (Uttaranchal).



1.3.3 Facilitate Technology Access and Market Access (through Public Procurement) for Innovative Products to Achieve Scale

Accessing cutting edge technologies is a big hurdle for small and medium enterprises. GOI should establish infrastructure and policies that help Indian biotech firms access frontier technologies.

A. Let the C-CAMP model flower- establish 3 more C-CAMPs across India to access technology and high end services

The Centre for Cellular and Molecular Platform was established by DBT with the mandate to be a core lab facility that would provide high end research services as well as provide access to cutting edge technologies to the biotech fraternity. The model though in its initial stages is attracting industry's attention. Similar such C-CAMP should be established at 3 other hubs of biotechnology viz. Pune, NCR and Hyderabad.

B. Incentivize R&D through tax policies

GOI should reduce import duties on high end equipment, manufacturers to establish cutting edge bio-analytical facilities. Technology accessibility barriers could also be reduced by providing tax breaks and rebates of 300% on R&D expenditure as well as preferential tax exemption for indigenously developed drugs and products.

C. Establish a public procurement policy for innovative products: Make the public sector the first and significant user of technology products. Procurement policies play an important role in the demand side in sustaining innovations and providing an access to the market. Dalpe et al (1992) showed that the public sector can be the 'first substantial user of innovations' [2]. It was also shown that in Canada organizations such as government hospitals and other public institutions such as federal administration consume around one quarter of all innovations generated in Canada. Further policy researchers have also shown that firms with procurement contracts in high technology areas such as microelectronics perform significantly better than those that receive subsidies [3].

The GOI has initiated a new public procurement policy for SMEs. The purview of this policy should also include biotechnology and healthcare firms.

For example national schemes such as National Rural Health Mission (NRHM) should have a procurement policy for medical devices and diagnostics. This could help in scaling up medical device and diagnostics industry. The implementation of procurement policies should be transparent and should not jeopardise the safety of end users especially in a sector like healthcare.

1.3.4 Promote Biotech Entrepreneurship & Provide Access to Risk Capital for All Stages of Biotechnology Product Development Cycle while Focusing on Seed and Proof of Concept Funding

For India to become a bio-economy a strong push for biotech-entrepreneurship is needed. Most of the future bio-innovations will emerge from academic labs that wish to take an idea forward or they will emerge from people who have spent a career in corporate polishing their business skills and then wish to take the entrepreneurship plunge- the so called 'Second Career Entrepreneurs'.

Policies should be designed to support both forms of entrepreneurships as well as other entrepreneurial activities.

A. Promote and foster entrepreneurship via Awards and Prize Incentive schemes
Prizes have been used as an inducement scheme by several governments to fast track innovation. This has been true historically as well. As reported in an article by Economist, a study by Liam Brunt who analyzed triggers for agricultural inventions in Britain during a hundred year period found a distinctive link between prizes and increase in patenting [4]. The article cites how Britain, Canada and Italy including other countries are partnering with the Gates Foundation and offering US $1.5 billion to firms under the Advanced Market Commitment (AMC) scheme to develop vaccines relevant for diseases of the developing countries [4].

One of the ways that GOI can foster entrepreneurship would be to throw 'problem challenges' in biotechnology areas relevant to India.

B. Populate back-end very early stage ideas of the innovation funnel through ring fenced funding
Each stage of innovation funnel requires unique set of policy intervention tools. As a strategy to spur innovation, numerous early stage ideas should be funded such that the probability of one idea making through the hurdles increases. Recently DBT has set up "Ignition Grant" scheme which will hopefully populate the innovation funnel at the back end especially those that are still at the idea stage or before pre-proof of concept.

As a strategy to spur innovation, numerous early stage ideas should be funded

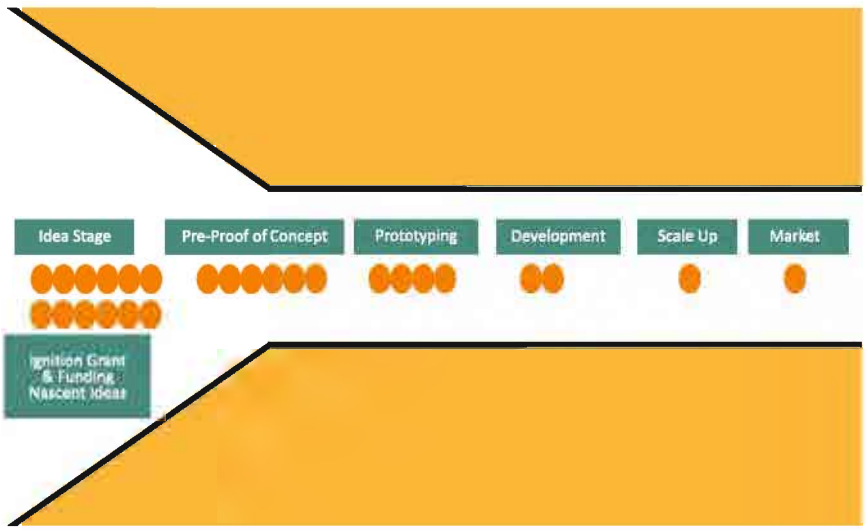


Figure 1.3 The Innovation funnel

C. No restriction on R&D funding to SMEs that are owned by non Indians if major part of the R&D is being conducted in India
Foreign SMEs especially start up firms that conduct major part of their R&D in India should not be restricted to seek public seed funding. These firms also play a role in nucleating the innovation ecosystem in India. Policies and modalities could be worked out such that some of the benefits derived from the funding could be accrued back into the country.

D. Provide early stage start-ups with access to scientific and market databases
Start up firms that are R&D intensive need continuous access to knowledge about current technology trends and peer reviewed scientific journals. It is expensive to access cientific and market databases. GOI should provide funding to incubation centers for accessing scientific databases such as Science Direct and others.

1.3.5 Nucleate and Foster Networks, Platforms and Triple Helix Collaborations

Innovation is popularly called as a "contact sport" but boundary spanning contacts need to occur several times for innovation to flourish. Networks and community platforms provide immense benefits such as exploration of collaborative projects and joint partnerships amongst the three stakeholders (triple helix) - the academia, industry and the government. For example the London Regenerative Medicine Networks allows scientists (both in academia and industry), venture capitalists and other stakeholders to interact with each other. Several such networks should be fostered through BIRAC. DBT could also establish a dedicated mentorship network for entrepreneurs to interact and share learning from other entrepreneurs especially in gaining valuable suggestions during the course of enterprise building. Leading S&T clusters such as Boston, Silicon Valley, USA and Cambridge, UK have many such mentorship programmes.

1.4 The Roadmap Report

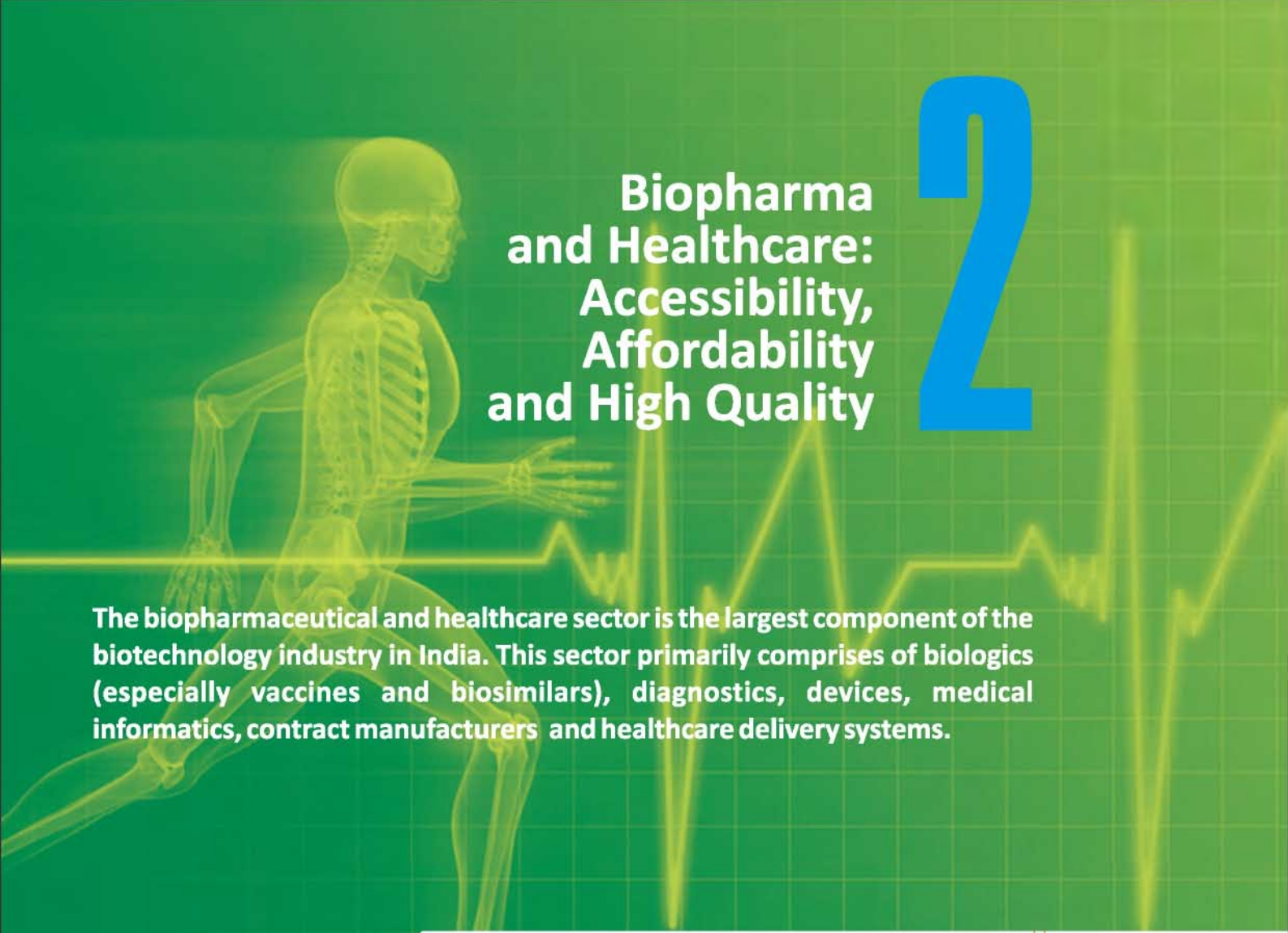
This report delves into the Indian biotechnology sector and attempts to understand the global dynamics within the biotechnology sector. The report identifies gaps and challenges that exist in the Indian biotech sector and recommends policy and procedural interventional measures that would hasten of the growth of Indian biotechnology sector such that India evolves to become a bioeconomy.

The report identifies gaps and challenges that exist in the Indian biotech sector and recommends policy and procedural interventional measures

Chapter 2 addresses the biopharmaceutical and healthcare aspects of the Indian biotechnology sector and covers vaccines, biosimilars, stem cells, medical device and diagnostics, traditional knowledge based drug discovery, synthetic biology and healthcare delivery models. Chapter 3 outlines the growing importance of India as a global destination for bioservices including contract research and manufacturing. It shows how firms in this segment are attempting to evolve into drug discovery firms with a collaborative approach. Chapter 4 delves into the agribiotechnology situation in India and identifies how technologies such as molecular assisted selection and genetic modification are helping to improve crop productivity yields. The chapter 5 addresses the bio-industrial sector while Chapter 6 shows how innovative Indian systems biology firms are using systems biology and predictive modelling approaches to conduct molecular marker and drug discovery studies, and create world leading platforms for data analysis. The chapter 7 concludes with the affirmation to the future growth potential of the Indian biotechnology sector and for India to become a bioeconomy. It recommends that positive policy interventions from GOI in partnership with industry and academia.

1.5 References

1. The Bioeconomy to 2030. Designing a Policy Agenda, OECD 2009
2. Dalpe, R., Debresson C, & Xiaooping, H. (1992) The public sector as first user of innovations. Research Policy, 21, 251-263
3. Doutriaux, J. (1991) High-Tech Start-Ups, Better Off with Government Contracts than with Subsidies: New Evidence in Canada. IEEE Transactions of Engineering Management, 38, No. 2, 127-135
4. 'Innovation prizes: And the winner is '; Economist. August 5th 2010. http://www.economist.com/node/16740639
5. Rutgers Institute for Pharmaceutical Industrial Fellowship http://pharmafellows.rutgers.edu/home/index.php
6. MRC People Exchange Program http://www.mrc.ac.uk/Fundingopportunities/Fellowships/PEP/index.htm
7. MRC Industrial Case Fellowship http://www.mrc.ac.uk/Fundingopportunities/Studentships/IndustrialCASE/index.htm
8. Tralau-Stewart, CJ et al. (2009) Drug Discovery: new models for industry-academic partnerships. Drug Discovery Today, Vol. 14, No. ½. 95-101.
9. Indian scientists turned entrepreneurs at Strand Lifesciences crack genetic code to save lives. The Economic Times, 25th May 2012.



2 Biopharma and Healthcare: Accessibility, Affordability and High Quality

The biopharmaceutical and healthcare sector is the largest component of the biotechnology industry in India. This sector primarily comprises of biologics (especially vaccines and biosimilars), diagnostics, devices, medical informatics, contract manufacturers and healthcare delivery systems.

There is an inherent dynamism within this area and it has the potential to provide affordable, high quality healthcare and wellness for all Indian citizens. From its position today of being the third largest supplier of quality, affordable medicines to the world by 2025, India should be an international leader in innovative medical technologies, therapeutics, diagnostics, and healthcare delivery of high quality and affordability [1].

One of the leading drivers for India to become a leading destination for innovation in biopharma and healthcare will be the growth of its domestic market fuelled by overall GDP growth and increasing prosperity amongst her citizens, especially the growth of the middle class who can afford medicine, and the changing profile of disease prevalence among the population. These developments require the implementation of India specific healthcare delivery models that take into account the evolving situation.

2.1 Healthcare as a Domestic Market Driver:

The public healthcare system in India in the present state is not adequate and needs an immediate overhaul. The healthcare providers are mostly private with most people paying out-of-pocket to access healthcare services. Figure 2.1 highlights that the per capita spending on health has not changed over the years and has hovered around the comparatively low figure of US $40. India ranks very low in several healthcare parameters and this status need urgent remediation. Table 2.1 illustrates a selection of healthcare parameters in India.

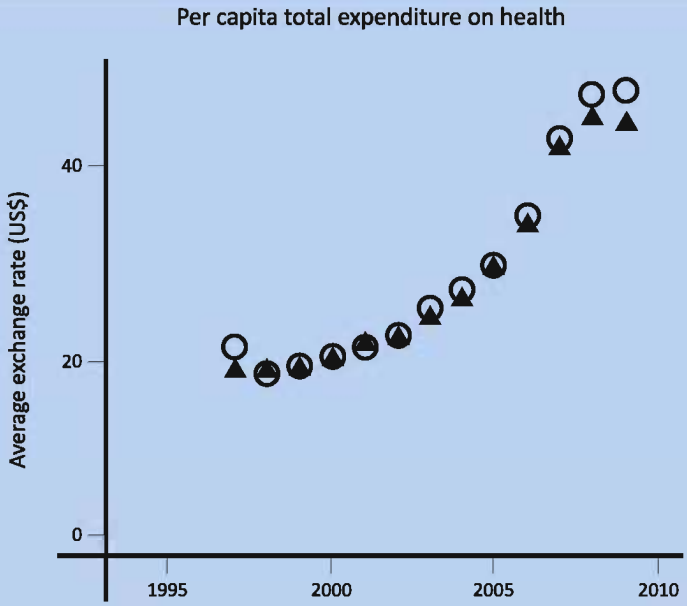


Figure 2.1: Per capita total expenditure on health (from WHO, India, [2])

Table 2.1: Healthcare indicators in India ([2], [3]).

Doctors/Physicians	60 per 100,000 people (PwC Report, 2009)
Nurses/Midwives	130 per 100,000 people (WHO estimate)
Pharmacies	367,000 (urban), 185,000 (rural). (PwC Report, 2009)
Hospitals	30,000 (67% public; 23% private). (PwC Report, 2009)
Hospital Beds	1.7 million. One per 1000 people. (PwC Report, 2009)
Health Centres	171,687. (PwC Report, 2009)
Population using improved water facilities	~90% (urban); ~80% (rural). (WHO estimate)
Access to improved sanitation	~60% (urban), 20% (rural) (PwC Report, 2009)

The Indian biotechnology sector especially biopharma and healthcare can play a key role in offering solutions to the myriad of healthcare related challenges the country presently grapples with. This sector will also be one of the key growth engines for the Indian economy, which is set to rise to US $10 trillion in 2025 and is predicted to reach US $41 trillion in 2050, powering India to be among the top three GDPs in the world.

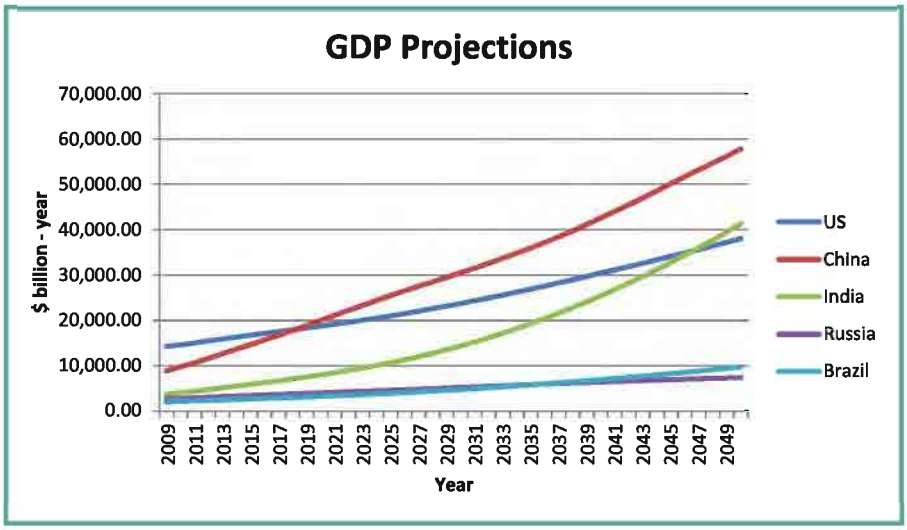


Figure 2.2 GDP projections, [4].

The Indian biotechnology industry can contribute $100 billion to the projected GDP by 2025; if it grows at 25-30% CAGR. Currently, the Indian biotechnology industry is valued at around US $4 billion and is growing at 20-22% year-on-year, so a favourable environment for the progress of the biotech sector would be a major growth driver for domestic and international markets.

The growing economy in India has provided the middle class with a greater amount of disposable income, and this has subsequently increased the expenditure towards healthcare services.

Thus, healthcare will emerge as an important market driver for both indigenous as well as multinational biotech/pharmaceutical companies. India exemplifies a dichotomous situation with respect to healthcare. On the one hand it faces typical health challenges of being a developing country such as rise in TB and other infectious diseases, while on the other hand the country shows atypical signs of a growing economy such as the prevalence of chronic diseases such as diabetes (currently India is estimated to have 50 million diabetics which is expected to grow to 75 million by 2025) and cardio-vascular diseases. These economic and epidemiological changes will create a demand for quality healthcare in the country. Influx of multinational corporations, growing healthcare infrastructure and increasing telemedicine and diagnostic centers in India have also fuelled the growth of the domestic market (Figure 2.3).

Figure 2.3 Healthcare as a market driver

The biopharma and healthcare sector, which is still in its early growth phase in India, mainly consists of Biosimilars, Medical Devices & Diagnostics including equipment, Regenerative Medicine, Systems Biology, Natural Product Based Medicines, Pre-clinical & Clinical Research, Contract Research & Manufacturing and Integrated Healthcare Delivery Systems.

Each sub-sector of the biopharma and healthcare industry in India is addressed individually in the following segments.

2.2 Immense Opportunities in Biosimilars & Vaccines

Vaccines and increasingly biosimilars will constitute the largest component of the Indian biopharma segment and immense opportunities lie in creating an ecosystem in India that will take India to the next level as a hub for global biologics including vaccine and biosimilars development and manufacturing.

2.2.1 Global Vaccine Scenario

Vaccines play a significant role in developing the world's economy as they reduce infant mortality and immunize against diseases. They are also cost-effective methods of ensuring good health on a long term basis. Some of the long-term impacts of vaccination drives have been shown in Figure 2.4 below.

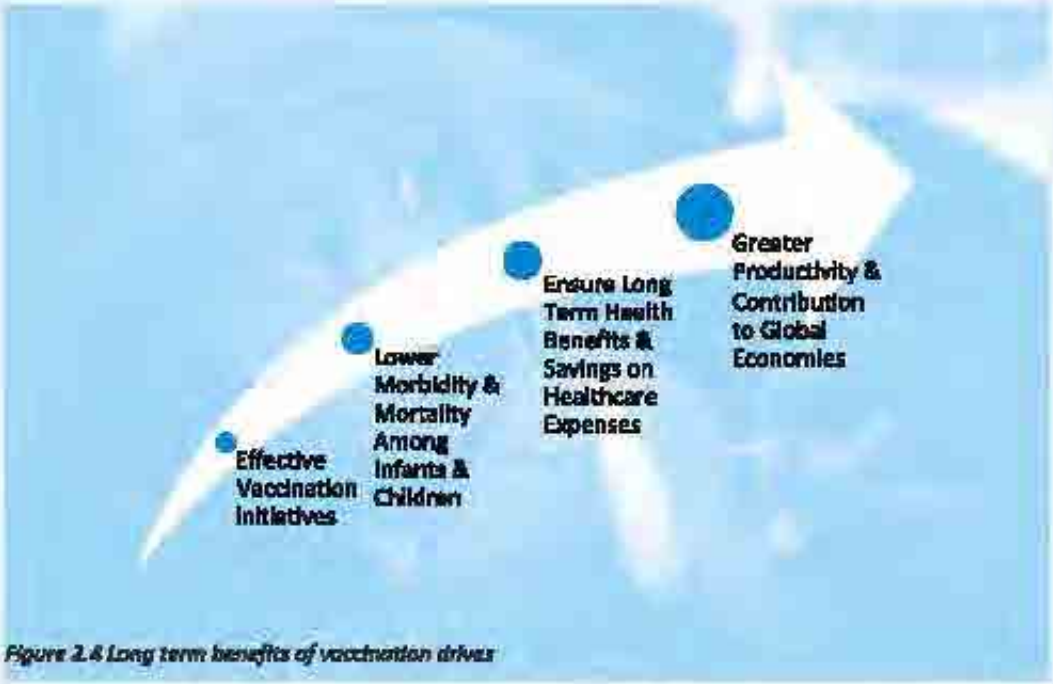


Figure 2.4 Long term benefits of vaccination drives

With the launch of global initiatives such as the "Decade of Vaccines" and the collaborative efforts of the Global Vaccine Action Plan (GVAP) by the Bill and Melinda Gates Foundation in 2010, the vaccines sector is set for major growth and development in the next few years.

The GVAP collaboration is a joint effort by World Health Organization (WHO), UNICEF, National Institute of Allergy and Infectious Disease (NIAID), and the Bill and Melinda Gates Foundation that aims to provide a global platform for collaborations among all stake holders to enable immunization efforts across susceptible populations in poor countries.

Despite the progress in this sector, there are still over two million children that die annually due to diseases that can be prevented by effective administration of vaccines [5]. Hence, it is essential to invest in this sector and expand its global outreach in order to ensure a sustained global economy.

2.2.2 Indian Vaccine Scenario

India is already an established player in paediatric vaccines with firms such as Serum Institute, Bharat Biotech, Shanta Biotech and Panacea Biotec contributing to India's emergence as a leading hub for vaccine manufacturing and supplier to global schemes run by global institutions such as WHO and UNICEF. With the increase in disposable incomes and the launch of new affordable vaccines by both domestic and international companies, the vaccine market is predicted to grow at a rate of 10-13 percent in the next five years. According to 2011 estimates, 60 percent of the global

health vaccines are produced in India [6]. Thus, it is very important to maintain high standards of healthcare delivery through vaccines and address immediate challenges to ensure a sustained growth of this sector in the near future.

Over the last 15 years Indian vaccine firms have been in the forefront of developing vaccines that are of high quality as well as affordable. The example of Shantha Biotech's Hepatitis B vaccine in 1997 that was available at a 30 times lower cost per dose than other competing brands was followed by similar examples from Bharat Biotech, Panacea Biotech and Serum Institute. Bharat Biotech for example has priced its indigenously developed Rotavirus vaccine at US $1 per dose thus making it the cheapest rotavirus vaccine in the world.

A notable development in this regard was the launch of Vaxi-Flu-S, the first Indian indigenous H1N1 swine flu vaccine developed by Cadila Healthcare in 2010. Subsequently, companies like Serum Institute of India and Bharat Biotech also launched their versions of the swine flu vaccine, which helped India emerge as a strong global competitor in the vaccines sector.

Despite India being a global hub for vaccine manufacturing, vaccination for a variety of human diseases among Indian children remains an issue and there is still some ground to cover in terms of universal vaccination of children. Figure 2.S from WHO India and Table 2.2 illustrate the case.

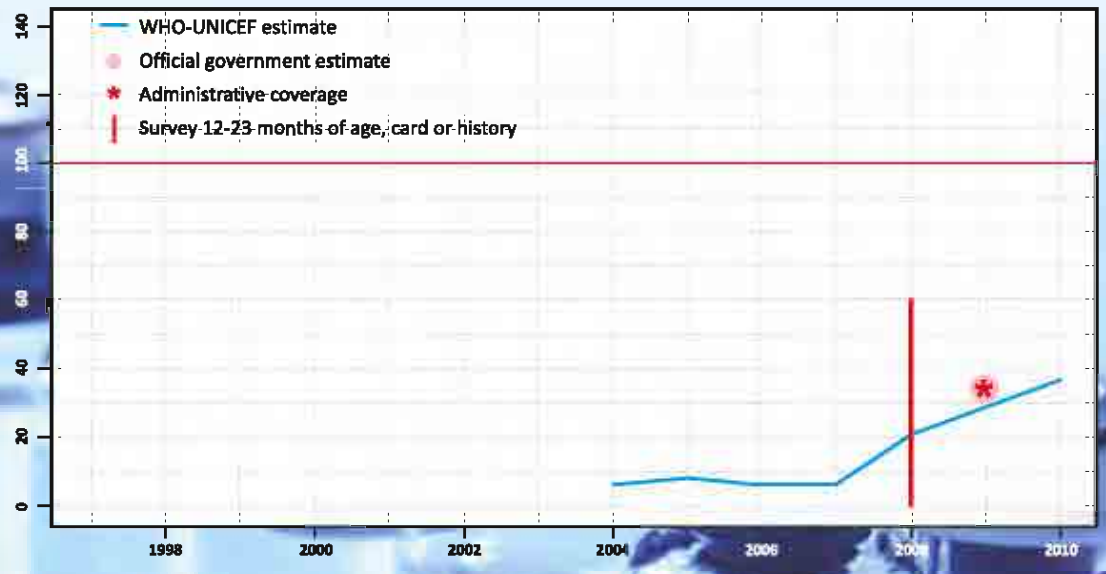


Figure 2.5: Hepatitis B vaccine caverage in India, (WHO, [7]).

Disease	Percentage immunization of nine year old children (2010 estimates)
Measles	74
HepB3	37
TB corresponding vaccines: BCG	87
DPT corresponding vaccines: DPT1	83
DPT corresponding vaccines: DPT3	72
Polio corresponding vaccines: polio3	70

Table 2.2 Immunization coverage of disease conditions among one year old Indian children, (UNICEF, [8])

The Department of Biotechnology (DBT) has established a national mission programme (the Vaccine Grand Challenge Programme-VGCP) for the development of vaccine candidates for a host of diseases that affect children and adults such as Rotavirus, Typhoid, Cholera, Japanese encephalitis, HIV, Influenza to name just a few. Other organizations such as Gates Foundation, GAVI and WHO are contributing to vaccine research, development and delivery in India with the aim of providing affordable vaccines to improve public health.

2.2.3 Biosimilars: The Opportunity on the Other Side of Patent Cliff

The follow-on versions of biologics (medicines derived from living systems), developed using recombinant DNA techniques are known as "biosimilars". They include products such as human growth hormones and biosynthetic "human" insulin among many others. Biosimilars, unlike conventional generics, are target-specific, large and complex molecules that have a stringent production protocol. Biosimilars, along with vaccines, diagnostics and devices, are predicted to be the key growth areas in the Indian Biopharma sector [9].

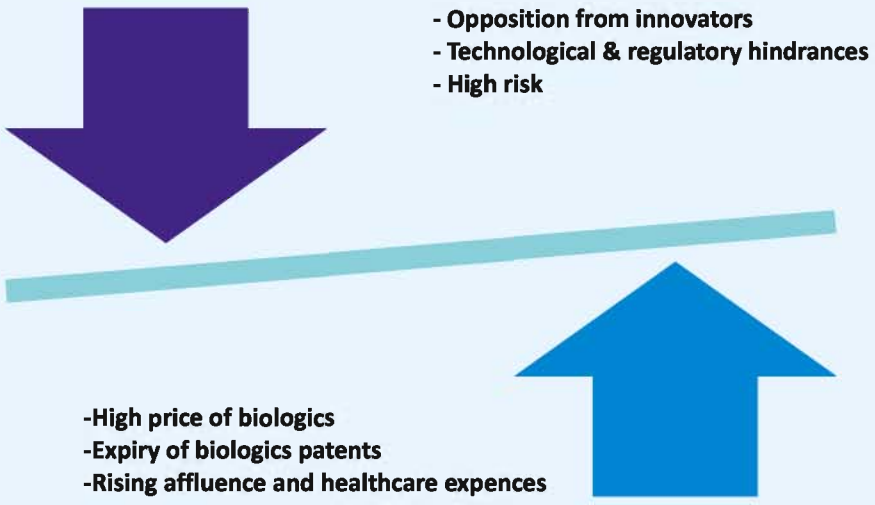


Figure 2.6 Biosimilars market – challenges and growth drivers, (ABLE-PwC, [9]).

Global sales figures for biosimilars in 2009 were US $1.23 billion and the market is predicted to reach around US $43 billion in 2020. Being an affordable yet equally-effective alternative for biologics, they can provide savings that range from 25% to 85% of the original versions. Moreover, the patent expiry of approximately 48 biologics (worth US $73 billion) in the next 10 years will also fuel the demand for biosimilars [9]. Despite the resistance from the innovator companies, and the regulatory hurdles involved in their production, biosimilars have immense market potential for both developed, as well as growing economies (Figure 2.3) [9].

As the patents for biologics move closer to their expiration dates and the challenging economic situation across the globe forces a decrease in healthcare expenditures, biosimilars emerge as the cost-effective therapeutic alternative across the globe [9].

In 2010, the USA, having the largest biopharma market, announced a new regulatory pathway for complex biosimilars. The European Union (EU) also announced that they will draft guidelines for biosimilars approvals by mid-2012. The investments and market potential for this sector are also increasing as leading global pharma companies continue to collaborate in this area. Some of the collaborative initiatives have been described in Figure 2.4 [10].

Recent Global Joint Ventures for Biosimilars		
Amgen and Watson Pharmaceuticals invested $400 million for cancer biosimilars	Baxter International and Momenta Pharmaceuticals invested $503 million	Biogen Idec and a unit of Samsung invested $300 million.

Figure 2.7 Global Joint Ventures for Biosimilars, [10].

2.2.4 Indian Biosimilars Scenario

The drug classes for biosimilars in India comprise of human insulin, human growth hormone, granulocyte colony stimulating factor (G-CSF), Erythropoietin, and Streptokinase. Recent estimates indicate that 20 companies in India are already developing biosimilars [8]. There are around 25 recombinant therapeutic available in India and 15 of them are manufactured within the country. About 50 brands are commercialized in the country by leading companies such as Biocon, Shantha Biotechnics, Reliance Life Sciences, Wockhardt and Intas Biopharmaceuticals among others. About 72 recombinant drugs are currently undergoing different stages of clinical trials (Figure 2.8) and their launch may cause an increase of 25% in the Indian Biopharma sector [11]. Some of the recent developments in this area are discussed below.

Figure 2.8 Biosimilars statistics in India, [9, 11].

In May 2011, Dr Reddy's Laboratories launched Peg-grafeel (pegfilgrastim). The product was priced at US $184.69, thus making the drug 95% cheaper than in the US and is valued at 25% of the cost of the originator brand in India. Moreover, Dr. Reddy's Laboratories has 11 other biosimilars in different stages of development [11].

In another development, Hyderabad-based generic drugmaker Natco Pharma partnered with Mabxience, the biosimilars division of Swiss firm Chemo SA for the manufacture of four drugs, mainly: trastuzumab, bevacizumab, rituximab and etanercept [12].

The demand for biosimilars is likely to increase as Indians become increasingly affluent and healthcare insurance coverage widens. Moreover, considering the cost advantages that India can provide, the country has a great potential for future growth in the biosimilars market. As mentioned in the previous section with several biologic drugs coming off patent, India stands on the shores of immense opportunity to become a world leading centre for biosimilars manufacturing that is fuelled both by domestic as well as global demand [9]. As there is an increase in the investments for biosimilars and general biologics undergoing clinical trials; the Indian market potential is predicted to rise significantly in the next few years. The subsequent launches of these biosimilars may contribute to more than 25% of the growth in the Indian biopharmaceutical market [9]. Table 2.3 provides a cursory glance at the biosimilars being marketed in India.

Table: 2.3 Biosimilars in India

Firm	**Biosimilar Product** (Description)
Biocon	**Biomab** (biosimilar nimotuzumab) **Eripro** (recombinant human erythropoietin (EPO) **Insugen** (recombinant human insulin) **Myokinase** (recombinant streptokinase) **Nufil** (recombinant G-CSF)
Dr. Reddy's Lab	**Cresp** (Darbepoetin alfa) **Grafeel** (recombinant G-CSF) **Reditux** (Rituximab)
Intas	**Epofit** (recombinant EPO) **Intalfa** (recombinant human interferon alpha-2b) **Neukine** (recombinant G-CSF) **Neupeg** (PEGylated G-CSF)
Reliance Lifesciences	**Reliferon** (recombinant interferon alpha 2b) **ReliGrast** (recombinant G-CSF) **Relipoietin** (recombinant EPO)
Shantha Biotech	**Shanferon** (recombinant interferon alpha-2b) **Shankinase** (recombinant streptokinase) **Shanpoietin** (recombinant EPO)
Wockhardt	**Wepox** (recombinant EPO) **Wosulin** (recombinant insulin)

A list of a few biologics coming off patent in the period ranging from 2012 to 2015; have been provided in Table 2.4 below [9].

Product	Company	Therapeutic Category	Patent Expiry
Enbrel	Amgen, Pfizer	Other anti-rheumatics	23-10-2012
Neupogen	Amgen	Immunostimulants	12-03-2013
Humalog	Eli Lilly	Anti-diabetics	07-05-2013
Avonex	Biogen Idec	MS Therapies	30-05-2013
Epogen	Amgen	Anti-anaemics	20-08-2013
Procrit/Eprex	Johnson & Johnson	Anti-anaemics	20-08-2013
Cerezyme	Genzyme	Other therapeutic products	27-08-2013
Rebif	Merck KGaA	MS Therapies	31-12-2013
NovoMix	Novo Nordisk	Anti-diabetics	06-06-2014
NovoRapid/NovoLog	Novo Nordisk	Anti-diabetics	07-12-2014
Rituxan	Roche	Anti-neoplastic Mabs	31-12-2014
Kogenate	Bayer	Anti-fibrinolytics	31-12-2014
Prevnar	Pfizer	Vaccines	01-01-2015
Lantus	Sanofi-Aventis	Anti-diabetics	12-02-2015
Actemra	Roche	Other anti-rheumatics	07-06-2012
Gonal-F/Gonalef	Merck KGaA	Fertility agents	16-06-2015
Neulasta	Amgen	Immunostimulants	20-10-2015
Nimotuzumab	YM BioSciences	Anti-neoplastic Mabs	17-11-2015
Norditropin SimpleXx	Novo Nordisk	Growth hormones	15-12-2015
Helixate	CSL	Anti-fibrinolytics	31-12-2015

Table 2.4 List of biologics coming off patent from 2012 to 2015, [9].

2.2.5 Challenges in the Indian Biologics Landscape

Several challenges remain in the biologics landscape in India both in the technological domain as well as infrastructural and regulatory domains. The most prevalent issues are discussed in the following sections.

2.2.5.1 Generation of Productive Cell Lines and Process Efficiencies

Only a limited number of Indian players have the technological ability to develop highly productive cell lines as well as to improve process efficiency. Five years ago most biosimilar developing firms were contracting out development of cell lines to USA and UK. Recently, however, this trend is changing with certain Indian firms, such as Reliance Lifesciences, CIPLA and Biocon being able to develop cell lines in-house.

2.2.5.2 Supply Chain Issues

Indian biologics manufacturers still depend on global suppliers for inputs such as fermentation vats and other technologies. Therefore the cost of goods on material inputs remains the same globally though the cost of labour is lower in India. The supplier base in India remains negligible.

Figure 2.9 Key challenges in the Indian biologics sector [1, 9]

2.2.6 Recommendations for Biologics (Biosimilars and Vaccines) Segment

India has the potential to become a true global leader in vaccines and biosimilars mirroring the strong position it has in small molecule generics. The goal for India should be to secure at least 10% of the global market for biosimilars by 2025 and to become a leader in vaccines in the paediatric, adult and animal segments [9]. For this to come to fruition India needs a concerted approach to boost both research and development in biopharma and strengthen the wider ecosystem supporting this segment of the industry [9].

The goal for India should be to secure at least 10% of the global market for biosimilars by 2025 and to become a leader in vaccines

2.2.6.1 Build GLP Certified Protein Characterization Facilities

India has only one GLP certified protein characterisation laboratory at NCBS, Bengaluru. These laboratories are essential in providing necessary support during two crucial stages of the biopharmaceutical product development cycle. The industry recommends that in the near term there should be at least four more such GLP certified protein characterisation laboratories spread across the country [9].

2.2.6.2 Establish Animal Testing & Breeding Facilities

For pre-clinical studies the industry needs high quality animals to generate animal experimentation data that adhere to global standards. In the near term the industry requires the establishment of at least one rodent and two large animal facilities especially primate experimentation facilities to facilitate testing of drugs, toxicity levels on large animals before studying them on humans [9].

GOI should also equip the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) to match international standards [9].

2.2.6.3 Expand Viral Testing Facilities

India does not have enough facilities for testing and evaluating the viral safety of biologics derived from characterized cell lines of human or animal origin, and compliance with International Conference on Harmonization guidance ICH Q5A (R1) [9]. Presently there are only few facilities for viral safety testing and assessment in Mumbai, Pune, and Bangalore. Therefore, GOI should support the expansion of five more viral testing facilities in the country- one each in Chandigarh, Delhi, Kolkata, Hyderabad and Chennai [9].

2.2.6.4 Simplify Import/Export Regulations

The procedures for importing comparator drugs, test materials, Genetically Modified organisms (GMOs) and Living Modified Organisms (LMOs) into India for research purposes and for exporting biologics out of India, for clinical studies in other countries, are currently very cumbersome [9].

GOI should simplify the process for importing biological samples and participate in negotiating government-to-government treaties for handling biologics. In addition, more cold storage facilities are needed in other important airports such as Hyderabad, Delhi, Pune and Chennai [9].

2.2.6.5 Form a Single Window System Approval Protocol for Establishing Manufacturing Plants
GOI must ensure that the format, content and interpretation of all such regulations is common throughout the country and introduce a single window system for securing all clearances and approvals from the various central and state agencies [9].

2.2.6.6 Formulate Biologic Specific SEZ Manufacturing Policy
Tax incentives are critical for fostering biopharma manufacturing as it needs substantial capital incentives. GOI should provide tax holidays to biologics/biosimilars manufacturing firms. These tax holidays should kick in only when the manufacturing site has been registered and successfully received approval from USFDA/EMEA. Countries such as Malaysia make it attractive for manufacturers to set up units in that country by providing tax holidays [9, 25].

India needs to create an industry friendly environment for contract manufacturing to scale. This will have a significant spill over affect. Learning from other industrial systems such as automobiles it can be seen that the automobile clusters of Pune and Chennai have created not only global manufacturing set ups but a vibrant ancillary industry that supports manufacturing. A similar policy needs to be laid out for biopharmaceutical manufacturing [9, 25].

Countries such as Malaysia make it attractive for manufacturers to set up units in that country by providing tax holidays

2.2.6.7 Strengthen Local Supplier Base
As mentioned earlier creating and strengthening a local supplier base is essential to reduce the cost of input material. The medium term goal should be to incentivize local suppliers of equipment that are needed to set up biologics manufacturing. Tax incentives to local OEMs are essential for fostering a domestic supplier base.

2.2.6.8 Need for National Vaccine Policy and Strengthening Procurement Cycle in Vaccines
India urgently needs a national vaccine policy that is driven by a inter-ministerial healthcare team that takes care of not just funding of vaccine research projects but sets an implementable policy on procurement based on robust forecasting. India should follow a 2-3 year procurement cycle especially for vaccines which is typically the case for WHO and UNICEF. To implement such a procurement cycle, a mission led approach for even greater penetration of national immunization programmes as well as improved co-ordination between demand forecasting and procurement is needed. For example, it is reported that China is able to follow high volume procurement because its healthcare agenda especially in vaccination programs is well coordinated [13]. Short procurement cycles have an adverse impact such as creating artificial shortages in the market [13].

2.2.6.9 Provide Common Infrastructure Support
India needs to provide world class infrastructures such as uninterrupted power and water supply as well as access to effluent treatment plants to boost economies of scale for biopharmaceutical firms.

2.2.6.10 Industry Oriented Curriculum Development
Research and development in biopharma requires highly specialized skill sets which are not abundant in India. While India does have courses in chemical engineering, however there are very few industrially relevant courses in biochemical engineering. Although there is an increase in well trained returnees, the numbers are not sufficient to fill the skills gap. If India is to become a global destination for biopharmaceutical research, development and manufacturing, the country needs to create an educational system that matches its global ambitions. Industry input for curriculum design is essential and hands-on training for undergraduates and postgraduate students in an industrial R&D set up is important for this sector to flourish.

2.2.6.11 Establish a National Centre for Biological Therapeutics

GOI should establish a National Center for Biological Therapeutics head quartered in Bangalore and with regional centers in Ahmedabad, Chandigarh and Hyderabad (refer section 6.8.2.4). India should use this opportunity to present herself as a biosimilar development and manufacturing hub that can mirror the country's growth in the small molecule generic space and emerge as a global leader in biosimilar manufacturing. The window of opportunity may not last for long as other countries particularly China, Malaysia, Singapore, Brazil and even East European countries such as Poland and Czech Republic are competing for the same space.

The Centre should close the technology gap and help in navigating the regulatory hurdles that many of the start-up companies are facing. This can be achieved by:

A. Training of manpower: Manufacturing biosimilars and other biologics such as vaccines requires highly trained staff and the industry will benefit substantially if the proposed centre can help in providing rigorous and hands-on training, especially in biochemical engineering - from cell line generation and manipulation techniques to batch processing. The Centre could incentivize the training process by providing scholarships (US $420/month) for 18 months.

B. Access to Information: The proposed centre and its affiliates should provide latest information to the firms in terms of new emerging technologies as well as the changing regulatory landscape across the world. The Centre should also provide help in navigating regulatory requirements.

C. Common Core Lab Facilities: The proposed centre should provide common core lab facilities that many firms in the biosimilar space can use. A common pool of high end instruments should be housed and a pay per use model should be brought in to facilitate the use of expensive, world-class technologies. The proposed centre can also be a place where industry could send samples for comparability testing besides other high end services.

2.3 Regenerative Medicine

Regenerative medicine is considered to be among the new, innovative medical therapies that have emerged in the last couple of decades. It is a multi-disciplinary field that involves basic sciences, cell therapeutics and bio-engineering techniques to enhance he functionalities of tissues or organs (refer Figure 2.10).

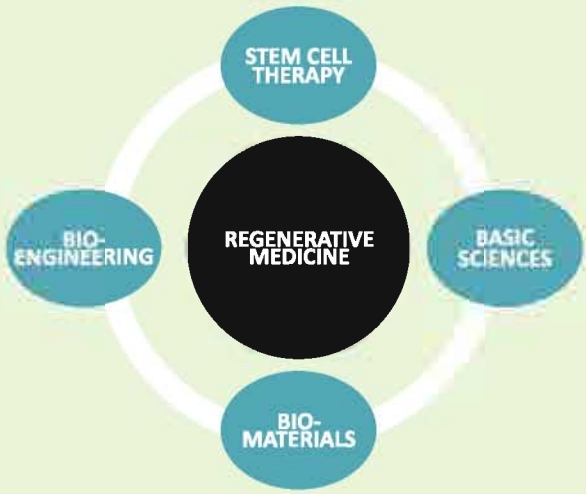


Figure 2.10 Components of regenerative medicine

The goal of cell therapy, overlapping with that of regenerative medicine, is to repair, replace or restore damaged tissues or organs

These new therapies have been defined by international healthcare authorities as follows:
The USFDA defines somatic cell therapy as, "The prevention, treatment, cure or mitigation of disease or injuries in humans by the administration of autologous, allogeneic or xenogeneic cells that have been manipulated or altered ex vivo" [14].

The US NIH defines "Regenerative Medicine" as the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects" [15]. The goal of cell therapy, overlapping with that of regenerative medicine, is to repair, replace or restore damaged tissues or organs [16]

Cell therapy may take the form autologous therapy where patient's own cells and tissues are used for therapeutic purposes or allogeneic therapy which uses cells and tissues that are derived from a donor [14, 15, 16].

Regardless of the type of cellular therapy, it involves several complex cell and tissue engineering techniques that manipulate cells during separation, selection, expansion and modifying the biological characteristics of the cells [14, 15 & 16]. Such therapies can be done at a single point of care or might involve logistical co-ordination amongst various laboratories spread across the globe [14].

Regenerative medicine (RM), as well as other cellular therapies, is a rapidly emerging area of bio-medical research with enormous therapeutic potential. They are expected to improve our understanding of fundamental biological processes, help in developing a model for human diseases such as birth defects or cancer, in establishing a platform for drug screening and toxicity studies while quickening the process of drug discovery and finally, they can be utilized for therapeutic applications involving repair of damaged tissues. It is envisaged that stem cells are going to be a major branch of medical treatment and are going to be a standard of cure and practice in the years to come [14, 15 &16].

2.3.1 Global Landscape of Regenerative Medicine and Tissue Engineering

RM especially stem cell therapy evolved from tracing from bone marrow transplants in the 1950s and 1960s as a procedure of choice. This field grew rapidly as stem cells were successfully derived in the form of adult stem cells and human embryonic stem cells (hESC) and shown to be plastic and advancement in in-vitro-fertilization (IVF), biomaterial engineering (especially by scientists in the USA such as Professor R Langer and Professor JP Vacanti). The 1990s and early 2000s saw the emergence of RM firms in the UK and USA such as Organogenesis, Advanced Tissue Sciences (ATS) and Ortec.

The field has grown rapidly over the last decade with the stem cells based product market expected to reach US $64 billion by 2015 [17]. The leading countries for stem cell research and development are the USA, UK, Germany, Japan, Canada and Israel with new growth countries such as South Korea, China and India.

Global stem cell policy has been shaped by governments across the world seeking to balance ethical and regulatory issues for the benefit of patients.

The USA: President Obama signed the executive order (EO) 13505, "Removing Barriers to Responsible Scientific Research Involving Human Stem Cells" on 9 March 2009. The EO withdrew the ban that President Bush had declared in 2001 on the use of federal funds for research using hESCs created after 2001. New NIH Guidelines for funding hESC research became effective following the EO on July 7th, 2009. However researchers are still not able to use the existing federal funds to derive or create lines (however, scientists are allowed to conduct research on existing approved lines created using other funding means). The reason for this is the Dickey-Wicker amendment, which became law in 1996, and has been renewed by the Congress every year thereafter. The law specifically bans the use of public funding to create human embryos, or for research in which embryos are destroyed, discarded or knowingly subjected to risk of injury. Beyond this national directive, there is a huge disparity of laws between individual US States [18].

Dickey-Wicker Amendment: The law specifically bans the use of public funding to create human embryos, or for research in which embryos are destroyed

From the time the policies were revised by the US government in 2009, the National Institutes of Health (NIH) has invested over US $300 million for human embryonic stem cell research [19]. The state of California has established the California Institute for Regenerative Medicine (CIRM), a world leading centre for stem cell research and development. Besides the NIH and individual state funds, Ministry of Defence (MOD) also supports stem cell research projects.

The United Kingdom: The UK was one of the first countries to have put in place and implemented a stem cell regulatory policy. The regulatory body Human Fertilization and Embryology Authority (HFEA) was established after the Human Fertilization and Regulatory Act was legislated in 1990. HFEA has the authority to implement the Human Fertilization and Embryology Act which governs the use of human embryos in research in the UK. Although the laws strictly forbid human reproductive cloning and somatic cell nucleus transfer (SCNT), the policies permit hESC research, and derivation of new hESC lines from supernumerary in-vitro fertilization (IVF) embryos under strict conditions [18].

This act has kept pace with the rapidly changing technological advancement including induced-pluripotent stem cell technology (iPS) [18]. UK has set up a publicly funded stem cell network and the focus has been on translation of stem cell therapy through combination of public and private funds. It has leading research centres in Edinburgh and Cambridge. The Office of Lifesciences (OLS) and Technology Strategy Board have dedicated grant funding for stem cell translation. In the UK and in the rest of the European Union, stem cells are now regulated by Advanced Therapeutic Medical Products (ATMP).

South Korea: It has a central coordinated strategy for development of stem cell product and therapy. The Ministry of Science, Education and Technology manages bioscience research policy and oversight. The Bioethics and Biosafety Act became effective on December, 2008 and allows for the derivation of excess IVF embryos and for somatic cell nuclear transfer SCNT. In addition, both reproductive cloning and interspecies SCNT are specifically banned [18].

China: The country has a very liberal environment for hESC. Research on both hESC and adult stem cells is supported by government funds. The Ministry of Health and Ministry of Science and Technology passed a guideline called the 'Ethical Guidelines for research on Human Embryonic Stem Cells' in 2003. The guidelines prohibit reproductive cloning and allow for the derivation of hESCs from excess IVF embryos and SCNT [18].

The first RM products to get FDA approval were Carticel (autologous chondrocytes manufactured by Genzyme) and ApligrafTM (by Organogenesis though marketed by Novartis until 2003) in 1998. In the last 5 years FDA has approved SynerGraftTM by CryoLife. Meanwhile in 2008, Spanish surgeons and scientists conducted the first successful tissue-engineered whole organ (windpipe) transplant. The windpipe was made using the patient's own stem cells [20]. Several products and therapies by leading stem cell firms such as Osiris (for myocardial infarction; Diabetes Type 1), Mesoblast (cardiovascular diseases, Osteo-arthritis), Gamida (autoimmune diseases and hematological disorders) are being developed for a range of disease conditions.

The stem cell market in India was worth approximately US $450 million in 2010 and is growing at a rate of 15%

2.3.2 Stem Cell Scenario in India

Stem cell research in India is still in a nascent stage with around 40 organizations, both public and private, involved in various aspects of regenerative medicine and stem cell research. The stem cell market in India was worth approximately US $450 million in 2010 and is growing at a rate of 15%.

2.3.2.1 Indian Public Funded Stem Cell Institutes

Public funded institutions have been supported by DBT and CSIR. DBT, in 2009, established The Institute for Stem Cell Biology and Regenerative Medicine (inStem), which is India's first dedicated institute for research in stem cells. inSTEM has recently signed a research partnership Memorandum of Understanding (MoU) with the US-based California Institute for Regenerative Medicine (CIRM) as well as a MoU with the Institute for Integrated Cell-Material Sciences (iCeMs), Japan to establish a satellite lab in NCBS.

Other leading institutes like Christian Medical College (CMC) in Vellore, National Centre for Biological Sciences (NCBS) in Bangalore, Jawaharlal Nehru Centre for Advance Scientific Research (JNCASR)- Bangalore, National Centre for Cellular Sciences (NCCS) in Pune, The Institute of Immunohematology in Mumbai, National Brain Research Centre (NBRC) in Delhi and Cellular and Molecular Biology (CCMB) in Hyderabad are also premier public establishments that conduct pioneering research on stem cells.

2.3.2.2 Private Stem Cell Firms

Private firms in India are in the early stages of producing stem cell therapies and products while mostly umbilical cord blood banking has emerged as a major revenue generator for the other players in this field. Home grown companies, such as Reliance Life Sciences, Stempeutics and L.V. Prasad Eye Institute (LVPEI) are at the forefront in the development of stem cell products and therapies in India. Companies like LifeCell, StemCyte India therapeutics and Cryo Stem Cell are involved with the collection and storage of umbilical cord blood stem cells.

Stempeutics is conducting phase-II clinical trials of its product Stempeucel in four disease conditions viz. osteo-arthritis, diabetes mellitus type II, liver cirrhosis and chronic obstructive pulmonary disease (COPD). Reliance Lifesciences is focussed on are cardiac disorders, neural

degeneration, metabolic disorders, ophthalmic diseases, burns and wound management, diabetic and venous ulcers, skin pigmentation disorders and bone disorders. They also have in house human embryonic stem cell lines that have been registered in the International Stem Cell Registry (UMASS, USA). RLS has established the safety and efficacy of the following therapies in clinical trials: Relinethra®, Relinethra C® and Cardiorel®. LVPEI has pioneered the treatment of corneal blindness in India using cultured limbal stem cell therapy and has established research partnership with University of Sheffield, UK.

Although only a few companies in India are working in the field of stem cell research, they have the potential to make important global contribution to the development of the emerging stem cell technological field. The key players in the stem cell industry, from both the public as well as the private sectors (in red) have been listed in Table 2.5.

Type of Stem Cells	Public/ Institutes
Embryonic Stem Cells	National Institute for Research in Reproductive Health, Mumbai National Centre for Biological Sciences (NCBS), Bangalore National Centre for Cell Science (NCCS), Pune National Brain Research Centre (NBRC), Maneswar Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvanthapuram Reliance Lifesciences, Mumbai
Hematopoietic Stem Cells & Bone Marrow Mononuclear Cells	Christian Medical College (CMC), Vellore, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPIMS), Lucknow Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh Manipal Hospital, Bangalore, All India Institute of Medical Sciences (AIIMS), New Delhi National Institute of Immunology (NII), New Delhi Indian Institute of Science (IISc), Bangalore Research & Referral Hospital, New Delhi Indian Institute of Technology (IIT), Chennai
Limbal Stem Cells	L V Prasad Eye Institute (LVPEI), Hyderabad R. P. Centre, AIIMS, New Delhi Regional Institute of Ophthalmology, Kolkata
Neural Stem Cells	NBRC, Maneswar National Institute of Mental Health & Neurosciences, Bangalore NCCS, Pune
Mesenchymal Stem Cells	CMC Vellore SGPIMS, Lucknow Manipal Hospital, Bangalore Stempeutics, Bangalore (focussed on therapy) Reliance Lifesciences, Mumbai
Liver Stem Cells	Centre for Liver Research and Diagnostics, Hyderabad Centre for DNA Fingerprinting and Diagnostics, Hyderabad
Pancreatic Progenitor Cells	National Institute of Nutrition, Hyderabad NCCS, Pune
Cardiac Stem Cells	Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram
Muscle Stem Cells	Centre for Cellular & Molecular Biology, Hyderabad
Cancer Stem Cells	IISc, Bangalore
Stem Cell Banking	Reliance Lifescience, Mumbai LifeCell International, Chennai Nichi-In Centre for Regenerative Medicine, Bangalore Cryosave, Bangalore

Table 2.5 Stem Cell Organizations in India (Both Public and Private), [Adapted from 11, 21]

2.3.2.3 Indian Stem Cell Regulation and Funding

In India stem cell regulation falls under the purview of multiple agencies involving Ministry of Health (Drug Controller General India-DCGI; and Indian Council of Medical Research-ICMR) as well as by Ministry of Science and Technology via DBT.

The ICMR, the apex body regulating medical research in India and the Department of Biotechnology (DBT) under the Ministry of Science and Technology, Government of India (GOI) drafted the guiding principles for stem cell research and therapy in 2007. In 2011, the ICMR also announced the completion of 'public consultations' for regulation of stem cell research and stated that they will provide the revised guidelines in 2012 [22].

DCGI established the Cellular Biology Based Therapeutic Drug Evaluation Committee (CBBTDEC) in Nov 2010. This committee is formed under the aegis of DCGI and the Director General of ICMR has been nominated as the Chairman of this committee. The NAC-SCRT (National Apex Committee-Stem Cell Research Therapy) is another regulatory committee that is under the aegis of ICMR. Moreover, all cord blood banks require mandatory registration with the DCGI.

With norms being formulated for stem cell research, banking and storage facilities, and the rise in public-private partnerships, India has the potential to emerge as a global leader

The ICMR-DBT guidelines have not yet approved any indications of stem cell therapies except for bone marrow transplantation (BMT) and the guidelines consider all other procedures excluding BMT as experimental. Clinical trials for stem cell based therapies require prior approval of DCGI.

The Department of Science and Technology (DST), along with the DBT, ICMR, and CSIR constitute the government funding agencies for basic as well as translational research in stem cells in India.

2.3.3 Stem Cell Recommendations

Considering the latent potential for this sector, stem cell research in India has started in a positive direction but still has a long way to go. With norms being formulated for stem cell research, banking and storage facilities, and the rise in public-private partnerships, India has the potential to emerge as a global leader in the areas of regenerative medicine and tissue engineering.

For this field to grow rapidly several issues have to be resolved. The following are the list of issues and recommendations to foster growth of RM in India.

2.3.3.1 Establish a Clear Regulatory Framework

Given the importance of this nascent field, there are still no laws that govern stem cell research and development in India. GOI had drafted guidelines for stem cell research and development; however a definitive law is yet to be drafted.

In November 2010 under the aegis of DCGI and under the Chairmanship of ICMR a committee called the "Cellular Biology Based Therapeutic Drug Evaluation Committee" (CBBTDEC) was formed. However, India still lacks a clear regulatory path for stem cell therapies oversight and it is hindering the growth of this field. Besides, stem cell therapies, there are also no regulatory laws for stem cell banking.

Further the industry opines that procedural delays increase the risk of projects specially since and it currently takes 12 to 18 months to get approval from the date of submission. This makes Indian stem cell firms look at destinations such as Malaysia. The Malaysian Biotechnology Corporation has a clear, un-ambiguous policy for regulatory approval. It provides a response within 45 days and an indication for 'go' and 'no-go' decision within 90 days.

2.3.3.2 Establish Infrastructure for Pre-Clinical Animal Model Studies in Stem Cells
India needs to establish and strengthen infrastructure and expertise for creating animal models for various diseases to conduct pre-clinical studies especially in stem cell. Indian stem cell firms depend on UK, USA or Singapore to develop animal models for the disease conditions that they focus on.

2.3.3.3 Strengthen Stem Cell Quality Control Regimes
Stem cell product manufacturing and therapy involves variety of specialized intervention and manipulation and involves stringent safety issues including different sets of unique GMPs. DCGI categorizes stem cell manufacturing within the general manufacturing protocols of Schedule M and audits the research and manufacturing labs. There should be specialized expertise within DCGI for assessing quality issues for stem cell manufacturing.

2.3.3.4 Streamline Policy for Import and Export of Human Tissue
The present policy for import and export of human tissues is cumbersome and should be streamlined immediately.

2.3.3.5 Dedicated Funding for Translational Stem Cell Therapy including Stem Cell
In India, while schemes for early stage and proof of concept exist for industrially relevant biotechnology projects (such as SBIRI, BIPP and NMITLI), no specific stem cell translational funds are available for industry.

In the USA, for example, organizations like CIRM function both as basic research as well as funding agencies for translational research in stem cell therapies. CIRM recently has recently expressed interest in funding clinical trials [23].

A stem cell firm spends close to US $1458.33 per patient for Phase II or Phase III trials thus the cost of conducting clinical trials is high. In India clinical trials by small stem cell firms could be subsidized by the GOI, especially procedures such as CT Scans and MRI Scans.

In India clinical trials by small stem cell firms could be subsidized by the GOI

2.3.3.6 Create a Platform for Academia-Industry Linkages in Stem Cells
While centres for excellence are present in the stem cell arena, especially institutes such as inSTEM, Christian Medical College Vellore, AIIMS among other organizations, many of these institutes are islands with minimal interactions with the industry. Incentivizing interactions among publicly funded stem cell institutes and stem cell firms would go a long way in bridging this gap.

2.3.3.7 Foster Skilled Talent Pool
Stem cell and cellular therapies have immense potential for growth in India. However, India lacks trained manpower that is well versed in stem cell techniques and management including embryonic stem cells. While efforts such as establishing inSTEM and other stem cell focused centres will enhance the skill sets of researchers in this field industry exposure in stem cell manipulation (especially in GLP facilities) is essential.

GOI should establish 100 PhD and postdoctoral industrial fellowships in Regenerative Medicine which would aim to provide cutting edge scientific training to researchers. Further GOI should tie up with leading Regenerative Medicine centres in the world such as California Institute of Regenerative Medicine (CIRM) and Roslin Institute (UK) and send at least 25 researchers each year for short term and long term training at these world renowned regenerative medicine institutes. A fund allocation of US $ 3.13 million will be required to over 5 years to implement these fellowships.

2.3.3.8 Focus on Disease Specific Stem Cell Research
There is a lack of information regarding the amount of funding that is being channelized for stem cell funding in different disease areas. GOI should identify and fund specific disease areas where stem cell research could make an impact in the next 5-10 years.

2.4 Medical Technology: Medical Devices, Diagnostics and Imaging

Medical technology primarily encompasses healthcare devices and imaging methods that aid clinical diagnosis, monitoring and therapy for patients. The medical technology industry in India is currently the fourth largest in Asia and comprises of varied segments like medical instruments, syringes, X-ray equipment, among many others. In 2011, PwC estimates stated that the Indian medical technology industry is predicted to grow 23% annually for the next five years and is expected to touch US $10.7 billion in 2019 [24].

Hence, with India being one of the emerging markets for medical technology, it is essential to identify its key players in this sector, the latest developments and market trends, the public institutions, the challenges currently faced by it, and also discover the potential areas of growth, collaboration and market opportunities for this sector.

2.4.1 Global Perspectives

The global medical technology industry revenue is US $350 billion and the USA remains the leader in the medical technology industry accounting for 40% of the world market [24]. The USA is home to 32 of 46 medical technology companies with annual turnover of more than US $1 billion. The 2011 PwC report on medical technology highlighted that the dominance of the USA in this sector is due to confluence of positive drivers:

A. Financial incentives, including a high level of reimbursement for medical procedures,
B. Effective innovation funnel through cutting edge research from academic medical centres,
C. Supportive regulatory system where FDA has taken a leadership position in setting standards and guidelines
D. Supportive funding landscape where medical technology is ranked as the second largest category among venture capitalist [24].

The rising cost of healthcare in the West especially in the USA and the European Union will influence global giants to increasingly look to developing countries such as India

Besides USA, which has global giants such as Johnson & Johnson, GE Healthcare, Bectin Dickinson, Stryker and Abbott other global players are based in Germany (B. Braun, Siemens Healthcare, Fresenius Medical Care, Drager), United Kingdom (Smith & Nephew), Netherlands (Phillips Healthcare), Japan (Olympus, Terumo) and Switzerland (Alcon). The global MNCs typically spend anywhere between 8 to 12% of their revenues on R&D.

In the USA, medical devices fall under the purview of the FDA in particular the Center for Devices and Radiological Health (CDRH). Laws governing medical devices were enacted as part of the Medical Devices Amendments of 1976 and the Safe Medical Devices Act of 1990 [25].

The rising cost of healthcare in the West especially in the USA and the European Union will influence global giants to increasingly look to developing countries such as India not just as markets but as destination to conduct part of their current R&D [24]. Highlighting the case of rising healthcare cost and the policy measures taken by countries like the USA is the 2010 Act, the Patient Protection and Affordable Care Act (PPACA), that has the intention to reduce soaring healthcare costs[24].

2.4.2 The Indian Scenario

The Indian market is suitably poised to provide innovations in medical technology in a quicker, efficient and affordable manner to a world that is dealing with dynamic changes in healthcare cost. The Indian device market, which was US $2.75 billion in 2008 is expected to reach US $10.7 billion by 2019 [24, 26]. The Indian device market consists of medical instruments, orthopaedic and ophthalmic devices, syringes, needles, catheters, scanning devices (X Ray, CT scan), bandages. A CII and Deloitte report quoting a Cygnus study on the sector in 2010 provided the market distribution of the device industry which is given in the Figure 2.11 [26].

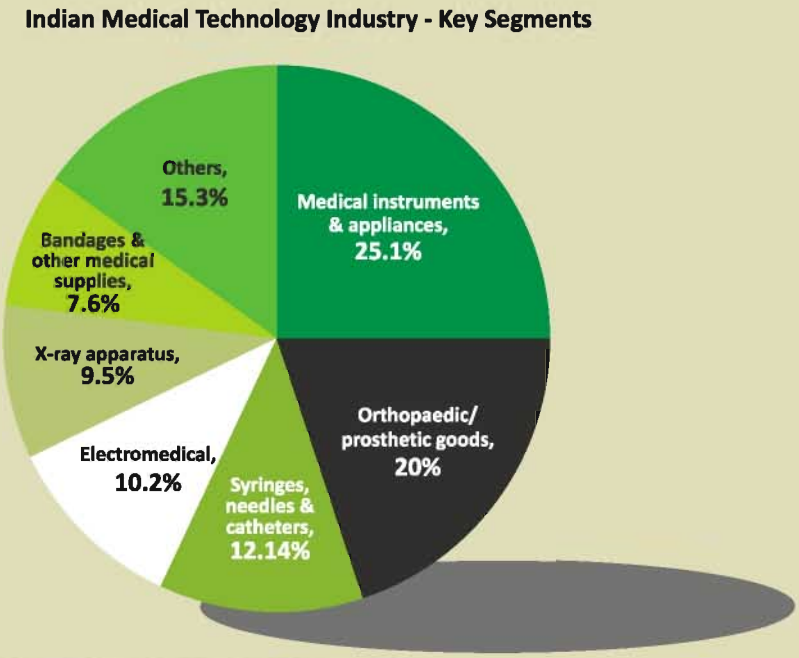


Figure 2.11 Key segments of the Indian medical technology, [26]

Despite the challenges recent developments in this sector look promising and are potential growth drivers for medical technology in India. Recently, the Indian Planning Commission marked the medical equipment sector as a priority area for the 12th Five Year Plan [27], and this promises to fuel the progress of the medical device market in India.

India faces the dual challenges of dealing with both atypical developing world disease patterns such as infectious diseases such as TB (India has a quarter of global TB patients), HIV, chikungunya and Malaria on the one hand and a continuing increase in chronic diseases such as diabetes, cardiovascular diseases and cancer. Further emerging threats from global pandemics such as SARS and H1N1 will have to be dealt with. These factors have strengthened the market potential for healthcare monitoring devices and diagnostics among many others.

Increasing healthcare coverage and medical tourism has also enabled the expansion of the medical technology industry in India. The growing healthcare infrastructure like the increase in the number of hospitals, dental clinic chains, and diagnostic centers and R&D facilities across India are also expected to drive the future prospects of the medical device industry.

Preventive medicine will be the key in keeping the nation healthy. This will require effective screening, rapid detection and implementation of healthcare measures. Medical technology products in India should be able to meet the three driving forces- affordability, accessibility and high quality.

Multinational medical technology firms such as GE Healthcare and Philips Healthcare have established R&D centres in India with the intention to develop products for Indian market that will also have relevance for other geographies. For example GE Healthcare, from its Jack Welch R&D Centre in Bangalore, developed a hand held ECG machine (named MAC 400) in 2010. The Mac400 costs US $800 and the cost of an ECG procedure has been reduced to $1per person thus increasing affordability and accessibility [28]. Hence, India is increasingly becoming a favoured destination for developing novel devices in this sector. However, India still needs to improve its regulatory infrastructure, promote domestic manufacture and penetrate further in to rural markets in order to meet the 2025 vision for the Indian medical device sector.

Medical technology products in India should be able to meet the three driving forces- affordability, accessibility and high quality

Leading international companies in this sector include Johnson & Johnson, Abbot, Roche and Siemens, where as domestic players comprise of Transasia Biomedicals, Tulip Group, J Mitra & Co., Perfint, Xcyton, Bhat Biotech, Remidio, Bigtec, Achira Labs, Trivitron, Optocircuits, Diagnova and Span Diagnostics among many others.

Many Indian firms are bringing innovative, high quality but affordable devices and diagnostic kits to the market. Bigtec uses micro-electromechanical-systems (MEMS) to design and manufacture innovative, high quality, affordable lab-on-chip microfluidic devices to detect multiple pathogens. These diagnostic kits are highly sensitive and offer rapid detection functionality. It has plans to bring to the market a lab-on-chip diagnostic kit that can detect malaria, hepatitis B, hepatitis C, chikungunya, HIV & HPV. Similarly Xcyton has developed immuno-diagnostic kits for detection of infectious agents such as HIV, Hepatitis C and Japanese encephalitis. Achira Labs is focussing on a microfluidic chip platform as well as an innovative integrated fabchip (fabric chip using locally sourced silk) based diagnostic kits.

Similar to start up diagnostic firms many device firms such as Remidio and Perfint are bringing medical devices that are of high quality yet at the same time are affordable. Based out of Bangalore, Remidio has designed and built a unique handheld monocular ophthalmoscope, eyedioVR10. The device can show a 45 degree field view of the retina, thereby providing a high clarity view of the retina. Perfint, a Chennai based medical imaging firm, has launched a product PIGA that facilitates image guidance and enables minimal invasiveness during CT scans thereby enabling radiologists to accurately perform important procedures such as biopsy and RFA in thorax. In the ophthalmic arena Aurolabs, an arm of Aravind Eyecare, manufactures world class intraocular lenses and medical sutures.

Many Indian firms are bringing innovative, high quality but affordable devices and diagnostic kits to the market

Private companies like Span Diagnostics, Optocircuits and Perfint intend to diversify their portfolio and are planning towards major expansion in the future.

Increasing investments in the private sector, government initiatives and academic collaborations predict a steady growth pattern for the Indian medical technology sector. Combination products such as drug-eluting stents are also expected to drive the future of this industry. Thus, medical technology in India shows a significant potential for future growth.

2.4.3 Collaborations & Future Perspectives

A co-operative effort from academic, industrial, healthcare and government sectors would ensure the progress of the medical devices and diagnostics industry in India. One such initiative, like the Stanford India Bio-Design, is an example of a step taken in this direction. However, more such collaborations need to be encouraged for fostering innovative and sustainable ideas in the medical technology ecosystem. Such initiatives would aid in bridging the industry-academic gaps that currently exist in India, and would also help in the development of a mutually beneficial environment that would be able to adapt to the changes in both the sectors.

Over the past few years many domestic firms and multinationals are partnering specifically in the medical technologies for example Trivitron has tied up with Celerus to launch cancer screening technologies in India [29].

A few of the significant partnerships and their outcomes have been listed in Figure 2.12 [30, 31 & 32].

GE-Healthcare, Government of Madhya Pradesh & Sanya Hospitals and Diagnostic Centre

- Set up a diagnostic centre at Netaji Subash Chandra Bose medical College Hosptial at Jabalpur and Installed CT,and MRI diagnostic facilities there
  Invested USD 1.6 million on equipments and provided medical professionals
- Consequently, diagnostic imaging costs were made affordable for patients.

B Braun and Government of Andhra Pradesh

- Made an investment of USD 7.29 million for 11 hemodialysis centers with a total of 111 hemodialysis devices.
- Free dialysis would be provided for patients and the state government would pay a sum of USD 22.5 per patient for the treatment.

Stanford India Bio-Design

- Medical technology training program funded by Department of Biotechnology, Ministry of Science and Technology, Government of India, Stanford University, and IIT Delhi in joint collaboration with All India Institute of Medical Sciences (AIIMS) and Indo-US Science & Technology Forum (IUSSTF)
- Many successful companies (like AUM Medical) have been launched and are receiving international attention.

Figure 2.12 Joint ventures in the Indian medical device sector [30, 31, & 32]

2.4.4 Indian Medical Device Regulatory Environment

India is a regulated market for medical device and diagnostic kits. The in-vitro diagnostic (IVD) kits in India are regulated by the Drug Controller General of India (DCGI) which is part of the Central Drug Standard Control Organization (CDSCO). Two different cells exist viz. Device Cell and Diagnostic Cells which are staffed with Drug Inspectors and Technical Data Associates that provide the oversight for medical devices and diagnostics firms (see figure 2.13).

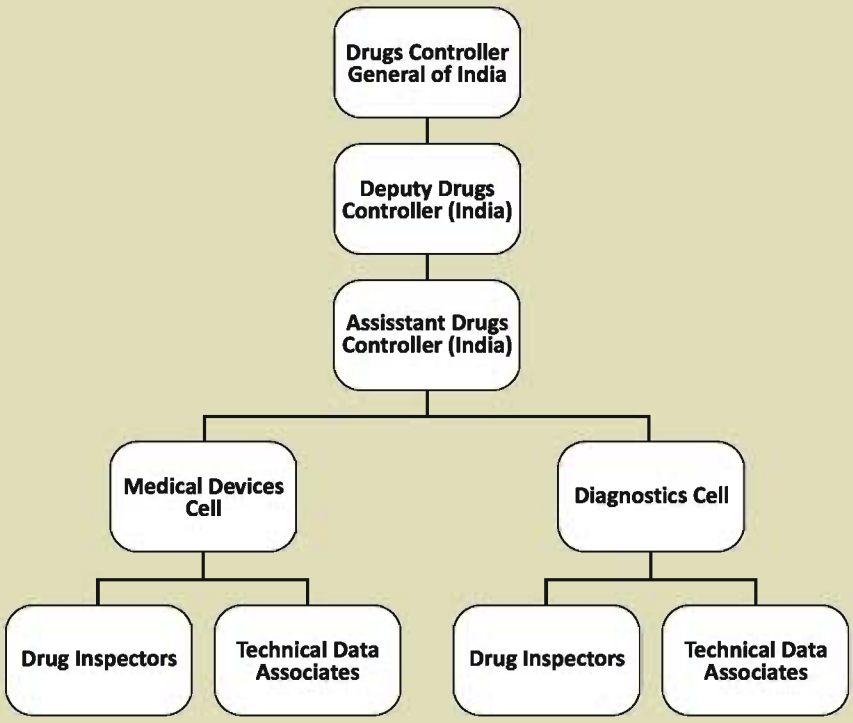


Figure 2.13 Organization of medical device regulation in India (from DCGI Website)

The state offices then directly monitor the medical technology in the respective states. This, quite often, leads to discrepancies among the rules administered by the different state offices as well as between the state and central offices. Moreover the custom officials at the ports also have their own set of guidelines. As a result, the regulatory process becomes time-consuming and difficult to manage at different levels.

All diagnostic products that are manufactured and sold in the country require a license. IVD are divided into two groups; viz critical and non-critical devices. Critical devices are the ones that are used for testing of HIV, HCV, Blood grouping, and Malaria. All other devices are considered as non-critical.

DCGI conducts batch testing (via the National Biological Laboratory or The National Institute of Communicable Diseases) and audit visit of the manufacturing site before providing an approval for a manufacturing license [111].

Figure 2.14 Challenges and growth drivers for medical technology in India

2.4.5 Recommendations for Medical Devices and Diagnostics

The Indian medical devices, diagnostics and equipment sector is growing. However, India imports 70% of all medical technology, which has a downstream affect on affordability of these technologies. Since costs are high, rural healthcare providers are unable to afford buying medical instruments.

India has the optimum skill sets in engineering, biology and chemistry to leverage this strength and be a leader in this sector and supply the domestic market with affordable technologies and products.

2.4.5.1 Promote Domestic Manufacture of Products through Procurement & Manufacturing Tax Incentives

As mentioned before India imports 70% of medical technologies. There is a dearth of initiatives that promote domestic manufacture of medical technology within the country. In some instances, government import laws also tend to favour the import of a medical device, as opposed to the domestic production of the device. Low level R&D investment, lack of capital investments for medical device companies and exemption of import duties for medical technologies absent in India are also factors that discourage local manufacture of such products [26].

Similar to the Biosimilars opportunity, India is at a threshold to leverage its strengths to become a significant global manufacturing destination for medical technologies. Several factors are important for India to gain recognition as a manufacturing destination.

A. Link domestic manufacture to procurement by scaling up national programmes such as NRHM

Indian medical device and diagnostic firms are able to bring out innovative, high quality products that are affordable. Up-scaling pan Indian programmes such as NRHM, Government hospitals and primary healthcare centres and sourcing medical devices and diagnostics from Indian medical technologies firms (as long as the products meet the criteria) would provide a huge impetus to firms in turn to scale up manufacturing as well as increase spending on R&D. In India, Ministries for funding (such as DST, DBT, CSIR) are not the Ministries that decide procurement (Ministry of Health) are different and hence there is no alignment in procurement policies. The Ministry of Health, for example, has the criteria that for procurement a product has to be 3 year in the market which does not help innovative medical device firms that have brought new products into the market. An explicit policy on procurement of 'made in India' medical devices and diagnostics are critical for domestic market creation in India. This will give a much needed impetus to manufacturing of medical technologies by both domestic and multinationals in India.

B. Enable the wider ecosystem for medical device and diagnostic for rural accessibility

The majority of the Indian population, around 68.84% [33], lives in rural parts of India. Hence, for the entire nation to develop and meet the vision for 2025, the advancements in healthcare technologies should reach the rural masses in an affordable and accessible way. For this to happen; training of staff in primary healthcare centre is essential. Besides; insurance coverage would enable use of medical technologies.

C. Provide tax incentives to boost local manufacturing as well as technology acquisition

GOI should provide tax benefits and import duty exemption in the case of technology acquisition and adoption for Indian market.

An explicit policy on procurement of 'made in India' medical devices and diagnostics are critical for domestic market creation in India

2.4.5.2 Establish an Independent Regulatory Framework

Currently medical devices are regulated as drugs under the Drugs and Cosmetics Act by the DCGI of CDSCO, the central governing body of the country. There is a lack of a dedicated centre in the country to oversee certification, approval or monitoring of medical devices. An independent body should be set up to oversee the regulatory aspect of this sector. This will reduce approval timelines as well.

It is also important that the DCGI has retained personnel who are experts in medical devices, diagnostics and equipment. For this continuous training and engagement with other leading agencies in the world is required. A budget allocation of US $1.04 million for continuous training is required.

2.4.5.3 Establish Testing Facilities for Medical Devices, Diagnostics and Equipment

Currently DCGI has identified two publicly funded laboratories for testing medical devices. India needs another four such testing facilities that work in close co-ordination with the industry. A budget allocation of US $20.83 million is required to establish these testing facilities and staff them with technically competent staff. These testing facilities could be moulded in the form of the recently established Ganit Lab or C-CAMP at Bangalore such that besides being testing facilities

these centres could also act as technology platforms for medical technologies. It is essential that we bring together experts in design, nanotech and electronics, biology and biomaterials for the growth of this sector. Government should also create a platform where clinicians and other end users can legitimately interact with medical technology firms.

2.4.5.4 Create Multi-Disciplinary Courses in Medical Technologies

There are a few institutions in India that have courses in biomedical engineering either at bachelors or post-graduate level. It is urgently required that all IITs, NITs and other leading engineering institutes offer extensive courses in medical technologies with intense industry exposure. Besides this, these institutions also must have trained teaching staff both academic and practitioners from industry. An integrated all India entrance examination for postgraduate education in medical technologies along the lines of the DBT-biotechnology national exam is essential.

A pilot initiative to offer BTech & MTech courses in biomedical engineering should be started at all IITs (presently only IIT Mumbai & Chennai offer MTech courses in biomedical engineering).

2.4.5.5 Encourage Mobility Schemes for Academicians and Industry Experts

Government should encourage and fund academicians to spend at least 3 years in a medical technology firm to carry out joint research. Similarly industry should be incentivised to send their R&D experts to spend R&D time in an academic lab of choice.

2.4.5.6 Build a Medical Technology Cluster

India indeed has a huge potential to tap into its existing skill sets in engineering, design and biology, and build a medical technology cluster. This cluster could be located in Bangalore, since it hosts several medical device start up firms, has precision engineering tool manufacturers and institutions such as IISc, NCBS and NIMHANS.

2.4.6 Companion Diagnostics

Companion diagnostics are tests that aid in selecting treatment protocols for patients by evaluating the safety and/or efficacy of the therapeutic product. These tests can be developed as a companion to the drug molecule or after the drug has been launched in the market. Thus, companion diagnostics can significantly impact the drug development process not only by increasing the efficacy and safety of the therapeutic product (& hence enabling personalized medicine), but also by decreasing the cost and time required for its commercial launch (see Figure 2.15).

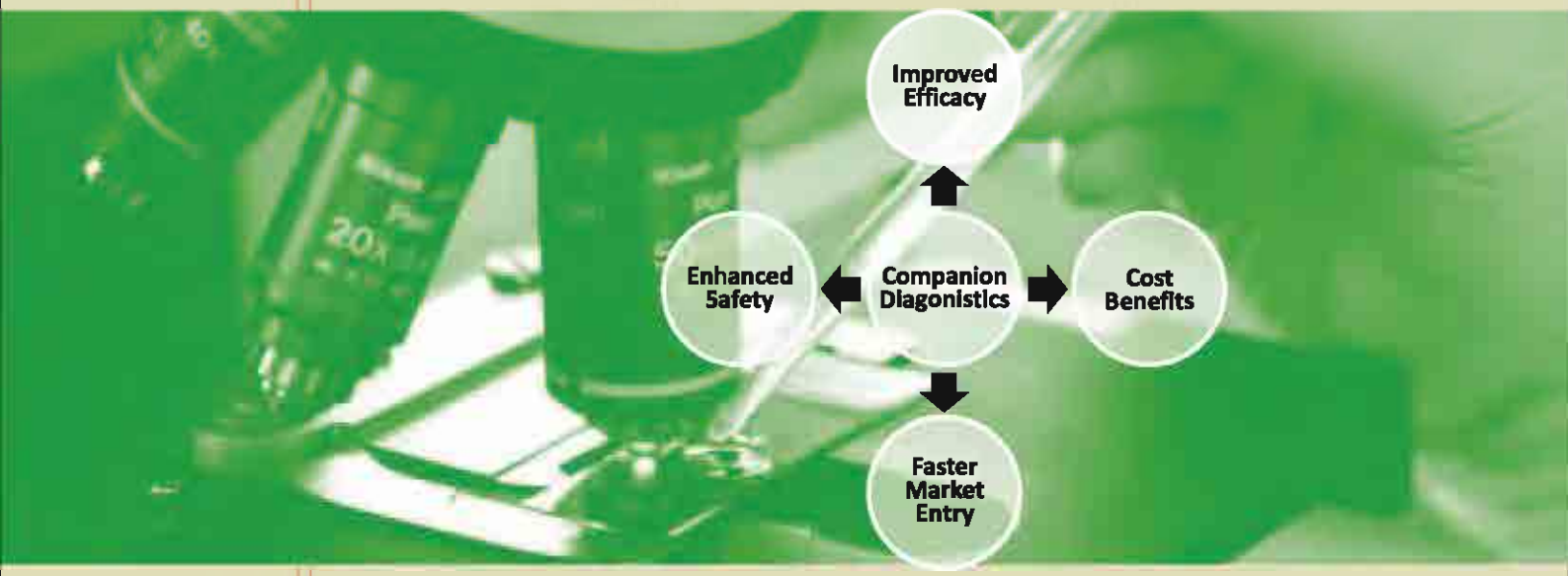


Figure 2.15 Advantages of companion diognostics

2.4.6.1 Global Outlook

Companion diagnostics is an emerging field in drug discovery and development today. In an analysis done by Visiongain, the global value of the companion diagnostic market in 2010 was US $1.3bn and the market is expected to grow steadily in the near future [34].

FDA has approved several companion diagnostic tests for example Trastuzumab treatment for HER-2 positive breast cancer for treating HER-2 positive breast cancer patients in 1998 with several strict rules on how it could be administered. FDA again expanded the rules for administration in 2006 [35]. It opened up new avenues for facilitating research in the pharmacogenomics sector. Similarly The Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis 2 (I SPY 2 TRIAL) launched in 2010 enables women with locally advanced breast cancer to check if investigational drugs can augment standard chemotherapy for the most favorable therapeutic outcomes. It will also help to personalize chemotherapy based on tumor genetics and hence can provide pharmacogenetic advantages for future patients [36]. Quintiles, a leading clinical research organization, has also supported I SPY 2 [37]. In August 2011, FDA approved Zelbograf and a companion diagnostic test by Roche's Cobas 4800 BRAF V600 Mutation test that can determine whether patient's melanoma cells have the BRAF V600 mutation [38]. Similarly, FDA approved companion diagnostic tests for Pfizer's Xalkori (crizotinib) and its companion diagnostic test that has been developed by Abbott.

Increasingly pharmaceutical firms are focussing on companion diagnostics as they seek to improve drug response profiles and hence improve clinical trial outcomes. A PwC report highlights the fact that the number of companion diagnostic partnerships increased from 19 in 2009 to 25 in 2010. The disease areas that global pharma and diagnostic firms are focussing on to develop companion diagnostics range from cancer (lung, brain, skin, gastric and pancreatic), neurology, infectious diseases (influenza, hepatitis C), autoimmune (lupus), ophthalmology (age-related macular degeneration) and kidney disease [39].

Increasingly pharmaceutical firms are focussing on companion diagnostics as they seek to improve drug response profiles and hence improve clinical trial outcomes

Some of the recent collaborations in the global companion diagnostic sector have been listed in Table 2.2 below.

Table 2.6 Global collaborations for companion diagnostics

Companies Collaborating	Date	Therapeutic area for collaboration
LabCorp and Merck	July 2010	Companion diagnostics to detect Il28 polymorphism in hepatitis C patients [39]
Dako and AstraZeneca	Jan 2010	Companion diagnostics for undisclosed cancer [39]
MDxHealth and GSK	Sept 2010	DNA methylation specific marker for unspecified cancer [39]
Abbott and GlaxoSmithKline Biologicals SA (GSK)	Nov 2011	Develop companion diagnostics for cancer immunotherapy research [40]
Metamark Genetics Inc. and Janssen Biotech	Dec 2011	Research and validation o cancer prognosis determinants [41]
Qiagen and Eli Lilly	Sept 2011	Companion diagnostics for blood cancer [42]
Qiagen and Pfizer	Aug 2011	Companion diagnostics for lung cancer [43]
Zinfandel and Takeda	Jan 2011	Companion diagnostics for Alzheimer [39]
bioMeriux and Ipsen	Feb 2011	Companion diagnosis for prostate cancer [39]

2.4.6.2 Overview of the Indian Landscape

While personalized medicine and pharmacogenomics expand their presence in the global healthcare markets, India can grow to be a strong competitor in this sector as it has expertise in the fields of clinical research and trials development. A recent BioSpectrum article stated that companion diagnostics, in India, can provide additional cost benefits of up to US $200-$500 million per drug [44].

The leaders in the Indian pharmacogenomics sector include OncQuest Laboratories, Acton Biotech, TCG Life Sciences, Mir Lifesciences, Mitra Biotech and Mazumdar-Shaw Cancer Centre (MSCC).

Some of the recent developments in the Indian companion diagnostic sector have been listed in Figure 2.16.

Roche Diagnostics submitted US-FDA approved 'cobas BRAF Mutation Test' for legal approval in India [45]

Mumbai-based Acton Biotech offers several new tests to genetically select cancer patients for chemotherapy [46]

Oncquest Laboratories recently launched 'NPM 1 Exon 12 Mutation Analysis' for the prognosis of Acute Myeloid Leukemia [47]

Figure 2.16 Developments in the Indian private sector for companion diagnostics

Acton Biotech offers a range of genetic tests that can predict response to chemotherapy drugs such as gefitinib, cetuximab, tamoxifen and other cancer drugs. Acton Biotech have also launched an MGMT epigenetics tests for glioma patients undergoing Temozolomide treatment. Similarly Oncquest Laboratories offers diagnostic tests such as NPM 1 Exon 12 mutation test for prognosis of Acute Myeloid Leukaemia (AML) and Imatinib Resistance Mutation Analysis (IRMA) for chronic myeloid leukaemia (CML).

MSCC is partnering with Mitra Biotech to develop a protocol for personalized medicine treatment for patients suffering from head and neck squamous cell carcinoma, (HNSCC). It is also concentrating on finding markers for oral tongue squamous cell carcinoma in partnership with Ganit Labs as well as conducting early studies in salivary markers for early stage cancer detection.
There are several institutions which are conducting research in companion diagnostics including molecular markers & pharmacogenomics.

1. Council of Scientific and Industrial Research (CSIR) initiated the Indian Genome Variation (IGV) Consortium project in 2003 among six constituent institutions. The participating institutions are studying SNPs and other genomic variations in diseases such as cancer, clot disorders, diabetes, and retinitis pigmentosa among other diseases.

2. National Institute of Biomedical Genomics (NIBMG), Kalyani, West Bengal
NIBMG is a DBT institution that participates in International Cancer Genome Consortium endeavouring to identifying biomarkers for oral cancers especially squamous cell carcinoma of the gingivo-buccal complex.

3. Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Mumbai
Tata Memorial Centre (TMC) Hospital, Mumbai established ACTREC to conduct research into biomarkers for oral, breast and pancreatic cancers.

2.4.6.3 Future Prospects and Recommendations

The companion diagnostic field is extremely nascent in India with only a few players both in the private and public arena concentrating on pharmacogenomics. It is however set to grow in India as the country becomes a global hub for clinical trials and it has immense potential in establishing personalised medicine in its truest of sense.

2.4.6.3.1 Support biomarker studies for several India specific diseases

India has multitudes of ethnicities who are also treatment naïve. It is crucial that the country embarks upon projects that identify biological markers candidates for variety of diseases which can later become candidates for further development of diagnosis and eventual therapy.

2.4.6.3.2 Involve physicians in formulating companion diagnostic strategies

It is imperative that physicians get involved for formulating appropriate treatment plans that includes diagnostics testing regimes such that treatments are standardized. Many physicians in India are still unaware of companion diagnostics. It is crucial that curriculum of Indian medical colleges and institutions incorporate the latest advances in diagnostics and especially companion diagnostics.

2.4.6.3.3 Support the overall ecosystem of diagnostic testing centres

The major challenges faced by the Indian companion diagnostic sector are primarily the lack of sufficient testing centres. Further there is a lack of trained staff who can conduct molecular testing. GOI should support training of staff in the existing testing centres as well as supporting the creation of further testing centres.

2.5 Natural Products Drug Discovery

Natural products have been an important source of active drugs and lead compounds. Around 75% of all anti-infectives and 60% of all anti-cancer drugs that were approved from 1981 to 2002 had natural product origins [48].

2.5.1 Global Perspectives

The global interest in drugs derived from natural sources especially plant based has taken a new urgency as lead generation has dwindled, pathogens showing drug resistant and side effects from chemical based drugs. The US National Cancer Institute for example has screened 50,000 natural substances for activity against cancer cell lines while Lily Research Laboratories markets vincristine and vinblastine (peri-winkle derivatives) to treat childhood leukaemia [48]. Similarly a plant derived anti-cancer drug paclitaxel had notched up sales of US $1.6 billion in 2000 [49]. A 2008 analysis by Alan Harvey in Drug Discovery Today showed that over 100 plant-based natural products were at different stages of drug development [50].

Development Stage	Number of Plant Based Natural Products in Year 2008
Preclinical	46
Phase I	14
Phase II	41
PhaseIII	5
Pre-registration	2
Total	**108**

Table 2.7 No. of drugs based on plant natural products at different stages of development [50].

One of the better known examples of a herbal drug receiving a FDA's New Drug Application approval in 2006 is Veregen. It is an extract from green tea leaves that is used for topical treatment of genital condyloma [51].

There is growing interest in understanding and exploring drug candidates from natural sources including plants, bacterial, fungal and animal sources.

FDA has a Botanical Drug Guideline with a dedicated Botanical Team under CDER. The FDA regulatory management system of botanical drug products is the same as for other drug products that includes IND filing and clinical trials under strict regulatory oversight [52].

Europe:

The European Union has a binding directive (originally released in 2001) for Medicinal Products for Human Use that from 2011 have made it mandatory to obtain full authorization and licensing go ahead before being marketed through EU member states [53].

China:

China is heavily investing in Traditional Chinese Medicine (TCM) and is inviting large pharmaceutical companies to establish R&D centres including research and development in TCM. In Shanghai, for example, Novartis' R&D centre (Novartis Institute of Biomedical Research) is engaged in research and development that also focuses on TCM and drug discovery [54]. According to a KPMG report, the Chinese Government spent US $1.7 billion on TCM in 2009 which is a 185% jump over the funding in 2005 thus showing the Chinese Government's intention to promote TCM [55]. The report also highlighted the fact that there has been a significant increase in TCM specific hospitals which in 2009 had 449000 hospital beds spread across 3299 hospitals. [55]. The Chinese

government is keen to build innovation systems around TCM by establishing a dedicated database for TCM, study of its basic principles and setting up clinical R&D centres, promoting technology transfers and quality control [55].The Biotechnology Research Institute based out of Hong Kong is involved in testing of efficacy of TCM products while Chinese firms such as Chengdu Kanghong group are involved in TCM product development. The subsidiary of Chengdu Kanghong Group, Kanghong Sagent is a 50:50 joint venture with US based Sagent Inc and the Government has set up a TCM focused index in Chengdu for TCM firms to trade [55]. The new European directive, which has been mentioned previously, on herbal medicine registration will impact TCM.

2.5.2 Indian Traditional Medicine Overview

India has a long history of using traditional medicines of different systems, the oldest being Ayurveda. Other traditional system include Yoga & Naturopathy Unani, Siddha as well as Homeopathy thus India possesses a vast amount of traditional knowledge relevant for healthcare. The government has a dedicated agency viz. the Department of Ayurveda, Yoga, Unani and Naturopathy (AYUSH).

The traditional medicine products in India are regulated by DCGI under the Drugs and Cosmetic Act 1940 amended in 1964. In May 2012, the GOI took a decision to establish a separate Drug Controller General for Ayurvedic, Unani and Siddha drugs with the hope that it will facilitate growth of this sector [56].

There is a huge potential for India to tap into the growing field of natural product based drug discovery. Of the total global market of US $60 billion India's share is US $1 billion while China's share is US $19 billion [56].

There is a huge potential for India to tap into the growing field of natural product based drug discovery

2.5.2.1 Government Initiatives

In order to utilize the emerging potential in this field, the Indian Ministry of Commerce has collaborated with South Asian Association for Regional Cooperation (SAARC) countries to advance the role of traditional medicines on an international platform [57]. The Department of Ayush is also gearing up towards the enhancement and standardization of ISM (Indian Systems of Medicine) drugs such as Unani, Ayurveda, and Siddha drugs for the subsequent Five Year Plan [58].

The Golden Triangle Partnership (GTP) initiative introduced in 2004 jointly by the Secretary of Department of AYUSH, the Director General of CSIR and the Director General of ICMR has also resulted in the development of several drugs that have been listed in Table 2.8 below.

Disease	Formulations
Benign Prostate Hypertrophy (BPH)	Varunadi kwatha Gokshuradi guggulu Triphala churna Narayana taila
Hypertension	GTP –HTN 01
Dyslipidemia	Haritakyadi churna GTP–DL II
Osteoporosis	Laksha guggulu Ashwagandha - Mukta shukti bhasma granules

Table 2.8 Drugs being developed through GTP partnership [59].

The New Millennium Indian Technology Leadership Initiative (NMITLI), of CSIR has been supporting projects in this arena such as development of herbal medicines for diabetes and psoriasis, and study of the medicinal plant Withania somnifera [60].

NMITLI has also funded a joint project with pharmaceutical company Lupin to develop a plant based drug for psoriasis from a drug candidate Desoris which is a single plant extract. It has a novel mechanism of action to lesses psoriatic induced lesions. It went through extensive preclinical studies and eventually Lupin filed an Investigational New drug (IND) application and has successfully conducted Phase I clinical trials. It has subsequently received approval to conduct combined PhaseIIb/III clinical trials [61, 62]. NMITLI has also supported projects that sought to develop drugs for arthritis and osteoarthritis [61]. Institute of Ayurveda & Integrative Medicine (IAIM) based in Bangalore engages in fundamental as well as clinical research that shed light on the scientific basis of Ayurveda. It is also involved in building capacity for scientific evidence based ayurvedic treatments.

Other Indian firms, besides Lupin, such as Indus Biotech, Natural remedies, Himalaya Drug, Dabur and Zandu Pharmaceuticals are all endeavouring to develop healthcare products using natural sources. Indus Biotech, for example, has a pipeline that covers disease areas such as Parkinson, Huntington's, Rheumatoid Arthritis, Intestinal Bowel Disease, Kidney ailments and depression as well as infectious diseases such as HIV in various stages of development. The company has obtained an IND approval from US FDA for HIV treatment [63].

Lack of clinical trial data, differences in batches and inherent variations present in phytochemicals further inhibit drug discovery research in this sector

Thus, it is evident from the above segments that India has an expansive knowledge in the field of natural products based medicines. However, lack of research, documentation and standardization of the traditional plant-based therapeutics impede India's progress in this sector, consequently delaying its advancement as a leader on a global platform. In order to meet the 2025 vision for this sector of biotechnology, India needs to overcome the challenges discussed in the following segment.

2.5.3 Limitations and Challenges

While traditional drug discovery techniques from natural resources have a notable history of use and efficacy, there are also a number of limitations that arise from such methods. Despite their economical advantages, the naturally occurring drug molecules cannot be directly used for therapeutic purposes because most of them do not have reference standards and validation records. Lack of clinical trial data, differences in batches and inherent variations present in phytochemicals further inhibit drug discovery research in this sector.

Controlling the quality of the natural therapeutics is a key challenge in this sector. Due to inherent differences in the presence of the phytochemicals, it is difficult to standardize and validate extraction protocols from natural compounds.

Figure 2.17 Key challenges of traditional medicine

This impediment can be partially overcome by introducing clear and consistent regulatory controls at various levels of drug development. Following Good Agricultural Practices (GAPs) and Good Manufacturing Practices (GMPs) will also standardize the quality of natural medicine formulations and substantiate India's presence in the global market [64].

Isolation of active leads from plants is a cost-intensive process and currently, there are very few industries in India that can afford it. Hence it is essential to improve the drug discovery infrastructure in India to promote pioneering research in this sector.

2.5.4 Future Perspectives

With pharmacogenomics being one of the emerging aspects of drug discovery research, the 'Prakiti' concept of Ayurveda has developed new found significance in the modern world and holds a promising future potential in this sector.

Novel techniques such as Reverse Pharmacology, Systems Biology Approach, Ethnopharmacology and Personalized Approach will aid economical, safe and efficient discovery of new drugs. For instance, using reverse pharmacology method can reduce the drug development phase from 10-15 years to 5-6 years and reduce costs from US $1-1.5 billion to US $2-20 million [65].

The World Health Organization (WHO) has also contributed to this developing field by drafting 'WHO General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine' and 'WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants.' These initiatives promise an exciting future for the discovery of drugs from natural products. Innovative PPP models as shown in the case of NMITLI and an optimal combination of traditional and modern drug discovery techniques will help to re-define the future of this sector.

2.5.5 Recommendations for Future Growth

Increasingly natural product based drug discovery is gaining a foothold and emerging as an attractive avenue for biopharmaceutical industry. India has always been a rich repository of traditional knowledge and practice of traditional medicine has continued for over 4000 years. India has a rich tradition of ayurveda, unani and many other traditional systems that help in meeting several health conditions.

Many countries such as China are focused in building their traditional systems on a rational approach and gaining global confidence and market share. Increasingly countries that have a traditional health knowledge base such as those in Asia Pacific (Thailand, South Korea), Latin America (Brazil and Argentina) and the Middle East and Africa (Turkey, South Africa) will start focusing on developing their own systems to global standards. South Korea, for example, has already started focusing on promoting its traditional knowledge healthcare firms.

2.5.5.1 Establish an Interdisciplinary Mission Led Drug Discovery from Natural Products

Traditional knowledge such as Ayurveda offer huge opportunities to the pharmaceutical and biotech industry in drug discovery. However for this to come to fruition several factors need to be in place.

First, a "mission oriented approach" that delves into evidence based research behind many traditional therapies and that combines efforts of several leading institutions in this field is needed. Second, India needs to identify five to ten disease conditions that are already being treated with Ayurveda and other traditional approaches and then delve into the scientific basis behind those treatments including discovering novel active candidates that might be responsible for effective treatment.

Many countries such as China are focused in building their traditional systems on a rational approach and gaining global confidence and market share

Third, India needs to expand and scale up successful pilot programs of natural product based drug discovery. For example, New Millennium Indian Technology Leadership Initiative (NMITLI) programs on herbal drug development for effective therapies and remedies for conditions such as Osteoarthritis, diabetes and hepatic disorders must be scaled up and several other natural product based drug discoveries should be funded by GOI. GOI should also earmark US $20.83 million per year for projects involving natural product based drug discovery.

Fourth, India needs to strengthen the Traditional Knowledge Digitization Library which was set up in 2001 to check biopiracy and establish a similar programme to the China "s "Herbalome" wherein China has strategized to create a high throughput screening, toxicity testing and initiate clinical trials to identify novel drug candidates.

Fifth, India needs to prepare monographs of all existing medicinal formulations

2.5.5.2 Create a Regulatory Framework for Development and Approval of Botanical Drugs

There lies a large gap between modern science and traditional science. There has been very little endeavour put in so far on a suitable, computerized documentation of the authentic formulations used in our traditional systems of medicine. On the basis of this documentation, using rational criteria, formulations could be then selected on a priority basis for consistency, validation and manufacturing. India needs to urgently set up a regulatory mechanism for natural product based drugs based on scientific evidence.

India needs to urgently set up a regulatory mechanism for natural product based drugs based on scientific evidence

There are several leading hospitals that are providing numerous successful traditional therapies to patients on a range of chronic conditions. These hospitals should be linked to public research centres and pharma/biotechnology firms through incentives to jointly work together. Part of the US $20.83 million earmarked could be channelized to incentivise collaborations among hospitals giving traditional therapies, biotech companies and public funded institutions.

India can uniquely apply its scientific and IT prowess to Ayurveda to present a new paradigm of healthcare to the world i.e. effective & affordable prevention plus acute-emergency care. By 2025 India can synergistically leverage Ayurveda, biotechnology, and IT to significantly alter the health-disease profile of the Indian population.

2.5.5.3 Integrate Ayurveda and Genomics for Personalized Medicine

Ayurvedic texts mention that each individual patient is a different entity and the relationship between environment and its influence on genomes has to be explored. It has been suggested that three databases be organized that eventually inform customised therapy. Those databases are for human constitution (genotype), disease constitution (phenotype) and drug constitution [66].

2.6 Synthetic Biology

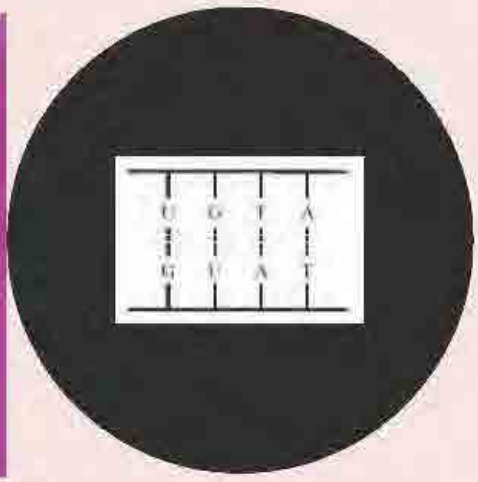
Synthetic biology is an emerging field that uses engineering methodologies to design biological systems. According to the European Commission's NEST High Level Group on Synthetic Biology it is defined as "the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures – from individual molecules to whole cells, tissues and organisms. In essence, synthetic biology will enable the design of 'biological systems' in a rational and systematic way" [67].

Scientists have classified synthetic biologists in to two broad classes. One that focuses on assembling non-natural or synthetic components to create chemical systems that behave according to the rules of biological evolution and another group that consists of scientists and engineers that focus on extractable and interchangeable parts from living systems that serve as building blocks of systems that may or may not resemble existing biological system [68].

Recent developments like construction of metabolic networks, signalling cascades and genetic circuits have opened new perspectives for fundamental biological concepts. This sector has enabled a holistic understanding of living systems. For example Craig Venter created a minimalistic artificial life Synthia (Mycoplasma laboratarium) by decoding, synthesizing and assembling the genome of Mycoplasma genitalium [69].

The enabling technologies for synthetic biology are rapid advances in cloning, synthesis and sequencing of DNA and other genetic material as well as computational modeling. This has resulted from the exponential drop in the price of synthesis of DNA oligonucleotides over the last decade.

Synthetic biology being a nascent science has the capacity to revolutionise a diverse array of fields from healthcare to agriculture and biofuels in the next decade and beyond if challenges such as the emerging biosafety issues are dealt with. The following section will focus only on the healthcare. Synthetic biology and its impact on other fields are described is discussed in the chapter on Industrial biotechnology.



Recent developments like construction of metabolic networks, signalling cascades and genetic circuits have opened new perspectives for fundamental biological concepts

2.6.1 Global Landscape for Synthetic Biology

On the global front, synthetic biology has been making significant advances in the fields of genetically engineered therapeutics and renewable energy resources.

A recent detailed paper by Oldham et al 2012 on the subject finds that around 40 countries globally are involved in conducting R&D in synthetic biology. The research in this field is dominated by the USA, UK, Germany, France and Switzerland with emerging economies such as China, India and Brazil, Mexico and South Africa increasingly joining the research fraternity in this field [68].

According to the BCC Report the global market for synthetic biology expanded five-fold from US $233 million in 2008 to US $1.1 billion in 2011 and is expected to touch US $2.3 billion by 2013 and predicted to touch US $10.68 billion in 2016 thus highlighting the exponential growth potential. The chemicals and energy was the largest segment and was worth US $80.6 million in 2008 [70, 71]. The biotechnology and pharmaceuticals segment was worth 80.3 million in 2008 and is projected to increase at a CAGR of 49.2% to reach US $594 million in 2013 [70, 71].

There are several firms in the USA that are endeavouring to use synthetic biology tools to create drugs including Amyris Biotechnology, Precision Biosciences, Sangamo BioSciences, Intrexon Corp., J. Craig Venter Institute, Blue Heron, GEN9 to name a few.

Amyris Biotechnology has artificially engineered microbial strains to produce artemisinic acid, a precursor of artemisinin (an effective anti-malarial). The company launched a non-profit organization to offer treatment for malaria across developing nations and intend to provide treatment for 300 million patients at 50 cents per treatment [72].

Large pharmaceutical firms Pfizer, Roche and Novartis are also engaged in synthetic biology projects. In particular Pfizer is engaged in research in PCR-less library mutagenesis, Roche is involved in the development of a software tool specifically for synthetic biology use, while Novartis is collaborating with the J. Craig Venter Institute and Synthetics Genomics in the area of vaccine development [68].

Intrexon Corporation, a next generation synthetic biology company, raised US $100 million in series E funding for synthetic biology initiatives. The funding will be use to develop the UltraVector® platform, which will aid the construction and design of transgenes to modulate cell functionality for varied biological, agricultural and bio-industrial application [73].

Other emerging uses of synthetic biology pertain to the construction of ribozyme switches which can be controlled to execute regulation, construction of E.coli, harboring synthetic plasmids which can invade cancer cells and promising applications are being explored in gene therapy and programmable personal stem cells [74].

Both private and public funds are available in the West to conduct R&D in synthetic biology

Both private and public funds are available in the West to conduct R&D in synthetic biology. In the USA, funding for synthetic biology is available from multiple sources such as NIH, and National Science Foundation (NSF), US department of Defense, DARPA and the Department of Energy [68]. In 2010, DARPA invested $6 million on a BioDesign programme and had plans to fund long term synthetic biology projects [68, 75].

University of California Berkeley and Agilent Technologies have collaborated to establish a Synthetic Biology Institute with the stated goal to "create an industrial revolution using synthetic biology" through research in deepening the knowledge of biological systems and develop transferable tools to engineer reliable biosystems as well as disseminate standardized design tools and analyze the ethical and social impact of synthetic biology [76]. Similarly, MIT has established a Synthetic Biology Center [77].

MIT also runs an educational programme, since 2003, specifically for undergraduates who wish to explore synthetic biology during summer break called The international Genetically Engineered Machines competition (iGEM) [78]. MIT has also built an open source standard repository of parts of DNA that are well defined in their structure and function and hence can be mixed and matched to construct biological systems [79].

In Europe major funding agencies in synthetic biology are the European Union's Framework Programme, the Biotechnology and Biological Sciences Research Council (BBSRC), UK and the Swiss National Science Foundation. In the UK, Imperial College London has established the Centre for Synthetic Biology and Innovation funded by the Engineering and Physical Sciences Research Council (EPSRC), UK.

2.6.2 Scientific, Environmental, Legal and Ethical Challenges

Although synthetic biology is a nascent field, it has already brought to attention the kind of risks it is associated with such as bio-safety and bio-security issues (environmental release and impact on bio-diversity, health issues and bioterrorism) as well as legal and ethical challenges.

Several stakeholders in the USA especially US FDA, NIH, US Environment Protection Agency (EPA), US Department of Defense and US Department of Agriculture are involved in analyzing the risks of synthetic biology. The National Science Advisory Board for Biosecurity (NSABB) has released recommendations for dealing with synthesis, screening and surveillance of select agents including DNA. Further, several companies have formed the International Consortium for Polynucleotide Synthetics (ICPS) and have published potential oversight framework [80]. There are also fears of bioterrorism and bioweapon production as synthetic biology advances and after the Anthrax scares, USA has drafted guidelines to screen genes [81].

There are also fears of bioterrorism and bioweapon production as synthetic biology advances

In Europe, too, regulations impacting the release and marketing of GMOs also govern synthetic biology especially the EU Council Directive (2001/18/EC) and EU Regulation 1829/2004 [82]. Europe has already initiated EU wide programmes on synthetic biology with the intention to foster synthetic biology research in Europe and understand its needs and impact. Some the of projects are Towards a European Strategy for Synthetic Biology (TESSY) that provides a EU wide research roadmap and framework for synthetic biology research [83].

It is also to be noted that international agreements such as the Convention on Biological Diversity (to which 163 countries are signatories) will also eventually address the issues emerging from synthetic biology. Moreover 163 countries are signatories to the Cartagena Protocol on Biosafety under the Convention of Biological Safety that influence the movement of living modified organisms. Furthermore, the Subsidiary Body on Scientific, Technical, and Technological Advice (SBSTTA) has invited stakeholders' opinion on synthetic biology [68].

The continuous growth of open source synthetic biology projects necessitates the formation of a standardized monitoring body to check their progress at regular intervals. Despite certain self-regulatory initiatives by open-source biologists, there is an urgent need to have a central network for regulating bio-security measures on an international platform.

2.6.2.1 Socio-Ethical and Legal Concerns

Ethical considerations and social regulations are also areas of concern in the field of synthetic biology such as the 'concept of minimal genome' and issues regarding ownership, rights and access are under a considerable amount of debate. A faculty in bioethics in University of Pennsylvania Prof. Arthur Caplan's had commented in a Nature article on Craig Venter's achievement that highlighted the ethical issues underlying synthetic biology *"Venter and his colleagues have shown that the material world can be manipulated to produce what we recognize as life. In doing so they bring to an end a debate about the nature of life that has lasted thousands of years. Their achievement undermines a fundamental belief about the nature of life that is likely to prove as momentous to our view of ourselves and our place in the Universe as the discoveries of Galileo, Copernicus, Darwin and Einstein."* [84]. The EU project, SYNBIOSAFE examined the ethics, perception and safety and security of synthetic biology research as well as public engagement [85].

2.6.3 Synthetic Biology Indian Scenario in Medicine and Health

Synthetic biology work especially in the field of medicine and health is still at a very nascent stage in India, however, there is an emerging group of scientists in public institutions who are working in synthetic biology pertaining to health, biofuels and green chemicals.

The continuous growth of open source synthetic biology projects necessitates the formation of a standardized monitoring body to check their progress at regular intervals

Scientists in IISc are working on synthetic biology approaches to study and understand and metabolism of Mycobacterium tuberculosis as well as understand metabolic modeling of pathways. Similarly groups in several IITs such as Mumbai and Delhi as well as national centres such as CCMB, Centre for Systems and Synthetic Biology (Kerala), IICB, NCBS, Rajiv Gandhi Centre for Biotechnology, Dhirubhai Ambani Institute of Information and Communication Technology and National Chemical Laboratory (NCL) are engaged in a diverse set of research in synthetic biology.

Very few companies are engaged in synthetic biology pertaining to healthcare in India. Only Evolva based out of Chennai and Reliance Lifesciences have projects that explore use of synthetic biology in the human disease and health context.

2.6.4 Future Prospects

There are innumerable possibilities in the field of synthetic biology, right from discovering quicker and affordable methods for creating artificial genes to synthesising entire micro-organisms for laboratory as well as industrial purposes. But, as discussed previously, the progress of synthetic biology projects should be monitored meticulously for safety as well as socio-ethical purposes.

2.6.5 Recommendations

Synthetic Biology is a revolutionary technology which has the potential to successfully transform human life and India has a great window of opportunity to harness this opportunity and emerge a global leader in this field of research.

Synthetic biology owes its roots to biotechnology and genetic engineering and it is a transformational science with immense potential for several disruptive innovations and discoveries. This has implications in areas such as affordable medicines, generation of innovative flavours, attractive fragrances, novel agricultural products, efficient biofuels and many other areas. This is a relatively new field and is yet to gain momentum in India.

2.6.5.1 Establish a Taskforce for Timed Implementation of Synthetic Biology Initiatives

Synthetic biology could open new avenues for healthcare, agriculture and industrial biology including bio-energy. The potential to design synthetic chromosomes, predictive genome engineering and custom designed genetic circuits could lead to engineered synthetic cells for a variety of applications.

As mentioned before, countries in the West such as the USA, UK and Germany have already constituted national roadmaps for growth strategies in this field and are evaluating the impact of synthetic biology.

A taskforce should be established by GOI under the aegis of the Secretary of DBT with the mandate and scope to evolve the national strategy in synthetic biology. It should explore opportunities in this space and foster the growth of synthetic biology in the country and also devise policies and regulation covering bio-safety and bio-security issues emerging from synthetic biology research and development. The taskforce should consist of experts from different government departments (MoEF, Department of Agriculture, Ministry of New & Renewable Energy, DRDO) research institutes, ethicists, legal experts, industry bodies and civil society. The taskforce should be entrusted with developing a comprehensive forward looking agenda in the field of synthetic biology and submit a report within 6 months of formation of the taskforce.

A taskforce should be established by GOI under the aegis of the Secretary of DBT with the mandate and scope to evolve the national strategy in synthetic biology

2.6.5.2 Provide Financial Support and Tax Incentives

At the moment this cutting edge technology is gaining entry into the country via licensing and multinational companies setting up their laboratories locally. In order to encourage more such initiatives, companies that are making efforts to establish this technology may be supported with appropriate funding even if they are not 51% owned by Indians. Mechanisms should be in place for the deployment of government funds for such companies in India itself. Also a bank of intellectual property is likely to be generated from such companies.

2.6.5.3 Customize Existing Regulatory Framework

Synthetic biology comes in two broad flavours. Creation of "artificial life" forms is one of them while making them produce "un-natural" products by tweaking their genome is the other. Although the former could have serious implications from an ethical point of view, the latter is effective in addressing human needs and welfare. But this may require some customized regulatory framework to enable safe and intended use of the products emerging from this technique.

2.6.5.4 Establish an India Specific Synthetic Biology Resource Pool

GOI should pool together relevant work being done across the country in synthetic biology to promote information access as well as collaboration. It should establish a programme along the lines of iGEM (organised by MIT) and Stanford India Biodesign.

2.7 Integrating Healthcare Delivery Models

India faces several challenges in its healthcare sector and it is struggling to meet the demands of a country that is growing on the one hand but has poor infrastructure on the other. Challenges in healthcare delivery are accessibility, affordability and quality. Data from World Bank statistics show that the health care expenditure as percentage of GDP for India has remained in the range of 4.1 to 4.5% over the last few years and is expected to climb up to 5.2% of the GDP by 2020 [86, 87]. In comparison, OECD countries will maintain high levels of expenditure on their healthcare from on an average 9.9% of the GDP in 2010 to 14.4% of the GDP by 2020 (please refer to Figure 2.18, [87]).

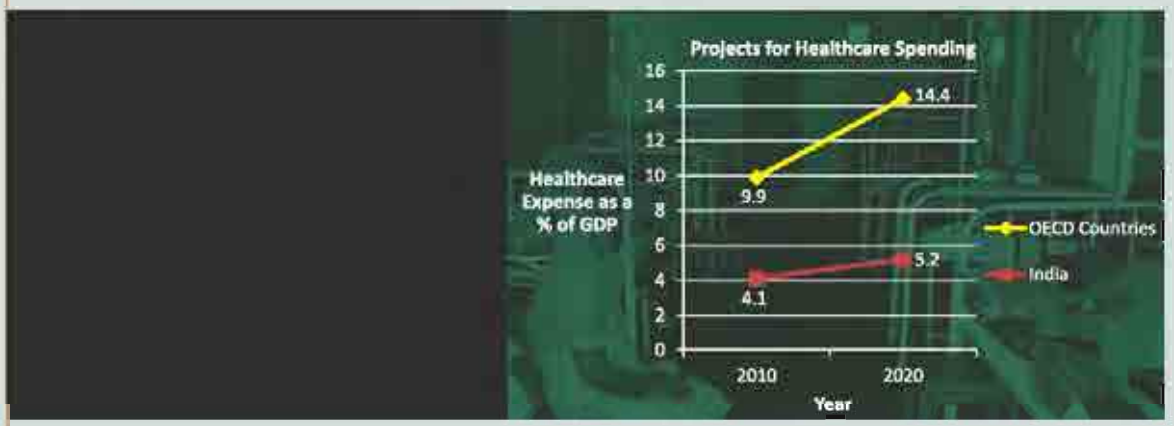


Figure 2.18 Projections for healthcare spending, PwC [86, 87].

Thus, the global healthcare market is expected to grow rapidly and open new avenues for improving healthcare delivery models across the globe.

The following segments address healthcare delivery models that are likely to influence the global as well as the local market.

2.7.1 Global Healthcare Delivery

As healthcare expenses continue to rise across the globe, most countries are looking towards developing innovative models to deliver faster, more efficient and economical healthcare solutions that are accessible to all citizens.

According to an analysis conducted by KPMG, global pharmaceutical sales are predicted to grow at 4–7% CAGR, increasing from US $825 billion in 2010 to US $975 billion by 2013 indicating an immense potential for future growth in the healthcare delivery sector [88].

Global developments in this sector have focused mainly on the expansion of the market and also ensuring wider and affordable outreach of healthcare deliverables for all its citizens. For instance, Singapore's Ministry of Health has appointed the Agency for Integrated Care to help re-structure the healthcare system in their nation and enable effective healthcare delivery to all citizens. They are setting up regional healthcare systems, expanding the network for primary healthcare and computerizing health records to improve the outreach of their health delivery model.

Healthcare restructuring is also currently underway in many of the OECD countries as healthcare costs have soared. The rising healthcare costs have caused a decline in insurance coverage across the US. Hence, the US government is also working towards restructuring healthcare delivery models to improve healthcare coverage across the country. Their healthcare reforms include 'The Health Care and Education Reconciliation Act of 2010', which was introduced in March 2010 to enable protection of patient and promote affordable healthcare measure for all US citizens [89]. In

the USA the Patient Protection and Affordable Care Act (PPACA) of 2010 [90] intends to reduce soaring healthcare costs. Healthcare in most Western European countries (such as the UK, Germany and France) is either completely sponsored by the state or is heavily subsidised. The access to healthcare remains very high in the West. The Digital Agenda for Europe in 2010 aims to provide secure and easy access to electronic health data and other eHealth services by the end of 2015 [91]. An ageing population in these countries has put pressure to reform the health system. Healthcare delivery models in India that provide high end care but at a fraction of a cost such as at Narayana Hryudayalaya, LV Prasad Eye Institute and Aravind Eye Care centre could have important lessons for the West too.

2.7.2 Healthcare Delivery in India

In India, 74.4% of private healthcare expense is out-of-pocket [88]. Hence, there is an urgent need to innovate and bring new models for healthcare delivery in order to provide affordable healthcare to all citizens across the nation. Some of the emerging healthcare delivery models in India are discussed in the following segments.

2.7.2.1 Low Cost Delivery Models

According to the census conducted in 2011 by the GOI, 68.8% of the Indian population resides in rural areas, and over 60% of the rural population live on an income that is less than US $0.73 per day [92, 93]. Hence there is an urgent need to provide economical and accessible healthcare facilities in the rural segments of India, which constitutes the majority of the Indian population (refer figure 2.19, [92]).

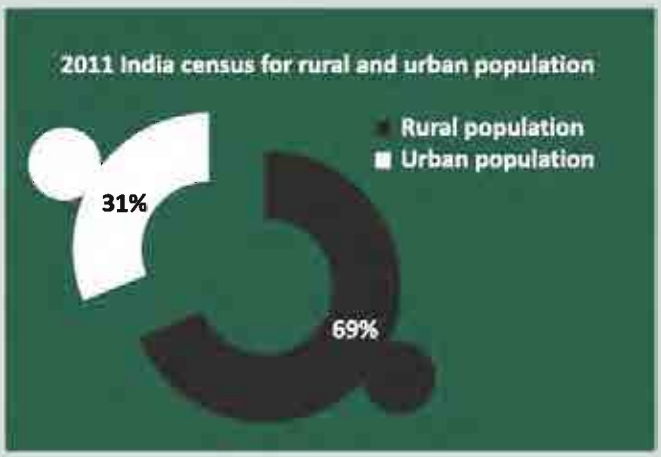


Figure 2.19 India census (2011) - rural and urban population [92].

Hospital chains like Dr. Devi Shetty's Narayana Hrudayalaya are developing interesting business strategies that address the diverse rural and urban healthcare demands in an economical manner. In 2010, Narayana Hrudayalaya announced the establishment of several hospitals in places such as Mysore, Bhubhaneshwar and Siliguri, that will provide cardiovascular healthcare to patients for as low as USD 1042 without comprising on quality or infrastructural facilities [94]. They also introduced the 'Yeshasvini Scheme' where Karnataka farmers can get healthcare insurances for US 10 cents per month [95].

Quality healthcare initiatives that safeguard rural health in an economical manner will also save on the travel expenses of the rural population to cities for medical facilities and thus will eventually have positive impact on both, rural health and the Indian economy at large.

Another example of a low-cost healthcare model is that of Vaatsalya, a chain of 15 hospitals in Tier II and Tier III towns of Karnataka and Andhra Pradesh, that caters to the medical needs of the rural populations [96]. Apollo Reach Hospitals in Karimnagar, an initiative of the Apollo Hospital chain, is another project aimed at delivering low-cost healthcare to patients in rural areas.

An additional novel healthcare delivery model is that of single specialty chains that focus their services on a core area. For instance, LV Prasad Eye Institute delivers quality eye care facilities at affordable rates. Dialysis centers such as Nephroplus are also examples of similar models where hospital chains focus on a single specialty and deliver it at cost-effective rates.

2.7.2.2 Telemedicine Initiatives

In order to ensure fast and effective healthcare delivery across a vast nation like India, several telemedicine initiatives, like the National Rural Telemedicine Network (NRTN) Project under the National Rural Health Mission (NRHM), are underway. Under this plan, four regional workshops for NRTN are currently being planned [97, 98].

Figure 2.20 m-Healthcare services [99]

The Indian mobile-phone driven healthcare service is valued at US $625 million compared to global estimate of US $23 billion. M-healthcare in India is mainly focused on providing diagnostic, healthcare monitoring and wellness services among the rural and urban population (Figure 2.20, [99]).

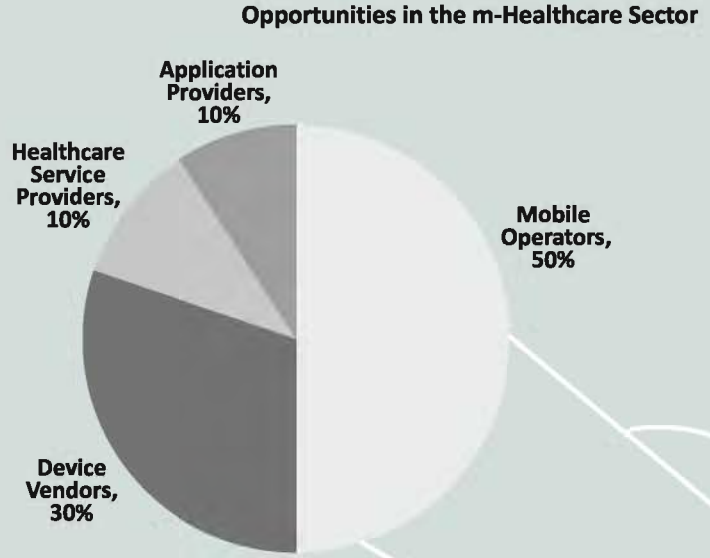


Figure 2.21 Mobile healthcare opportunities in India, [99]

These m-health opportunities are primarily distributed among mobile service providers, device vendors, application providers and healthcare service providers (Figure 2.21, [99]).

On the private front; Narayana Hrudayalaya and SANA (research group at MIT/Harvard) have jointly launched a mobile healthcare initiative in 2010 to facilitate the early diagnosis and screening of chronic diseases in an accessible and affordable manner. This initiative will also significantly save on healthcare risks and expenses that are usually associated with late stage diagnosis of ailments such as cancer [100]. Narayana Hrudayalaya has the world's largest telemedicine network, having treated over 30,000 patients using their tele-consultation facilities. They also use their telecommunication network for teaching and academic purposes [101].

Adding to the growth in this segment, ISRO has also established telemedicine facilities in 60 rural and 20 urban healthcare firms until 2006 and that positively impacted the networking of hospitals, thus enabling faster and more effective healthcare service delivery [102].

Forus Health Pvt Ltd, established in 2010, is an interesting case-in-point where mobile technology has been used effectively to provide preventive healthcare to patients. Their innovative product, 3nethra, is a portable, non-invasive eye-care diagnostic kit that can detect five major ailments without any assistance from a doctor. This invention helps alleviate the need for specialized physicians for early screening and thereby provides accessibility to diagnostic services in remote places [103, 104].

Hence, telemedicine networks have the potential to reach out to a large network of patients not only for consultation and treatment, but also to promote healthcare education and awareness. This can have a significant impact in promoting healthcare accessibility, affordability and awareness among Indian citizens; especially in remote parts of the country.

2.7.2.3 PPP Models for Healthcare Delivery

PPP models in India can be leveraged to bridge infrastructural and economic gaps in the healthcare delivery system. Some of the PPP working models like B-O-T, contracts and subsidies are described in Table 2.9 below [105-109].

PPP Model	Description	Example
B-O-T Model	The private sector receives a contract from the public sector to build, operate and transfer a capital asset, like a healthcare facility or a diagnostic center.	B. Braun in partnership with the Government of Andhra Pradesh will set up 11 dialysis centers to provide affordable healthcare to poor patients [105, 109]. GE Healthcare partnered with the Gujarat Government, to set up diagnostic centers in public hospitals [106, 109].
Management Contracts	The Government engages the private sector to manage and upgrade public health facilities.	Under Tamil Nadu Health Systems Project, the State Government partnered with the World Bank to improve healthcare infrastructure and facilities [107].
Subsidies	Government funds private groups to provide affordable healthcare facilities.	Under the 'Chiranjeevi Yojana' Plan, the government of Gujarat has partnered with the private sector to improve the delivery of maternal healthcare services in the rural parts [108].

Table 2.9 PPP Models for healthcare delivery India [105-109].

2.7.3 Healthcare Delivery Challenges

Although there are some healthcare programs that target the rural parts of India, more such initiatives should be developed in the future to encourage rural healthcare services. There is also a need to focus on preventive treatment measures in these parts of the country.

While Ayurvedic treatment centers are being developed abroad, there are very few initiatives in India that deliver alternative healthcare solutions. There should be an increased focus towards healthcare measures such as Ayurveda, Homeopathy, Siddha and Unani among many others, as they provide economical and effective healthcare solutions.

Moreover, there should be an increase in focus towards providing a healthy environment for living. Lack of clean drinking water, food and hygienic sanitation facilities are also key challenges that need immediate attention.

2.7.4 Future Prospects

With the emergence of low-cost delivery models that deliver high quality treatment to the rural segments, India's healthcare market is garnering increased global recognition. US markets are also looking to adopt Indian trends for effective healthcare delivery.

Thus, there is immense potential for growth and development in the Indian healthcare sector. The emergence of alternative treatment measures and rising awareness of the healthcare sector among Indians are potential growth drivers for the healthcare industry in India. India's growing economy will also enable the delivery of quality healthcare among Indians.

Telemedicine initiatives also have immense future potential as they encourage effective healthcare delivery to the rural segments of India at affordable rates. Thus, the Indian healthcare delivery market holds a promising future for growth and development.

2.7.5 Recommendations

The Indian healthcare system is in critical need of reform, especially the public healthcare system. India spent 0.95% of its GDP on healthcare between 1995-2005 as compared to China which spent 1.82% and Sri Lanka which spent 1.89% of GDP. It has been reported that the GOI spending on healthcare per person is 22% of that spent by Sri Lanka and 16% of that in China thereby highlighting the urgent need for public investments to creating a functional and effective national healthcare system [110].

Several other indicators in terms of healthcare accessibility and reach also remain low. For example a leading report by PwC in 2009 found that there are only 60 doctors and 80 nurses per 100,000 people in India thus highlighting the severe shortages in healthcare human resources which impacts accessibility for basic healthcare consultation and care in India. Close to 70% of hospitals are private and the rest are public or semi-public funded [3].

2.7.5.1 Integrated Approach

India faces a unique situation in its healthcare burden. On the one hand there is a prevalence of infectious diseases such as TB (a quarter of world's TB patients are in India) and on the other hand prevalence of chronic diseases such as diabetes and cardiovascular diseases are increasing as the Indian economy grows influencing lifestyle changes. The Indian healthcare sector is one of the fastest growing sectors due to a rapid increase in diseases prevalent among its population. Despite the speedy economic growth, healthcare suffers with an augmented rate of infant mortality and deaths due to chronic diseases and inadequate healthcare facilities. The following recommendations aim to prevent the existing health status from deteriorating further.

2.7.5.1.1 Establish Integrated Public Health Systems

Despite economic growth over the last decade, the Indian public health system remains a huge challenge as many parts are of India are still unserved by basic human health needs and less than 20% of healthcare costs are met by public resources. The National Rural Health Mission (NRHM) needs to be scaled up in the next five year plan. There should be a massive inflow of public expenditure in healthcare. GOI should spend at least 7% of the GDP on healthcare for the next 10 to 15 years especially building up primary healthcare systems across the vast rural hinterland, semi-urban (Tier 2 & Tier 3 cities) as well as in the larger cities such that the pressure on hospitals in the city is reduced. However, it is also important to note that urbanisation is increasing rapidly and Delhi & Mumbai are set to become megacities with populations greater than 25 million each. Other metros and tier 2 cities are also set to expand. This will create great pressure on "urban healthcare" systems too. An integrated healthcare system should include electronic medical records, health insurance coverage for Indian citizens, use of m-health, rapid and affordable diagnostics leading to personalised medicine and an understanding of delivery business models through local healthcare experts.

2.7.5.1.2 Provide Financial Protection through Healthcare Insurance Schemes

A Lancet paper (2011) [110] reported that in 2005-2006 only 10% of households in India had at least one member of the family covered by medical insurance. The medical insurance sector remains fragmented in India. India should find a sustainable model for health insurance schemes and healthcare payment models. The government could work with the private sector in a PPP model to deliver its healthcare schemes.

2.7.5.1.3 Focus on Technology Especially m-Health Initiatives to Deliver Healthcare

One of the technologies that GOI should leverage to provide healthcare delivery is via m-health initiatives, which can help bridge the divide between rural and urban healthcare accessibility.
m-health initiatives could also become a part of disease surveillance. It is important that India maintains population healthcare information which could in turn help in making informed policy decisions.

m-Health initiatives should also be integrated with NRHM programme and hospitals providing m-health initiatives such as Narayana Hrudayalaya, Apollo, Aravind hospitals and many others should be given incentives to scale up their operations across India.

2.7.5.1.4 Educate People on Healthcare Issues

Awareness about health related problems and risks associated must be created especially in the rural and urban areas of India. Cancer and lifestyle diseases are likely to account for nearly 75% of the deaths in India. Therefore, nationwide programmes should be conducted to promote the lifestyles changes like reducing the intake of tobacco, alcohol and junk food.

2.8 References

1. Biotechnology-Industry Recommendations to Department of Biotechnology (DBT) for the 12th Plan, A report prepared by Association of Biotechnology Led Enterprises (ABLE), July 2011.
2. http://www.who.int/gho/countries/ind.pdf
3. PwC Report, 2009: Global Pharma Looks to India – Prospects for Growth
4. http://www.guardian.co.uk/news/datablog/2011/jan/07/gdp-projections-china-us-uk-brazil
5. http://www.gatesfoundation.org/vaccines/Documents/vaccines-fact-sheet.pdf
6. http://www.asianscientist.com/tech-pharma/international-vaccine-symposium-ashwani-kumar-minister-science-technology-india-2011/
7. http://www.who.int/immunization_monitoring/data/ind.pdf
8. http://www.unicef.org/infobycountry/india_statistics.html
9. Vision 2020: A Biopharma Strategy for India, an ABLE–PwC report for Department of Pharmaceuticals, Ministry of Chemical and Fertilizers, Government of India.
10. http://www.fiercebiotech.com/story/baxter-momenta-team-potential-503m-biosimilars-deal/2011-12-22
11. ABLE-BioSpectrum Survey, Volume 9, Issue 6, June 2011
12. http://www.thepharmaletter.com/file/108602/natco-in-biogenerics-in-deal-with-mabxience-plans-generic-launches-in-south-africa.html
13. http://forbesindia.com/article/boardroom/a-shot-of-india-the-vaccine-market/24822/1?id=24822&pg=1
14. http://www.pall.com/medical_38848.asp
15. http://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=62&key=R#R
16. http://www.parliament.uk/documents/post/postpn333.pdf
17. http://finance.yahoo.com/news/Global-Stem-Cells-Market-to-iw-2507966313.html
18. http://www.mri.gov.on.ca/english/publications/documents/Regenerative_Medicine_Asset_Map_FULL_EN_WEB.pdf
19. http://www.boston.com/news/science/articles/2011/08/07/most_gop_candidates_oppose_stem_cell_funding/?page=full
20. http://news.bbc.co.uk/2/hi/health/7735696.stm
21. Alka Sharma (2006), Stem Cell research in India: Emerging Scenario and Policy Concerns. Asian Biotechnology & Development Review, Vol 8, No. 3, 43-53
22. http://www.pharmabiz.com/NewsDetails.aspx?aid=66670&sid=1
23. http://articles.latimes.com/2011/may/03/news/la-heb-cirm-funding-clinical-trial-stem-cells-20110503
24. http://www.pwc.com/es_MX/mx/publicaciones/archivo/201106-medical_technology.pdf
25. http://www.perdcentre.com/niperahd/download/finalbook-events.pdf
26. Medical Technology Industry in India Riding the growth curve. CII & Deloitte, July 2010 (http://www.deloitte.com/assets/Dcom-India/Local%20Assets/Documents/Medical_technology_Industry_in_India.pdf)
27. http://www.pharmabiz.com/NewsDetails.aspx?aid=65592&sid=1
28. http://articles.economictimes.indiatimes.com/2010-05-19/news/27566936_1_ecg-mac400-product
29. http://trivitron.com/press-release.htm
30. http://www.thehindubusinessline.in/2010/03/19/stories/2010031952611900.htm
31. http://biodesign.stanford.edu/bdn/india/
32. http://www.pharmaquest.biz/Overview-of-the-Industry/Company-News/GE-Healthcare-in-agreement-with-MP-Govt-and-Sanya-Hospitals-to-provide-advanced-diagnostic-care.html
33. http://censusindia.gov.in/2011-prov-results/paper2/data_files/india/Rural_Urban_2011.pdf
34. http://www.visiongain.com/Press_Release/66/'Global-companion-diagnostics-market-will-be-worth-3-45bn-by-2015'-predicts-a-visiongain-report
35. http://www.gene.com/gene/products/information/oncology/herceptin/factsheet.html
36. http://www.ispy2.org/

37. http://www.outsourcing-pharma.com/Clinical-Development/Quintiles-backs-I-SPY-2-breast-cancer-trial
38. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm268241.htm
39. Diagnostics 2011: M&A Surges, companion diagnostics accelerate and early detection offers new prospects PwC
40. http://www.pharmabiz.com/NewsDetails.aspx?aid=66281&sid=2
41. http://www.pharmabiz.com/NewsDetails.aspx?aid=66680&sid=2
42. http://www.pharmabiz.com/NewsDetails.aspx?aid=64906&sid=2
43. http://www.pharmabiz.com/NewsDetails.aspx?aid=64541&sid=2
44. http://biospectrumindia.ciol.com/content/BioSpecial/11010074.asp
45. http://www.roche.com/media/media_releases/med-cor-2011-08-17.htm
46. http://www.actonbiotech.com/home
47. http://www.oncquest.net/news/16-n-f.jpg
48. B. Patwardhan & ADB Vaidya (2010): Natural products drug discovery: Accelerating Clinical candidate development using reverse pharmacology approaches. Indian Journal of Exp. Boil. 48, 2202-227
49. YW Chin et. al. (2006) Drug discovery from Natural Sources. The AAPS Journal, 8 (2), E239-E253
50. Alan Harvey (2008) Natural products in drug discovery. Drug Discovery Today, 13, No. 19-20, 894-901
51. Chen et. al. (2008) New therapies from old medicines. Nature Biotechnology, 26, 1077-1083. http://www.nature.com/nbt/journal/v26/n10/full/nbt1008-1077.html]
52. http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ucm106137.pdf
53. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0085:0090:en:PDF
54. http://www.pharmaceutical-technology.com/projects/novartis-institute/
55. China's Pharmaceutical Industry: Poised for a giant leap. KPMG (2011)
56. Traditional Medicine to get a controller. Times of India. May 5th 2012
57. http://pharmabiz.com/NewsDetails.aspx?aid=67148&sid=1
58. http://pharmabiz.com/NewsDetails.aspx?aid=66919&sid=1
59. http://www.ccras.nic.in/Golden_Tiangle/20081011_Golden_Tiangle.htm
60. http://www.csir.res.in/csir/external/heads/collaborations/NM.pdf
61. Patwardhan B & Vaidya A (2010) Natural products drug discovery: Accelerating the clinical candidate development using reverse pharmacology approaches. Indian Journal of Experimental Biology, 48, 220-227
62. http://www.biospectrumasia.com/Content/180707IND3973.asp
63. http://www.indusbiotech.com/discovery/pipeline.asp
64. http://whoindia.org/LinkFiles/Traditional_Medicine_GAP_book.pdf
65. http://nopr.niscair.res.in/bitstream/123456789/7393/1/IJEB%2048%283%29%20199-207.pdf
66. Patwardhan B et. al. (2004) Ayurveda and natural products drug discovery, Current Science, 86, No. 25, 789-799
67. Synthetic Biology: Applying Engineering to Biology: Report of NEST High Level Expert Group. ftp://ftp.cordis.europa.eu/pub/nest/docs/syntheticbiology_b5_eur21796_en.pdf
68. Oldham et al. (2012) Synthetic Biology: Mapping the Scientific Landscape. PLoS, Vol. 7, Issue 4, e34368, 1-16.]
69. http://www.bbc.co.uk/news/10132762
70. http://www.bccresearch.com/report/BIO066A.html
71. http://bccresearch.wordpress.com
72. http://www.amyris.com/markets/artemisinin
73. http://www.dna.com/content.aspx?ContentID=1371
74. Editorial (2007): Synthetic Biology: promises and challenges. Molecular systems Biology, 3, Article No. 158 and George Church (2010), 2020 Visions Synthetic Biology, Nature, Vol. 463, 28

75. http://www.wired.com/dangerroom/2010/02/pentagon-looks-to-breed-immortal-synthetic-organisms-molecular-kill-switch-included
76. http://www.agilent.com/about/newsroom/presrel/2011/19apr-gp11012.html
77. http://synbio.mit.edu/faculty.html
78. http://igem.org/About
79. http://partsregistry.org/Main_Page
80. http://www.thehastingscenter.org/Publications/BriefingBook/Detail.aspx?id=2250
81. Wadman, M (2009) US drafts guidelines to screen genes. http://www.nature.com/news/2009/091204/full/news.2009.1117.html
82. Lloyd's (2009) Synthetic Biology Infuencing Development
83. http://www.tessy-europe.eu/public_docs/SyntheticBiology_TESSY-Information-Leaflet.pdf
84. Nature (2010) Sizing up the synthetic cell. http://www.nature.com/news/2010/100520/full/news.2010.255.html
85. http://www.synbiosafe.eu
86. http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS/countries/1W-IN?display=default
87. http://www.pwc.com/us/en/health-industries/publications/build-and-beyond.jhtml?WT.mc_id=gx-industry-health_us-health-buildbeyond
88. http://www.kpmg.com/Global/en/IssuesAndInsights/ArticlesPublications/Documents/HCI-ntegration-oct-2010.PDF
89. http://voices.washingtonpost.com/44/2010/03/obama-signs-higher-education-m.html?hpid=topnews
90. http://www.ppaca.com/
91.http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/10/200&format=HTML&aged=0&language=EN
92. http://censusindia.gov.in/2011-prov-results/paper2/data_files/india/Rural_Urban_2011.pdf
93. http://articles.economictimes.indiatimes.com/2012-05-04/news/31559329_1_rural-areas-mpce-nsso-survey
94. http://articles.economictimes.indiatimes.com/2010-10-24/news/27630804_1_heart-surgeries-hospitals-narayana-hrudayalaya
95. http://www.narayanahospitals.com/services/corporate-social-responsibility/ngo-support-work/yeshasvini-a-co-operative-farmers-healthcare-scheme/
96. http://vaatsalya.com/online/About_Us
97. http://www.cdacmohali.in/S_NationalRuralTelemedicineNetwork.aspx
98. http://mohfw.nic.in/NRHM.htm
99. http://www.thehindubusinessline.com/industry-and-economy/info-tech/article2954780.ece
100. http://articles.economictimes.indiatimes.com/2010-08-30/news/27610987_1_chronic-diseases-detection-smart-phones
101. http://www.narayanahospitals.com/services/telemedicine/introduction/
102. Bagchi S (2006) Telemedicine in Rural India. PLoS Med 3(3): http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0030082
103. http://www.forushealth.com/about_us.htm
104. http://www.forushealth.com/products.htm
105. http://www.thehindubusinessline.in/2010/03/19/stories/2010031952611900.htm
106. http://www.expresshealthcare.in/200810/market13.shtml
107. http://www.tnhsp.org/
108. http://www.gujhealth.gov.in/chirnajivi-yojana.htm
109. http://www.expresspharmaonline.com/20101231/pharmacistforbetterhealthcare09.shtm
110.Shivakumar AK et. al. (2011) Financing health care for all: challenges and opportunities. India: Towards Universal Health Coverage 6.
111. FINPRO: Diagnostic Centre Feasibility Study in India. November 2008.

3 Bioservices: The Emerging Collaborative Hub

The Bioservices industry consists of contract and clinical research organizations (CROs) as well as contract manufacturers (CMOs). Together they are often classified as Contract Research and Manufacturing Services (CRAMS).

3.1 The Global Flux in Pharmaceutical and Biotechnology R&D and Drivers of Development of the Bioservices Industry

The traditional model of drug discovery and development which was followed by pharmaceutical and biotechnology firms involved complete integration of all processes in-house; that is euphemistically referred to as 'vertically integrated firm'. This meant that processes such as target identification, assay development, lead generation and optimization, preclinical and clinical development (through trials) and marketing was all done within the boundaries of a firms. This pharmaceutical model worked very well during the initial years, however as the pressures of development cycle increased chiefly due to rising cost structures and declining approvals and other regulatory hurdles, big pharmaceutical companies began to engage and outsource parts of the value chain to other smaller pharmaceutical/biotechnology companies.

Studies by Munos (2009) [1] and Scannell et al 2012 [2] have shown that R&D costs have steadily increased while the number of approvals from FDA has been stagnant. Figure 3.1 shows that the cost per New Molecular Entity (NME) has increased drastically over the last couple of decades.

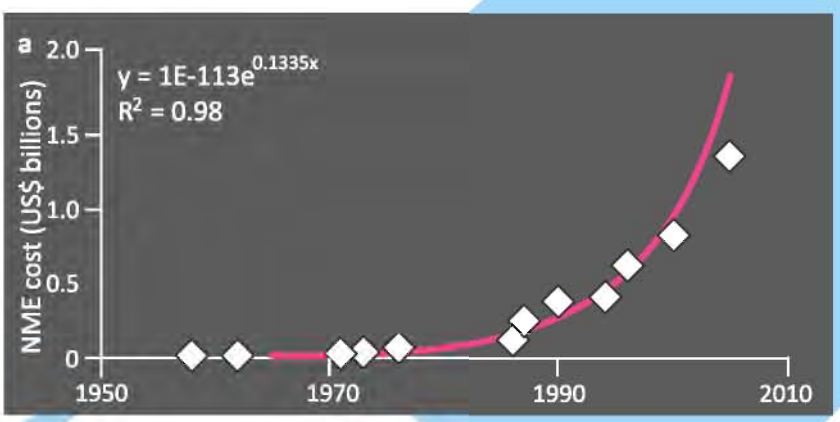


Figure 3.1 The rising cost of NME (from Munos 2009, [1])

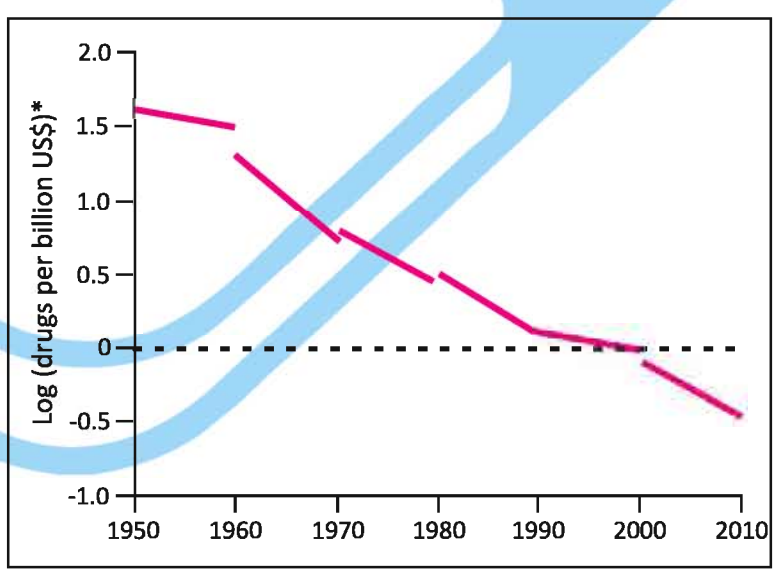


Figure 3.2 The Rate of decline of approval of new drugs per billion dollars spent (Scannell JW et. al. (2012), [2])

A BCG report (2011) estimated that the cost per drug molecule to bring to the market has risen from US$800 million in 2000 to US$2.3billion in 2010

A BCG Report (2011) has estimated that the cost per drug molecule to bring to the market including the cost of failure has risen from US $800 million in 2000 to US $2.3 billion in 2010 and is expected to touch US $3.8 billion by 2020 [3].

Furthermore, the number of drugs submitted for approval has remained flat over the last eight years and the average timelines of development have increased from 6.3 years in 1990s to 7.4 years in 2000s [3].

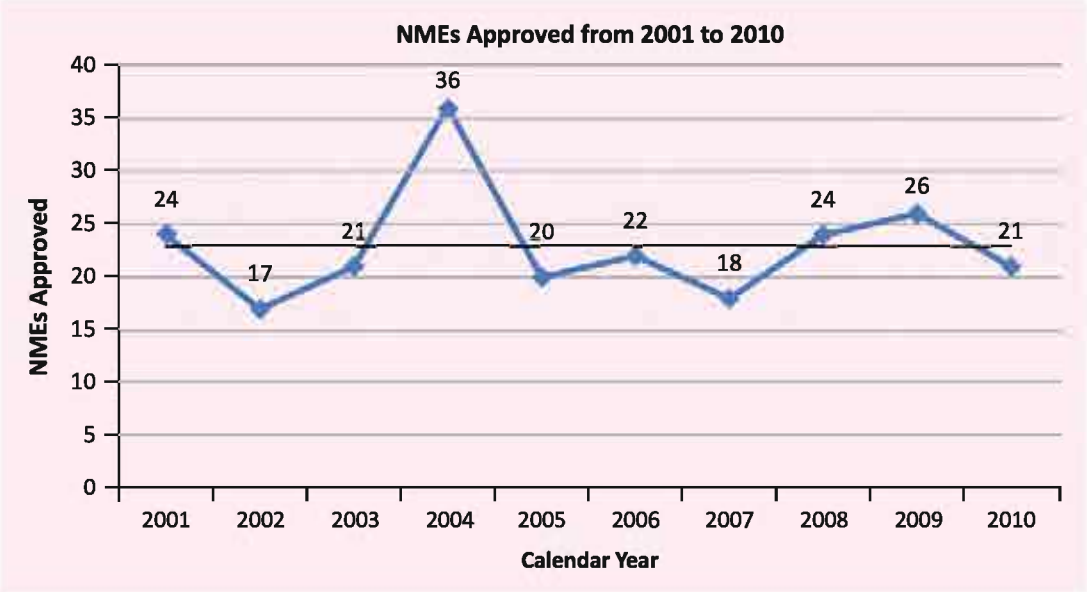


Figure 3.3 Ten year average of NMEs approved by FDA [from 4]

These cost pressures have been the drivers for big pharmaceutical firms to outsource parts of the value chain in drug discovery and development to other smaller firms and this has fuelled the growth of CRAM industry.

3.2 Global Bioservices Market: An Overview

The Bioservices industry sector was worth US $67 billion in 2010, of which 64% was contract manufacturing amounting to US $42 billion while contract research represented US $25 billion (ICRA 2011, [5]).

This industry is globally dominated by firms in the developed markets such as the USA, UK and Germany including ICON, Covance, Charles River, Quintiles, Kendle Research and PharmaNet. According to the ICRA 2011 report only 20% of global spend is being outsourced thus highlighting the growth potential. However Asian countries (such as China, Singapore and Malaysia) and other European geographies are soon emerging as strong competitors in this area [5].

China

The Chinese outsourcing industry is strong and is growing at more than 20% year on year; it was valued at US $2.05 billion in 2010. China, like India, offers unique advantages for global pharmaceutical firms to outsource some of their research and development and clinical trials to Chinese organizations [6].

There are 400 CRO companies in China whose main focus remains pre-clinical and clinical testing of novel drugs. These firms are clustered around Beijing and Shanghai [6]. Many multinational contract research organizations are active in China, either expanding operations or buying local firms. For instance, Quintiles, in 2011, launched a new CRO in China and plan to double the number of workers in the near future [7]. Charles River Laboratories paid US $1.6 billion to buy Wuxi Pharmatech in 2010 while ICON set up a partnership with Tigermed Consulting [6].

As mentioned before, China offers advantages in cost savings, a well trained talent pool; especially a high returnee culture and access to a treatment naive population. China also has a large number of patients in gastrointestinal cancers (esophageal, gastric and liver), nasopharyngeal cancer and neural tube defects [6].

3.3 The Indian Bioservices Sector

The Indian bioservices sector is the second largest sector of the biotechnology industry. The Indian bioservices industry has been steadily rising over the past few years as shown in Figure 3.4. It grew by 23% to register market revenues of US $721 million in 2010-2011, which accounted for 19% of the total revenue of the biotech industry [8].

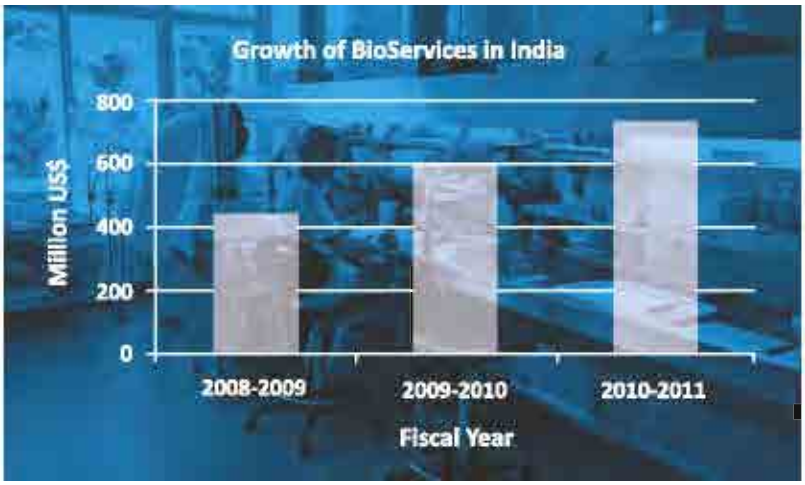


Figure 3.4 Growth of bioservices in India (ABLE-BioSpectrum Survey 2011, [8])

Some of the leading CROs in India include Quintiles, Syngene International, SIRO Clinpharm and Ecron Acunova, Lambda Therapeutic, Advinus, Aurigene, Jubilant, Sai Advantum, Suven Lifesciences among many others. The ABLE-BioSpectrum 2011 list of top 10 Indian CROs as per their revenue is shown in Figure 3.5 [8].

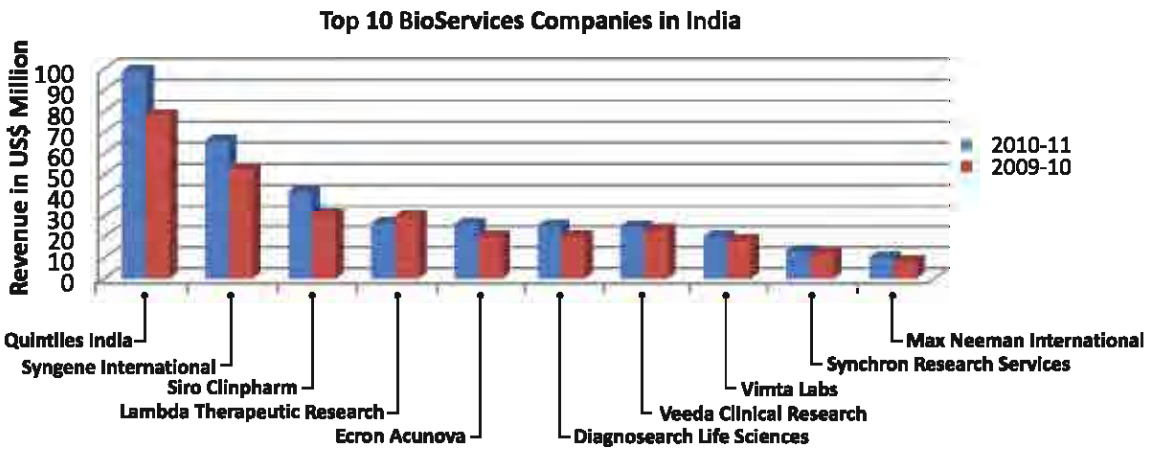


Figure 3.5 Top 10 Indion bioservices companies, (ABLE-BioSpectrum Survey 2011, [8])

The competencies of the Indian CRO industry are diverse. CRO firms provide a range of services from target identification and validation, screening, BA/BE studies, pre-clinical studies to all the way up to clinical trials and data management.

According to ABLE-BioSpectrum estimates there are 30 CROs that conduct Bioavailability (BA)/Bioequivalence (BE) trials and around 50 CROs that are involved in Phase I-IV trias (as shown in Figure 3.6, [8]).

The competencies of the Indian CRO industry are diverse. CRO firms provide a range of services from target identification and validation, BA/BE studies, pre-clinical studies, all the way up to clinical trials and data management.

Figure 3.6 The nature of Indian CRO industry (ABLE-BioSpectrum Survey 2011, [8])

Leading Indian CROs like Jubilant Biosys provide an integrated platform for drug discovery right from target validation to clinical trials and data management. GVK BIO is another company that provides an equally wide range of competency. Advinus (a TATA enterprise) is an end-to-end bioservices company and is strategizing to be a drug discovery company. Figure 3.7 (below) shows the competencies of the Indian CRO industry.

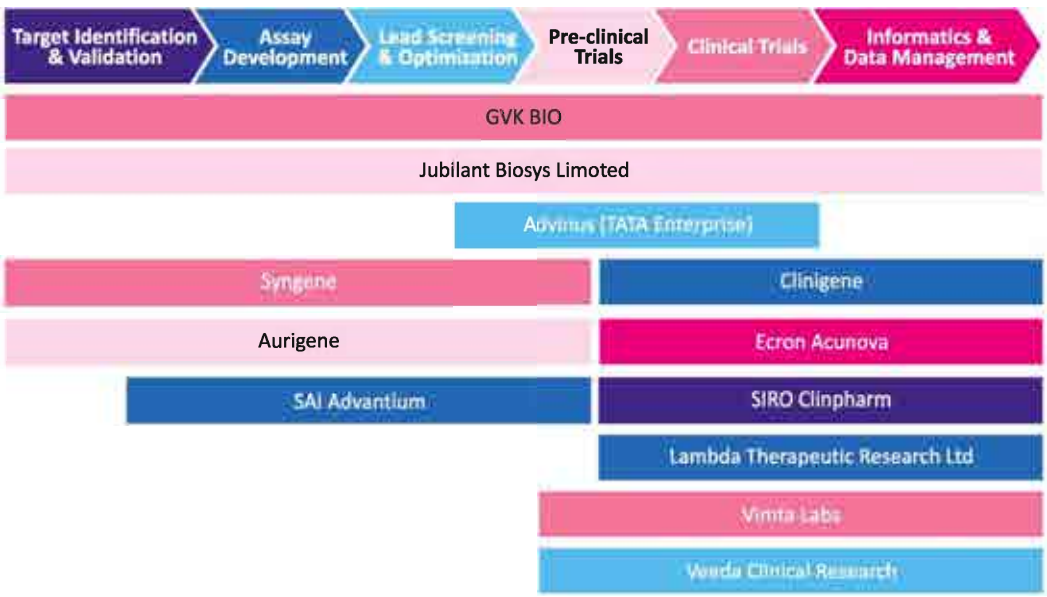


Figure 3.7 Competencies of Indian CROs (Adapted from BCG (2011), [3])

India has an opportunity to become a leading hub for clinical trials. According to the Biospectrum-ABLE survey of 2011, the number of ongoing clinical trials in 2011 was 1584. Further, the DCGI has introduced a compulsory registration process with CTRI for all clinical trials being conducted in India [8].

As per 2011 ABLE-BioSpectrum estimates, Quintiles India conducts the largest number of clinical trials in the country. Big pharmaceutical firms such as GSK, Novartis, Roche, Eli Lily and many other companies conduct part of the global studies in India. This sector is expected to grow steadily as more multinational corporations are looking to India to expand their clinical trials business markets and Indian CROs are looking overseas for collaborative opportunities [8].

Total Number of Clinical Trials (2011 Estimates)

- 1,584

Regulatory Initiative

- DCGI, in 2009, introduced compulsory registration with CTRI before starting any clinical study

Key Therapeutic Areas

- Diabetes
- Cardiovascular Diseases
- Cancer

Figure 3.8 Overview of clinical trials in India (ABLE-BioSpectrum Survey 2011, [8])

As mentioned before, there is a large patient population in India across several diseases. For example, there are around 50 million diabetics, close to a million new cases of cancer each year and 47 million people with coronary heart disease (which is expected to rise to 61 million by 2015) [3].

The therapeutic areas covered in the trials include diabetes, cardiovascular disorders, cancer (breast and head & neck cancer), infectious diseases, endocrine diseases, psychiatric abnormalities, central nervous systems dysfunctions and respiratory disorders [8].

3.4 Growth Drivers for Indian Bioservices

India's large, genetically varied population coupled with professional/IT skills and English literacy have made it an attractive hub for contract research outsourcing in the bioservices sector. Besides these advantages, India also has a large, diverse treatment naive patient population. This provides an ideal environment for conducting successful clinical trials. Hence, these characteristics are expected to fuel the development of this sector in India.

Figure 3.9 Growth drivers for bioservices in India

Moreover, India can provide the much needed cost benefits required for the recent global financial challenges. The cost of bringing a novel therapeutic from the bench to the market could be as high as US $1.5 billion, and these estimates are predicted to rise in the future. However, India is in a beneficial position as it can provide the much needed the cost benefits that can attract out-sourced projects. A recent BCG report (2011) had stated that the current cost advantage provided by India is estimated to be approximately 60% and is predicted to remain significant until 2025 at about 20% [3, 9]. Thus, the cost advantages would aid the long term progress of CROs in India.

The developing regulatory framework is also another key growth driver for the bioservices market in India. The recent focus towards quality and the regulation of clinical trials is predicted to drive the future of this segment in the country. Government regulatory bodies such as the DCGI, ICMR and GEAC are involved in proactively regulating this sector in India, thus paving the way for future growth and development.

It is also essential to understand global perspectives in this regard and use that information to drive the expansion of the Indian bioservices industry.

A recent BCG report (2011) had stated that the current cost advantage provided by India is estimated to be approximately 60% and is predicted to remain significant until 2025

3.5 The Evolving Collaborative Landscape

The BioServices industry took off in the 2000s and today India can claim to have a vibrant bioservices industry that meets the high standards of global delivery.

Recent collaborative initiatives have enhanced the growth of the bioservices sector in domestic and international markets. Current partnership models for bioservices include licensing partnerships, strategic alliances for pre-determined R&D segments of a project, and the nascent risk-sharing models, where the partnering CROs share the risks of developing and marketing innovations.

Some of the significant joint ventures in the bioservices sector are listed in Table 3.1.

Collaborations	Year	Purpose
Nostrum & Institute of Microbial Technology (IMTECH)	2009	Licensing Caerulomycin A [10]
Endo Pharmaceuticals & Aurigene Discovery Technology	2009	Cancer drugs R&D [12]
Abbot & Zydus Cadila	2010 2011	-Abbot marketed Zydus products for cardiovascular, neurological and respiratory disorders, as well as for pain and cancer [13] -Abbot to commercialize 25 Zydus therapeutics in 14 emerging markets in 2013 [14]
Syngene & Endo Pharmaceuticals	2010	Drug discovery for cancer [15]
TCG Life Sciences & Carna Biosciences	2010	Drug discovery for kinase targets [16]
SIRO Clinpharm & Dream CIS	2010	Expansion of the clinical trials business [17]
Jubilant Biosys & Endo Pharmaceuticals	2010	Expanded their drug discovery alliance in cancer [18]
Jubilant Biosys Ltd & Norgine	2011	Drug discovery for Gastro-intestinal disorders [19]
SIRO Clinpharm & Peregrine	2011	Monoclonal antibodies for cancer and viral diseases [20]
Advinus & SignalChem	2011	Anticancer drugs
Advinus & Celgene Global Health	2012	Visceral Leishmaniasis (Kala Azar)

Table 3.1 Joint ventures in the bioservices sector [10-20]

The typical CRO model in India is that of companies beginning with bio-availability and bio-equivalence studies, gaining increased competencies, and gradually occupying higher levels in the value chain [Figure 3.10]. Another emerging scenario is that of CROs increasingly taking a partnership route and sharing greater risks by involving themselves in the drug discovery process. This risk and reward model will strengthen in years to come as Indian CROs rises up the value chain.

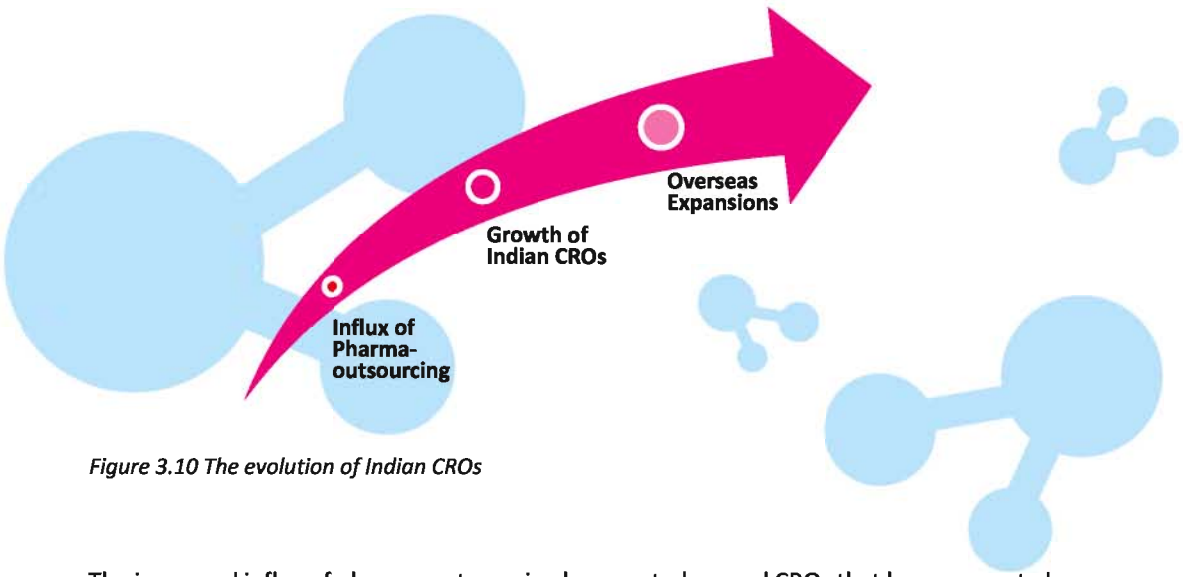


Figure 3.10 The evolution of Indian CROs

The increased influx of pharma-outsourcing has created several CROs that have grown to become independent industries and are now looking to branch out in South East Asian markets. For instance, SIRO Clinpharm and Veeda Clinical Research have expanded into the Malaysian market [21, 22]. Synchron Research has also branched to Thailand and is currently looking at expansion in Vietnam [23].

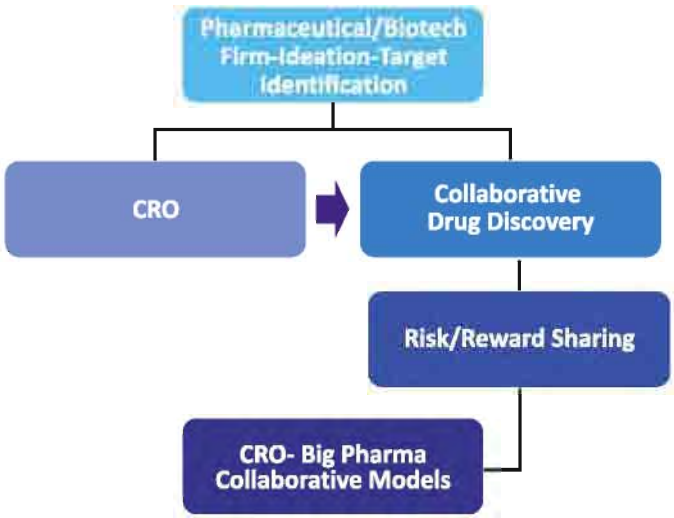


Figure 3.11 The evolution of the Indian CRO industry into nascent drug discovery firms

Another emerging scenario is that of CROs increasingly taking a partnership route and sharing greater risks by involving themselves in the drug discovery process

3.6 Contract Manufacturing in Biopharmaceuticals

India has built a reputation as a manufacturer of small molecule generics and invited global admiration with more than 200 USFDA and UK MHRA approved manufacturing plants [5].

As mentioned in Chapter 2, there is a huge opportunity for India to seize the emerging opportunity in biosimilars and vaccine development and manufacturing to become the world leader in biopharma manufacturing by 2025. Many biologics with global sales revenue of $73 billion in 2009 are coming off patent in the next ten years [24] and coupled with the high cost of healthcare in Western economies is driving many countries to look for cheaper but high quality alternatives and hence biosimilars will gain acceptance across all geographies across the world including India and Asia Pacific as well as the developed markets.

Despite the significant advancements in bioservices, India faces multiple challenges that impede the future growth of this sector. Some of the setbacks for the Indian bioservices industry are discussed in the following sections.

3.7 Key Challenges

There are several key challenges that Indian firms need to overcome to seize the opportunity that is within their grasps. These include lack of capital and infrastructure, regulatory issues, human resources and finally, many competitors such as China, Malaysia, and South Korea provide incentives to their local players that make biopharma manufacturing lucrative in their geographies.

Figure 3.12 Key challenges in the Bioservices industry

3.8 Recommendations for the Bioservices Industry

The CRAMS industry especially biotechnological contract services and manufacturing in India barely existed in the middle of the 1990s, but has grown today to be an important contributor to India's bio-economy. As an emerging segment of the Indian Biotechnology landscape, it is essential to address the issues that impede the development of the bioservices sector and suggest possible solutions for ensuring its sustained growth in the future. Some of the recommendations for this sector are discussed below.

3.8.1 Recommendations for Contract Research Services including Clinical Trials

3.8.1.1 Focus on Capacity Building

Capacity building is an important area that the GOI should focus upon. Current funding schemes, while rightly focusing on innovation driven firms, miss out on firms which focus on services as well as manufacturing products that have come out of patent cliff. Firms that have delivered on the grants must be given special rating to be eligible for further funds and grants. DBT, through BIRAC, can also work with DSIR and provide emerging start-up companies more services and support.

3.8.1.2 Establish Academic Courses for Contract Research and Clinical Trials Management

There are a few institutions in India that offer courses in clinical studies and management. It is urgently required that all leading academic institutes offer extensive courses in clinical trials management with intense industry exposure. Besides this, these institutions also must have trained teaching staff with academic as well as industrial experience.

3.8.1.3 Streamline Regulatory Framework

India's regulatory processes need complete review. The current regulatory process in cumbersome and takes an enormous amount of time and these delays bring down India's competitive advantages and become a negative driver for this industry. There are several critical areas where regulatory reforms are required immediately so that India can leverage its current advantages of cost and manpower. Some of the changes that are needed are as follows:

A. All things remaining equal, it should not take more than three months to get approval of a Schedule Y Phase I study. It should not take more than 30 days to receive a BE study approval.

B. IND Committee meeting should be called mandatorily every month and once a protocol is approved then the approval letter should be released within a week.

C. After receiving IND approval, all subsequent protocols should be allowed by the institutional ethics committee.

D. Allow Phase I study for a molecule that belongs to a multinational company.

E. Establish one rodent and two large animal facilities. The industry needs high quality animals and hence the industry needs proper large animal facilities.

F. Conduct a yearly inspection of GLP facilities in a time-bound manner.

G. Equip the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) to match international standards.

H. Simplify the approval process for import of animals. The current regulation needs multiple approvals from multiple Ministries such as Animal Husbandry (Ministry of Agriculture), Directorate General of Foreign Trade (DGFT), Ministry of Commerce and Industry and animal quarantine (Ministry of Environment & Forest) and hence is cumbersome. Plus separate approvals are required for each type of animals.

I. Simplify and streamline the current process of approvals for Phase III global trials which is lengthy and takes 9 months thus leading to unnecessary delays. This is in contrast to other countries where the approval time could range from 30 days (USA) to 90 days (Malaysia).

J. Abolish the cap on subject numbers from India for multinational studies. This will foster India's participation in global studies.

K. Align toxicology requirements in line with the requirements of the US FDA and/or EMEA.

L. CDSCO should consider introducing a pre-filing discussion in case of IND/NDA filings.

3.8.1.4 Encourage CROs to partner with academic institutions for drug discovery

Many Indian CRO firms have developed competencies to conduct drug discovery research as well as development which is evident from the partnerships Indian CROs are establishing with global MNCs.

Indian CROs should be incentivized to partner with leading Indian academic laboratories to jointly conduct drug discovery research. Incentivization tools could include establishing and implementing "Drug Discovery Funds" which only allows for joint industry-academia bids. This will not only foster industry-academia interface but also help many CROs to take calculated risks to become true drug discovery firms.

R&D partnering models such as the Translational Medicine Research Collaboration (TMRC), Scotland, Johnson & Johnson's pre-competitive collaboration with Imperial College, UK and the University of Dundee's School of Life Sciences partnerships with pharmaceutical companies should be studied and the best practices from these cases can be adapted to the Indian context [26].

Indian CROs should be incentivized to partner with leading Indian academic laboratories to jointly conduct drug discovery research. Incentivization tools could include establishing and implementing drug discovery funds.

GOI must ensure that the format, content and the interpretation of all such regulation is common throughout the country and introduce a single-window system for securing clearances and approvals from both the central as well as State agencies.

3.8.2 Recommendations for Biopharmaceutical Contract Manufacturing

India stands at the threshold of becoming a global giant in biopharmaceutical manufacturing within the end of this decade. For this opportunity to materialize several concurrent policy decisions have to be taken, some of which are discussed in Chapter 2 as well.

3.8.2.1 Establish Single Window for Approvals and Clearances

Currently there are multiple agencies under different Government Ministries to secure approvals and no-objection certificates. GOI must ensure that the format, content and the interpretation of all such regulation is common throughout the country and introduce a single window system for securing clearances and approvals from both the Central as well as the State agencies [25].

3.8.2.2 Create Independent Inspection Facility

GOI should establish an inspection body under the aegis of DCGI and the State drug Controller levels to audit the manufacturing and containment facilities of all biopharmaceutical manufacturing firms such that it helps to ensure that products meet the highest levels of international standards [25].

3.8.2.3 Revise Regulations on Process Validations

There is an anomaly in regulations that have an oversight of manufacturing and clinical development. Presently, it is required that the process validation batches be manufactured prior to clinical development phase [25]. It also requires representative samples of commercial scale up batches to be sent for clinical trials and export registration [25]. This is required to be done even before a local manufacturing license has been issued. Furthermore, the local manufacturing license is provided once a drug is approved by the regulator. Many industry experts opine that the regulations must be changed such that the use and launch of validated product is allowed from commercial scale up production if the product still has a shelf life [25].

3.8.2.4 Establish a National Center for Biological Therapeutics

As mentioned previously in section 2.2.6.11, the GOI should establish a National Center for Biological Therapeutics head quartered in Bangalore and with regional centers in Ahmedabad, Chandigarh and Hyderabad. GOI should use this opportunity to present herself as a biosimilar development and manufacturing hub that can mirror the country's growth in the small molecule generic space and emerge as a global leader in biosimilar manufacturing. The window of opportunity may not last for long as other countries particularly China, Malaysia, Singapore, Brazil and even East European countries such as Poland and Czech Republic are competing for the same space.

The Centre should close the technology gap and regulatory gap that many start-up companies are facing. As mentioned previously this can be achieved by providing training in several aspects of biochemical engineering and creating core lab facilities for biosimilar product testing.

3.9 References

1. Munos B (2009) Lessons from 60 years of pharmaceutical innovation. Nature Reviews, drug discovery, 8, 959-968
2. Scannell JW et. al (2012) Diagnosing the decline in pharmaceutical R&D efficiency, Nature Drug Discovery, 11, 191-200
3. Life Sciences R&D: Changing the Innovation Equation in India, BCG 2011
4. http://www.fda.gov/downloads/AboutFDA/Transparency/Basics/UCM247465.pdf
5. http://www.icra.in/Files/Articles/CRAMS%20Note,%20Overview%20and%20Outlook.pdf
6. KPMG (2011) China Pharmaceutical Industry Poised for the Giant Leap
7. http://www.fiercebiotech.com/press-releases/quintiles-launches-china-cro-kun-tuo-0
8. BioSpectrum ABLE Biotech Industry Survey 2011
9. http://www.thehindubusinessline.com/industry-and-economy/economy/article2090928.ece
10. http://www.csir.res.in/External/Heads/collaborations/MOU/nostrum_imtech.pdf
11. http://www.evaluatepharma.com/Universal/View.aspx?type=Story&id=177259
12. http://www.thepharmaletter.com/file/59145/endo-enters-rd-deals-with-harvard-univ-and-aurigene.html
13. http://www.abbott.com/news-media/press-releases/Press_Release_0856.htm
14. http://articles.economictimes.indiatimes.com/2011-12-14/news/30515979_1_abbott-india-zydus-cadila-abbott-plans
15. http://www.business-standard.com/india/news/syngene-ties-upendo-pharmaceuticals-to-develop-anti-cancer-drug/389348/
16. http://www.tcgls.com/news2010_12_oct.htm
17. http://www.siroclinpharm.com/siro_article_clinical_alliance_dreamcis.html
18. http://www.clinsys.com/news/01-27-10.html
19. http://www.jubilantbiosys.com/index.php/news-a-events/press-releases/22
20. http://www.siroclinpharm.com/siro_article_peregrine_pharmaceuticals_collaboration.html
21. http://www.siroclinpharm.com/siro_article_malaysia_launch.html
22. http://www.veedacr.com/veeda-announces-the-opening-new-unit-in-se-asia
23. http://www.biospectrumasia.com/Content/010411IND15840.asp
24. Vision 2020: A Biopharma Strategy for India, an ABLE–PwC report (2010) for Department of Pharmaceuticals, Ministry of Chemical and Fertilizers, Government of India.
25. Shaw KM (2011), India: A Global Manufacturing Hub for Biopharmaceuticals, ABLE-Biocon Whitepaper.
26. Tralau-Stewart, C et. al. (2009): Drug Discovery new models for industry-academic partnerships. Drug Discovery Today, Vol. 14. No. ½, 95-101.

Bio-Agri: Solutions for Food Security

4

Agriculture has been one of the most important anthropogenic activity for humankind and its growth has been facilitated by use of modern science and technology over the last few centuries [1]. More recently, the so called "Green Revolution" helped countries of Asia and Latin America to overcome chronic shortages of food. However the recent price increases of food commodities in 2008 brought issues regarding agriculture and food security back to the forefront and the need to address issues in this sector [1].

4.1 Global Bio-Agri Landscape

A 2012 ICRIER report highlighted that the Food and Agriculture Organisation (FAO) has estimated that the number of people who do not have food security increased from 800 million in 1998 to over 1 billion in 2009 because of the rise of global food prices from 2006 until 2008 [2].

The global population is set to increase to touch 9 billion by 2050 and it is inevitable that it will create increased demand for food and fuel [1]. Per capita calorie intake has increased by 550 kcal between 1963 and 2007 [2]. A policy paper by John Beddington quoting FAO sources mentioned that between 2008 and 2030, the total crop and livestock demand and production will increase by 40% and the World Bank predicts that there will be a 50% rise in cereals and 85% rise in demand of meat products between 2000 and 2030 as dietary lifestyles change in developing countries [3]. Many other forward looking estimates suggest that the world food demand will double by 2050 putting greater stress on usage of land and water as well as a substantial increase in energy requirements [4].

It has been estimated that currently 1600 million hectares (Ha) are under cultivation for crops and projections differ widely in the extra amount of land that would be required to meet the demand for food by 2030 [1]. There are varied estimates on how much land can be expanded for cultivation and it ranges from 50 to 1600 million Ha [1]. FAO estimates that an area of 120 million Ha would be needed to meet the demands of food by 2030. To put this requirement in perspective the area corresponds to double the size of France or one third of the size of India [5].

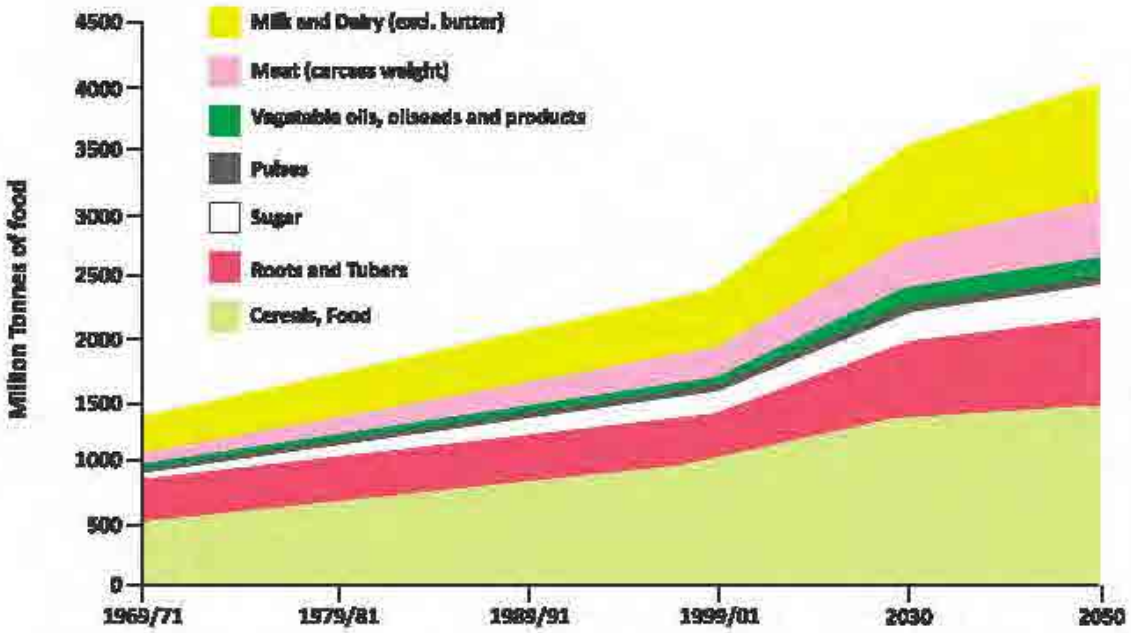


Figure 4.1 The Future demand for food products [3]

Figure 4.2 shows the global forest cover as percentage of land area and Figure 4.3 shows the land area per capita [6]. The implications of the pressure to increase land for agriculture are felling of more forest and conversion of natural grasslands, thereby dramatically affecting natural ecosystems.

Figure 4.2 World forest cover as percentage of land area in different regions [6]

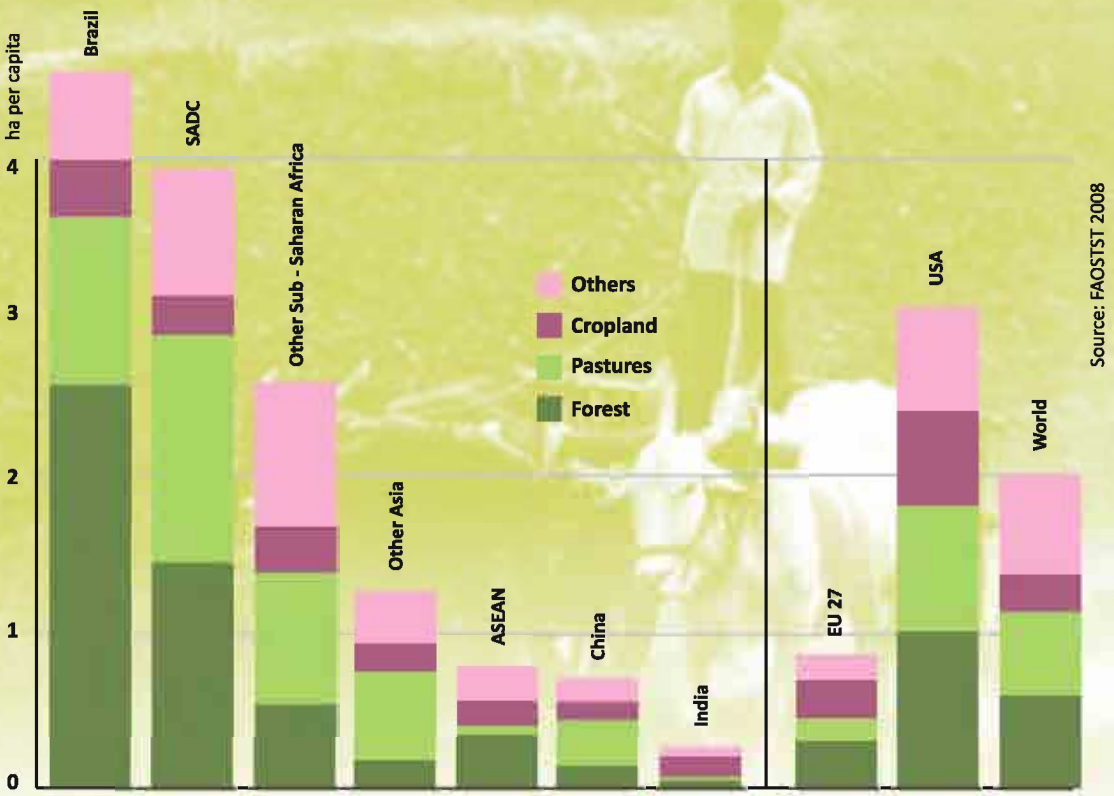


Figure 4.3 Land area per capita [FAO Stat 2008]

The solution to these global challenges lies in increasing agricultural productivity through technology. According to 2011, estimates, biotechnology advancements helped increase the net farm income by US $65 billion during the period ranging from 1969 to 2009 and developing nations contributed to 50 percent of this increase. Moreover, biotech also enabled the global increases in corn and soybean production by 130 million and 83 million tonnes respectively [7]. As shown in Figure 4.4, biotech can improve agricultural production by promoting the use of disease resistant crops, enhance the flavour and nutritional value of food products and subsequently impact global health and economies, especially among developing nations [8]. Thus, biotechnology can have a lasting impact on the global agriculture sector and can play a significant role in improving economies across the globe.

Figure 4.4 Benefits of biotech in the global agricultural sector [8]

4.1.1 Molecular Assisted Selection (MAS) and Molecular Breeding Technology

Progress in agriculture has depended on improved crop varieties. Modern molecular biology and genomic techniques such as MAS help in identifying desirable traits therefore allowing agricultural scientists to select varieties that have improved traits such as high yields and resistance to environmental stress resistance such as drought and pest [9]. MAS is used for a multitudes of functions such as [10]:

- Genetic variability assessment and germplasm characterisation
- Determining linkages between cultivars, inbreeds
- Determining the sequences of useful candidate genes
- Monogenic and quantitative trait loci (QTL) determination
- Identification and genotyping crop varieties [10]

MAS has been used to make improved maize variety with high protein content as well as those that are resistant to maize streak virus [9]. Other successes include disease resistant cassava [1, 10]. More than 40 genes that confer disease resistance have been mapped and these maps have helped in stacking several disease resistant genes into one genotype [10].

A detailed report on MAS and its use in agriculture and animal livestock breeding is available in the 2009 FAO publication titled Marker Assisted Selection Current Status and Future Perspectives in crops, livestocks, forestry and fish [11]. Enabling technologies such as next generation sequencing and mapping are helping in MAS. MAS is also being used to improve wheat (especially targeting diseases such as Fusarium Head Blight (FHB), Septoria tritici blotch (STB) and yellow rust), rice (especially targeting dieases such as bacterial blight, borr as well as for environmental stresses such as salinity, submergence among others. There are already more than 2200 simple microsatellite repeats identified for rice. Other plant species that are the focus of MAS are soybean, cotton, sugarcane, grape, banana, sweet potato, egg plant, potato, groundnut, cucumber and sugarbeet to name a few [11, 12].

In 2011, GM crops were cultivated in 29 countries (19 developing and 10 developed economies).

4.1.2 GM Crops

Genetically modified (GM) crops are among the leading aspects of agricultural biotechnology across the world. In 2011 GM crops were cultivated in 29 countries (19 developing and 10 developed economies) across the world with 160 million hectares being cultivated with GM crops- a rise in 12 million hectares over the previous year [13].

Figure 4.5 shows the growth of GM crop acreage from 1996 until 2011 [13]. The figure also illustrates developing countries now have an equal share of acreage of GM crops as developed countries.

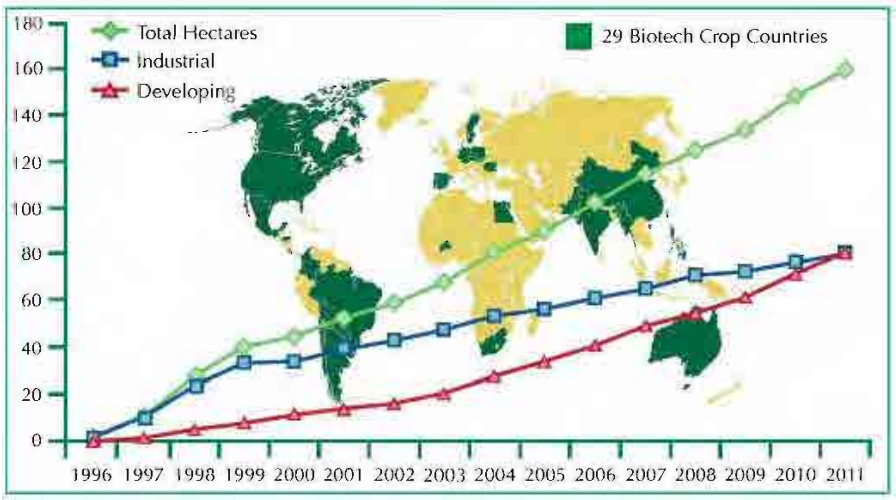


Figure 4.5 GM crop ocreage in million hectares from 1996-2011 [13]

The global market for GM crop in 2011 was US $13.2 billion an increase of US $1.5 billion from 2010. Multinational firms such as Monsanto, Bayer CropScience, BASF, Syngenta are major players in the GM crops space.

Table 4.1 shows the list of 29 countries growing GM crops [13].

Rank	Country	Area (million hectares)	GM Crops
1	USA	69	Maize, Soybean, Cotton, Canola, Sugarbeet, Alfalfa, Papaya, Squash
2	Brazil	30.3	Soybean, Maize, Cotton
3	Argentina	23.7	Soybean, Maize, Cotton
4	India	10.6	Cotton
5	Canada	10.4	Canola, Maize, Soybean, Sugarbeet
6	China	3.9	Maize, Papaya, Poplar, Tomato, Sweet Pepper
7	Paraguay	2.8	Soybean
8	Pakistan	2.6	Cotton
9	South Africa	2.3	Maize, Soybean, Cotton
10	Uruguay	1.3	Soybean, Maize
11	Bolivia	0.9	Soybean
12	Australia	0.7	Cotton, Canola
13	Philippines	0.6	Maize
14	Myanmar	0.3	Cotton
15	Burkina Faso	0.3	Cotton
16	Mexico	0.2	Cotton, Soybean
17	Spain	0.1	Maize
18	Columbia	<0.1	Cotton
19	Chile	<0.1	Maize, Soybean, Canola
20	Honduras	<0.1	Maize
21	Portugal	<0.1	Maize
22	Czech Republic	<0.1	Maize
23	Poland	<0.1	Maize
24	Egypt	<0.1	Maize
25	Slovakia	<0.1	Maize
26	Romania	<0.1	Maize
27	Sweden	<0.1	Potato
28	Costa Rica	<0.1	Cotton, Soybean
29	Germany	<0.1	Potato
Total	**160**		

Table 4.1 GM crop growing countries [13]

The USA is the largest producer of GM crops with GM varieties of corn, cotton, sugarbeet and papaya being adopted rapidly. GM alfalfa and GM sugarbeet are cultivated in 200,000 and 450,000 Ha respectively. In the EU, GM crops is now cultivated in 114000 Ha across six countries (Czech Republic, Spain, Portugal, Poland, Romania and Slovakia) which grew mostly Bt maize. Sweden and Germany allowed GM potato to be grown in a very small area [13]. Other agricultural products that would create an impact are golden rice (with high beta carotene levels) which is being developed by the International Rice Research Institute (IRRI) in the the Philippines. IRRI has successfully bred the Golden rice traits into IR64 and PSBRc82 in Philippines and with BRRI Dhan in Bangladesh [13].

GM crops provide several benefits. Improved varieties provide increased yields, reduced production costs (enabling food security & economic benefits to the farmers) and reduce agriculture's environmental impact such as reduction in pesticide used and indirectly through higher productivity gains helping to save forests by decreasing land requirements [9, 13].

4.1.3 Global Regulation Status of GM Crops

Besides the 29 countries where GM crops are grown and commercialised, another 31 countries have granted regulatory approval for the import of GM crops for food and feed with Turkey most recently giving a go ahead for import of GM crops in 2011 [13]. The ISAAA 2012 report cites that globally 1045 approvals have been granted for 196 events for 25 crops. Among GM crops, maize has been given most events approval numbering 65 followed by cotton which has 39 events approved [13].

However, there is opposition to GM crops from many quarters especially in Europe. Concerns regarding GM food pertain to possibilities of horizontal transfer of genes from GM to the wild varieties, development of resistance to herbicides and possible negative affect on human health [9]. In March 2010, the European Commission approved overturning a 12 year moratorium in cultivation of GM crops in Europe by allowing BASF to grow Amflora (a GM potato) for cultivation in Germany and the Czech Republic [14].

Many countries in Europe follow the Cartagena Protocol on Biosafety with the doctrine of the Precautionary Principle

In January 2012, BASF announced the closure of its development research in GM crops in Europe and that it is moving existing projects to the USA due to negative sentiments and a lack of interest for commercialization among various stakeholders, especially consumers, farmers and politicians. It also announced that the headquarters of BASF Plant Science will be shifted from Germany to Raleigh, North Carolina, USA [15].

Many countries in Europe follow the Cartagena Protocol on Biosafety with the doctrine of the "Precautionary Principle" that makes governments restrict and regulate new technologies and products until conclusive proof of safety is obtained first [9].

Calestous Juma, an international expert on biotechnology policy and a professor in Harvard Kennedy School opines that the opposition to GM by the public could be shaped by psychological factors that are triggered by food safety scares such as mad cow disease and dioxin contamination thus objective discussion on science based policy becomes a casualty [9].

4.2 Indian Scenario

The Green Revolution during the mid 1960s helped India become self sufficient in food grains, especially wheat and rice. Food grain production increased from 108 million tonnes in the 1970s to 234 million tonnes in 2008-09 [2].

Agriculture continues to be the largest sector in terms of employment with 52% of India's workforce employed in this sector, however the sector's contribution to the economy (India's GDP) has fallen from 30% in 1990-1991 to 14.5% in 2011-2012 thus highlighting the fact that while the economy is transitioning from an agrarian to a service based one; the dependency on agriculture for sustenance and livelihood has remained [16]. The average size of agricultural land holdings has declined from 2.28 hectares in 1970-71 to 1.23 hectares in 2005-06. The number of marginal holdings, i.e. holdings less than 2 hectares is 64.8% thus highlighting the fragmentation of land holdings [16].

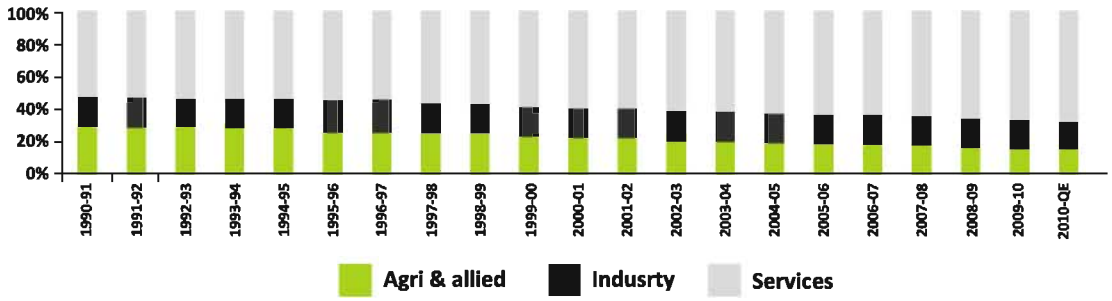


Figure 4.6 The contribution of agriculture sector to the Indian overall GDP [16, Central Statistical Office (CSO)]

Agriculture continues to be the largest sector in terms of employment with 52% of India's workforce employed in this sector, however, the sector's contribution to the economy has fallen from 30% in 1991 to 14.5% in 2011.

The agriculture sector holds the key to food security for the future as India's population continues to grow. Close to 240 million people in India suffer from chronic hunger, which means that India has the world's largest population of undernourished people [2]. The share of household expenditure on food for India is 50% according to 2004 estimates indicating that the economically disadvantaged bear the brunt of food security [2].

Over the last decade, while the Indian economy grew at an average of 7-9%, the agriculture sector grew at an average rate of 3%. Three factors, increasing population, increasing demands for food and declining agricultural productivity will have severe consequences on India's food security status.

Organisations such as the Indian Council of Agricultural Research (ICAR), The International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), M S Swaminathan Research Foundation and University of Agricultural Sciences (UAS, Dharwad) among many others, are leading agricultural research and development.

4.2.1 Indian Bio-Agri Industry

The bio-agri sector consists primarily of firms that are either technology development firms such as Metahelix and Monsanto, or seed firms such as Rasi Seeds to name a few.

The revenue generated from the bio-agri sector of India in FY 2010-2011 totaled US $516.67 million, thereby recording a year on year growth of 10.98% over the previous financial year [17].

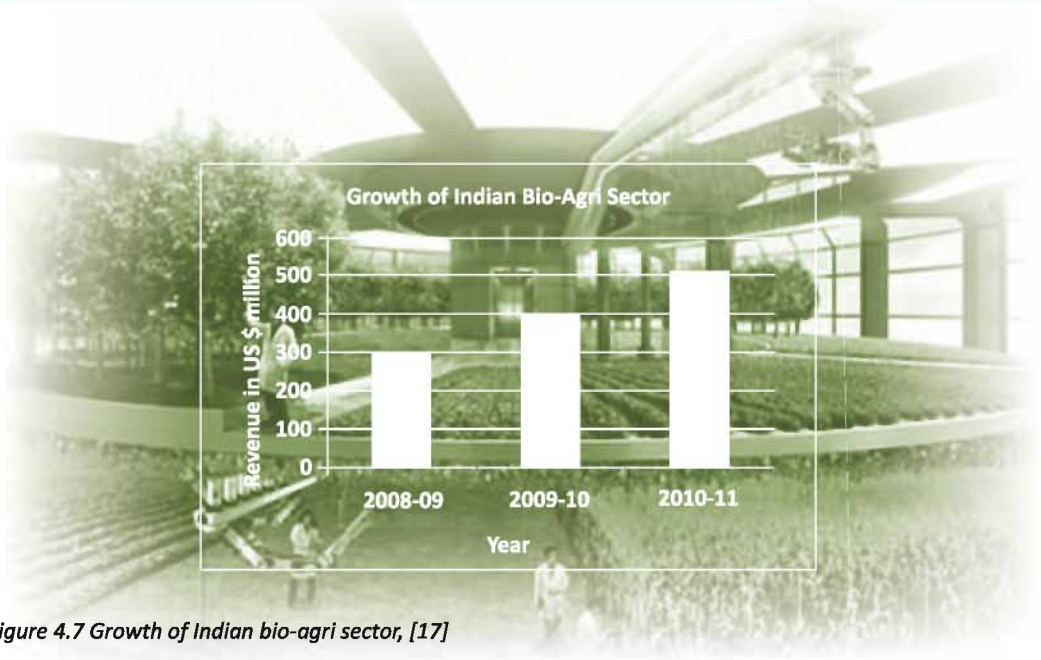


Figure 4.7 Growth of Indian bio-agri sector, [17]

The bio-agri sector has a mix of both multinationals such as Monsanto as well as Indian players. The leading players in this sector are Nuziveedu Seeds, Rasi Seeds, Mahyco, Metahelix, Ankur Seeds, Advanta, JK Agrigenetics, DuPont and Krishidhan Seeds to name a few. Currently, agricultural companies are among the fastest growing enterpirses in India, with companies like Ankur Seeds having a record revenue growth of 197 percent in 2010-11 compared to the previous fiscal year (Figure 4.8, [17]).

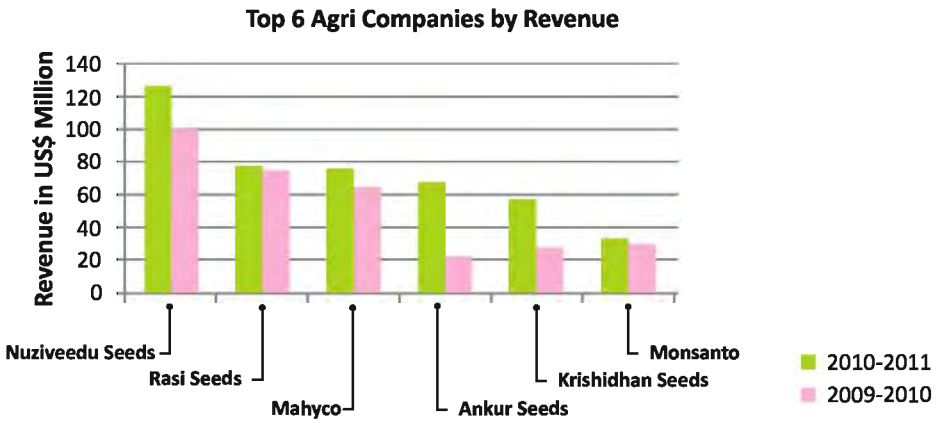


Figure 4.8 Top Indian agricultural companies by revenue, [17]

The Bt cotton has been a success story in India. Starting from 2002, when Bt cotton was introduced for the first time in India, it has continued to grow exponentially. Now Bt cotton acreage is close to 90% of all cotton cultivation (12 million Ha) and yields have increased substantially, while pesticide application has reduced by 50% [17].

Firms such as Metahelix have developed two versions of Bt cotton with its proprietary cry1C and cry1Ac based genes for Spodoptera and Bollworm control respectively. They are developing a combination of cry1C and cry1Ac as a stack. These products currently are in the process of regulatory approval as biosafety studies for Cry1C protein were completed and the event was found to be safe [18].

Indian contributions to the R&D sector in this space include multinational seed companies like Advanta India, which develops molecular marker technology and other biotech methods to enhance seed traits for agricultural crops such as sunflower, rice and tomatoes among several others [19]. JK Agrigenetics Ltd. has also contributed to this sector by collaborating with several national and international institutes, as well as agricultural universities to share agricultural technologies. JK Agrigenetics have successfully enhanced the yield and quality of crops such as pearl millet, sorghum and cotton [20].

Some of the major developments in this space, such as improvements in soil metagenomics, conservation of biodiversity and resolving productivity challenges are discussed in the following segments.

4.2.2 Addressing Productivity Challenges

As stated earlier, one of the primary challenges faced by the agri-biotech sector in India today is increasing agricultural productivity. The two primary methods of resolving this challenge is via hybrid technology and through reducing losses through environmental and pesticide stresses via MAS and genetic engineering techniques.

India has released MAS derived products, such as Samba Masuri and Pusa Basmati 1 that possess bacterial blight resistance and Swarna Sub-1 that tolerates submergence

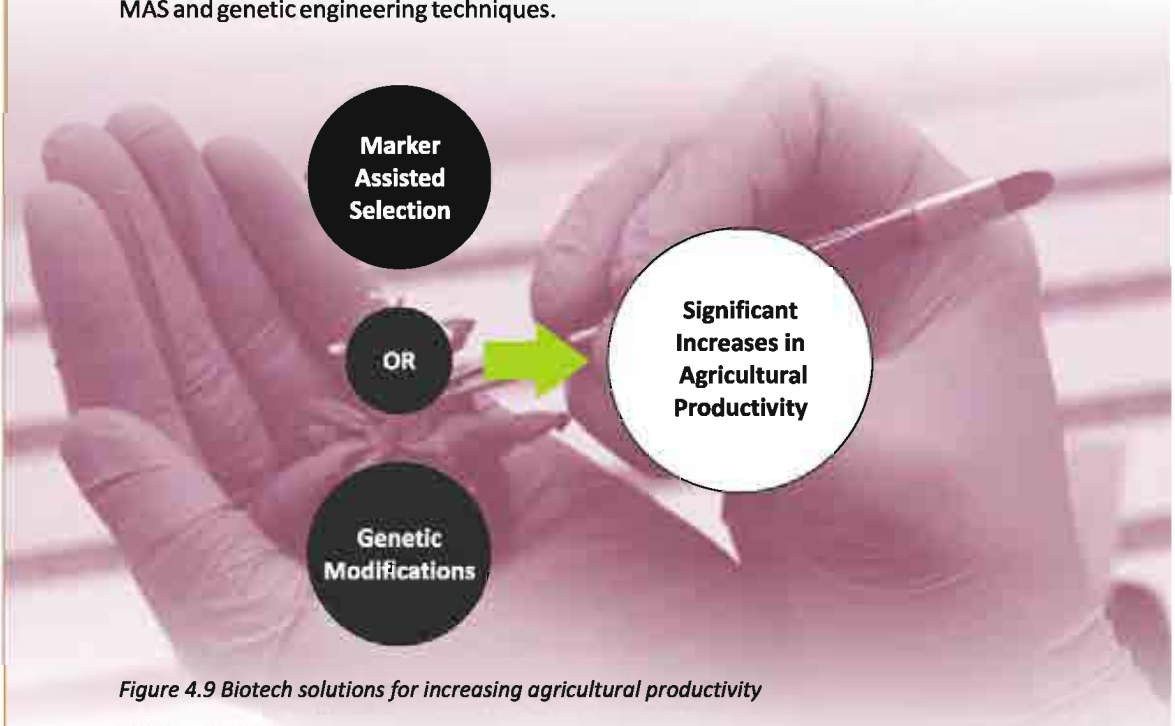


Figure 4.9 Biotech solutions for increasing agricultural productivity

MAS is now used widely to improve crop varieties especially endowing existing varieties with traits that help them to be resistant against diseases as well as become more productive by with standing environmental stresses such as salinity, water logging, drought and other stresses.

India has released MAS derived products such as Samba Masuri and Pusa Basmati 1 that possess bacterial blight resistance and Swarna Sub-1 that could tolerate submergence [16]. As mentioned before, GM crops deliver several benefits and Indian farmers have already derived benefits from Bt cotton. Currently 54 events developed by private and public organizations are undergoing testing. Crops that are currently under field trials are cotton, rice, potato, sorghum, sugarcane, castor, chickpea and tomato. In 2010, GEAC gave approval to the National Research Centre for Plant Biotechnology (NRCPB) for confined field trials to analyse the effect of Azotobacter mutant strains on wheat especially on yield, protein content and biomass as parameters. Similarly the Indian Institute for Horticultural Research (IIHR), Bangalore was allowed by GEAC to conduct event selection trials on five transgenic crops, some of which are: watermelon (resistant to watermelon

bud Necrosis virus), tomato (resistant to tomato leaf curl virus) and papaya [21]. In the same year, GEAC also had given permission to conduct Biosafety Research level (BRL-1) second field trials on two transgenic corn hybrids by Monsanto, India as well as permission to DuPont India to conduct event selection of transgenic hybrid rice and to the Sugarcane Breeding Institute (of ICAR) to conduct event selection for borer resistance on sugarcane. Further, GEAC had also given permission to conduct field trials on genetically modified potato resistant to potato virus to Indian Agricultural Research Institute (IARI) [21]. Public institutions such as ICAR have established a research consortium involving IIT Kanpur, Indian Institute of Pulses Research and IARI to study plant-nematode interaction using RNAi technology.

4.2.3 Soil Metagenomics

Soil metagenomics essentially involves the analysis of a mixture of microbial genomes isolated from a soil sample in a particular environment. This technique also enables the study of microbial species that cannot usually be studied under standard laboratory culture techniques and provides insights into the biodiversity of the environment. Such studies can facilitate the mapping of the soil metagenome to crop productivity, thereby increasing their yield without extensive utilization of pesticides and chemical fertilizers.

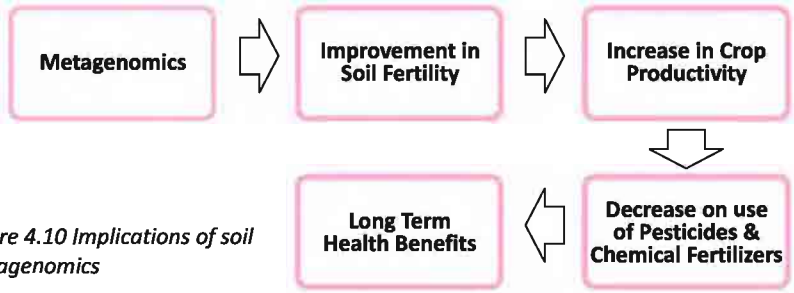


Figure 4.10 Implications of soil metagenomics

With food grain production decreasing in 2011-12 by 25% as against the previous financial year [7], it has become increasingly essential to adopt alternative methods such as soil metagenomics to increase agricultural productivity. Moreover, metagenomics studies can also improve the nutritional benefits of food crops; which have a long standing positive impact on public health (Figure 4.10).

ICAR National Fund for Basic, Strategic and Frontier Application Research in Agriculture had initiated a programme to study the dynamics of soil microflora with participation from IARI, GB Pant University of Agriculture and Technology and Tamilnadu Agricultural University.

Biotechnological advancements can also have a significant impact on protecting the biodiversity of the environment. Some of the aspects regarding biodiversity conservation through biotechnology are discussed in the following segments.

4.2.4 Biodiversity Conservation through Biotechnology

Biotechnological advancements can not only be effectively used to provide insights into environmental biodiversity, but also can play an important role in conserving it. Moreover, with the growing food demand across the nation, it is essential to focus on increasing food productivity while maintaining its rich diversity across different segments. Diligent use of biotechnological methods can aid the achievement of both these goals simultaneously.

In this context, an interesting biodiversity conservation model has been developed by M S Swaminathan Research Foundation called the '4C Model' that addresses conservation, cultivation, consumption and commerce requirements for crop plants. This method aids the preservation of biodiversity among local crops through the utilization of Gene-Seed-Grain Banks that help scientific selection and preservation of good seeds from several local landraces [22].

Molecular and genetic analysis of plants will also help provide deeper insights in to the bio-diversity of the environment. For instance, the Neem plant genome that was sequenced by Ganit Labs in 2011 will enable the understanding of plant bio-diversity at the molecular level [23]. Similarly, the pigeonpea sequenced by the joint efforts of National Research Centre on Plant Biotechnology (ICAR), Banaras Hindu University, Indian Institute of Pulse Research (ICAR), University of Agricultural Sciences Dharwad and ICRISAT, Hyderabad will also provide valuable insights regarding plant biodiversity [16].

Biotechnology has helped agricultural scientists by providing extensive knowledge about genetic diversity. Currently, there is an increased focus towards the preservation of local crop varieties. Thus, despite the emergence of transgenic crop varieties, the increasing demand for local crops and the growing seed banks that help to store different seed varieties are predicted to positively impact agricultural biodiversity.

4.3 Recommendations

The bio-agri sector will hold a key role in the transformation of India into a bio-economy since this is the sector that will provide solutions to several challenges that India faces currently.

The Neem plant genome that was sequenced by Ganit Labs in 2011 will enable the understanding of plant bio-diversity at the molecular level

Technology infusion will be a key determinant in making this sector dynamic by improving productivity of the sector. However, several bottlenecks need immediate attention such that an innovative sector can be built for the future.

4.3.1 Educate the Public on Benefits of GM Crops

The country has benefitted immensely with the introduction of Bt cotton in the last decade. The benefits of this technology have to be leveraged to boost the productivity of food crops like rice and maize. However, there are still unfounded fears among sections of the public, stoked by deliberate misinformation campaigns, which are standing in the way of technology development and commercial deployment. Major efforts are needed to educate the public about the benefits of GM crops and about the myths propagated by activists, to change public perception regarding cultivation and consumption of GM crops. This should be done by ICAR and DBT on a massive scale through TV, newspapers and other media of mass communication.

Biosafety regulations need to be simplified, particularly in areas, where we have sufficient evidence that no risks are present.

4.3.2 Regulatory Reforms Based on Scientific Data

GM crops regulation in India is riddled with uncertainties leading to considerable delays and wastage of precious resources and time of the applicant. This is not so much for want of a proper system, but because of the desultory implementation of the existing system. There is a serious credibility crisis stemming from the lack of consistency in its positions, and the frequent and open disagreements between the scientists, bureaucrats and politicians, who are associated with the system. Decisions are not always based on scientific convictions, but tend to get swayed by misleading propaganda.

The lack of harmonization between the policies of the Centre and the different states only adds to the problem. Some of the recent ad hoc decisions have added to the crisis by smudging the clear delineation of authority between the various statutory bodies. The system, in its implementation, needs a thorough overhaul. A competent committee which includes representatives from the National Agricultural Research System, relevant private sector scientists, officials from the different

stakeholder ministries, and other representatives should be immediately constituted and vested with the task of making specific operational recommendations within a 6-month time-frame. The goals of this exercise should be to restore credibility of the system by laying out principles/guidelines for science-based decision making; prescribing appropriate qualifications and experience for the decision making personnel; fix response times and detail processes to improve transparency and efficiencies in terms of time and money; delineate clear-cut authority between the different bodies in the system; and create appropriate mechanisms to harmonize GM Crop policies between the States and Centre, irrespective of differences in ideologies and political dispensations.

GOI should pass the Biotechnology Regulatory Authority of India Bill soon which will harmonize many regulations across India and provide a single window system.

4.3.3 Promote Large Scale Practice of MAS in Both Public and Private Sector

Marker Assisted Selection (MAS) has already been used for the production of improved cultivars of rice (Improved Pusa Basmati-1 & Improved Sambha Mahsuri by pyramiding genes for Bacterial Blight and Swarna Sub1A for submergence tolerance), hybrid maize (Vivek-QPM9 for quality protein maize) and hybrid pearl-millet (HHB-67-2) through the efforts of the public sector. There may also be success stories about MAS from the private sector, which are not widely known. However, MAS is not being widely practiced on a large-scale either in the public sector or in the private sector due to the following reasons, which need to be addressed immediately to realize India's Vision 2025 for crop productivity.

DBT should think of introducing a nationwide mechanism for mentoring plant breeders in the use of MAS in a large scale, so that MAS becomes an integral part of conventional plant breeding

(1) Crop-wise traits need to be identified, where marker technology can prove useful in improving crop productivity. These traits should include tolerance against biotic (a variety of fungal, bacterial and viral diseases) and abiotic stresses (drought, heat, salinity, alkalinity, freezing, submergence/flooding, etc.). Robust markers need to be developed for these traits and be deployed for MAS on a large-scale for improvement of crop productivity. Pyramiding of genes for resistance against each important crop-specific disease is also an important area, where MAS can be used. Synergy of traits for crop productivity and strategic breeding involving several synergistic traits (the so-called physiological breeding) should also be taken into consideration. Connectivity with a number of other countries may also help in achieving what we want to achieve in this area.

(2) Although enormous funding for research projects involving development of markers for specific traits (study of marker-trait associations = MAT) and MAS has been provided by ICAR and DBT, the projects involving MAS are not being taken up so far in a mission-mode, so that the agencies like ICAR and DBT have been functioning as mere funding agencies and not as mission agencies. For instance, ICAR provided funds through 5 year network projects, and DBT kept on providing funds for MAT and MAS through its various task forces (e.g. Agriculture & Plant Biotechnology), but no mission-mode approach has been followed. Only recently, DBT took an initiative for a mission-mode approach by establishing a new Task Force named "Accelerated Crop Improvement Programme" (ACIP), under which nine projects (including some mega-network projects in wheat and rice) amounting to about US $5.21 million were sanctioned in Phase I [projects have been shortlisted for Phase II].

There is an urgent need for providing guidance at site to the plant breeders, who want to adopt the new technology of MAS, as a component of conventional plant breeding. DBT should think of introducing a nation-wide mechanism for mentoring plant breeders in the use of MAS in a large scale, so that MAS becomes an integral part of conventional plant breeding. This activity is an extension of activity at the level of the laboratory.

4.3.4 Use Platform Technologies to Analyze and Characterize Indian Bio-Diversity and Promote Industrial Applications

The GOI should promote large scale projects that characterize and analyze Indian bio diversity such as large scale soil metagenomics projects through use of modern platform technologies such as next-generation-sequencing. For example, biodiversity of soil in Western and Eastern Ghats, Gangetic Plain, Himalayan ecosystem and other ecosystems should be characterized to identify unique microorganisms and plant and animal species that might turn out to be economically beneficial by helping scientists to improve crop yields. India has several unique soil ecosystems that have been used to grow several crops over several millennia. These soil systems should be studied and analyzed, for example, cyanobacterial diversity of different crop growing regions should be conducted.

4.3.5 Provide Subsidies to Farmers for Adoption of New Technologies

Affordability of the new technologies has to be promoted by increasing the efficiencies in its development and deployment. By increasing the predictability of the regulatory system, by making it time-bound, and by cutting out unnecessary steps/studies which do not add any value, the cost of technology development and commercialization can be significantly reduced. This combined with free market policies that encourage fair competition, the price of new technology products in agriculture can be moderated, while at the same time choices to the farmer increased. Furthermore, the Government could provide subsidies for proven biotech products.

4.3.6 Promote Public-Private Partnership for Marketing Agri-Biotech Products

There are a number of public institutions where the Government is spending considerable amounts on research on crop biotechnology. The chances of these investments resulting in commercially viable products would be much more if meaningful collaborations can be forged between the public institutions and the Industry at an early stage of development. Involvement of private sector scientists and industry captains in various decision making bodies of the Government would be a step in the right direction.

4.4 References

1. Beddington, J (2010) Food security: contributions from science to a new greener revolution, Philosophical Transactions of The Royal Society B, 365, 61-71
2. Sharma P & Gulati A (2012) Approaches to Food Security in Brazil, China, India, Malaysia, Mexico and Nigeria: Lessons for Developing Countries. ICRIER Policy Series
3. Beddington J (2009) Food, energy, Water and the cliate: A perfect storm of global events. Government Office of Science, UK http://www.bis.gov.uk/assets/goscience/docs/p/perfect-storm-paper.pdf
4. http://www.sciencedaily.com/releases/2011/11/111121194043.htm
5. http://www.grida.no/graphicslib/detail/potential-for-cropland-expansion_1178
6. Global Forest resources Assessment 2010. FAO;
http://www.pefc.org/images/stories/documents/external/KeyFindings-en.pdf
7. Inderscience Publishers (2011, September 19). The benefits of biotech to agriculture. ScienceDaily. (http://www.sciencedaily.com/releases/2011/09/110919131612.htm)
8. http://www.ctahr.hawaii.edu/oc/freepubs/pdf/BIO-3.pdf
9. Juma C (2012) Technological Abundance for Global Agriculture: The Role of Biotechnology. Faculty Research Working Paper Series. Harvard Kennedy School
10. http://isaaa.org/resources/publications/pocketk/19/default.asp
11. ftp://ftp.fao.org/docrep/fao/010/a1120e/a1120e.pdf
12. Marker Assisted Selection, FAO 2009.
13. James, Clive. 2011. Global Status of Commercialized Biotech/GM Crops: 2011. ISAAA Brief No. 43. ISAAA: Ithaca, NY
14. Move to allow EU ban on GM crops. Financial Times, UK,, June 4th 2010
15. An End of GM crop development for Europe. Financial Times, UK, January 12 2012.
http://www.ft.com/cms/s/2/6e074ee4-403e-11e1-82f6-00144feab49a.html#axzz1ur8lEPou
16. The State of the Indian Agriculture 2010-2011. Report to the Parliament, Ministry of Agriculture.
17. ABLE-BioSpectrum Survey, Volume 9, Issue 6, June 2011
18. http://www.meta-helix.com/main/pbt_cotton.html
19. http://www.advantaindia.com/rnd.php
20. http://www.jkseeds.net/display.asp?ch=24
21. GEAC Approves 17 Bt crops for trials. Biospectrum. June 22 2010.
http://biospectrumindia.ciol.com/content/BioSpecial/11006221.asp
22. http://www.mssrf.org/bd/bd-wayanad-cabc.html
23. http://www.strandls.com/viewnews.php?param=5&param1=68

5 Bio-Industrial: The Future is Green

The bio-industrial sector mainly comprises of enzymes that have multiple industrial use, generation of bio-energy through sources such as biomass and bio-fuels as well as bioremediation techniques (Figure 5.1).

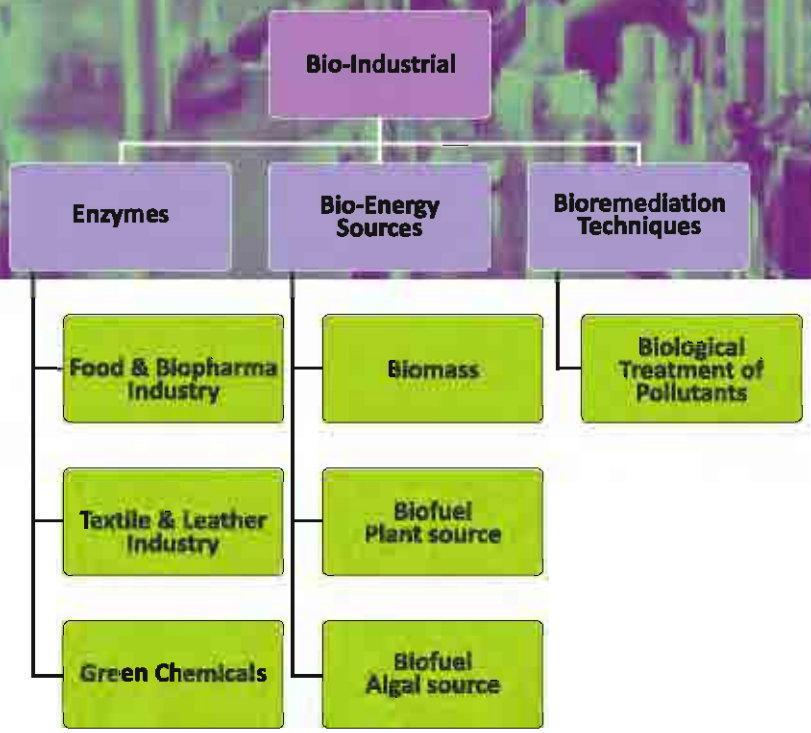


Figure 5.1 An overview of the bio-industrial segments

Enzymes are used in different industrial processes, be it in biopharmaceutical, food and nutrition, textile, leather and Green Chemicals i.e polymers derived using bio-based enzymes (Green Chemistry).

5.1 Global Enzyme Scenario

The global markets in this space are dominated by Western Europe, USA and Canada. The developing countries in Asia, Eastern Europe and the Middle-East are emerging destinations as markets as well as in R&D.

The global enzyme market is expected to touch US $3.74 billion with demand staying stable across mature economies while showing rapid growth in emerging markets in Asia Pacific and Eastern Europe [1]. The growth will be fuelled by rising demand for diagnostic enzymes and pharmaceutical enzymes, the animal feed industry and for production of biofuels.

Europe remains the largest region for industrial enzymes, followed by the USA [1]. The Food and feed industry represent the largest end user segment followed by detergents in the global industrial enzyme market. Global enzyme majors are Novozymes, AB Enzyme GmbH, Verenium Corp., Asahi Kasei, Advanced Enzyme Technologies, Genencor International Inc., NEXGEN Biotechnologies and DSM Food Specialities among several others [1].

The trend in the enzyme sector is a rise in investments in the manufacturing of the cellulosic enzymes especially for biofuels production. For instance in 2011, Genencor launched Accellerase® TRIO, a novel enzyme product that will enable affordable manufacture of cellulosic ethanol from varied sources of renewable non-food feedstock like wheat, straw, switchgrass, corn stover and municipal solid waste [2]. Similarly, Novozymes also launched Cellic® CTec3, another enzymatic product that facilitates the production of advanced bio-fuels from biomass [3]. Continuing this pattern, Royal DSM, and POET, LLC, collaborated to market cellulosic bio-ethanol, thus paving the way for the development of this next-generation biofuel [4].

5.1.1 The Global Food, Fuel and Energy Challenge

As previously mentioned in this report the world population is predicted to touch 9 billion by 2050, which is a 34% increase from 2010 levels. Most of this population growth will occur in the developing countries. The average calorie intake of the world population is increasing along with increasing energy usage (Figures 5.2, 5.3). In the developing countries, energy usage is set to increase by 84% by 2035 [5]. These statistics highlight the seriousness of the challenge in the food and fuel sector that the world will encounter in future.

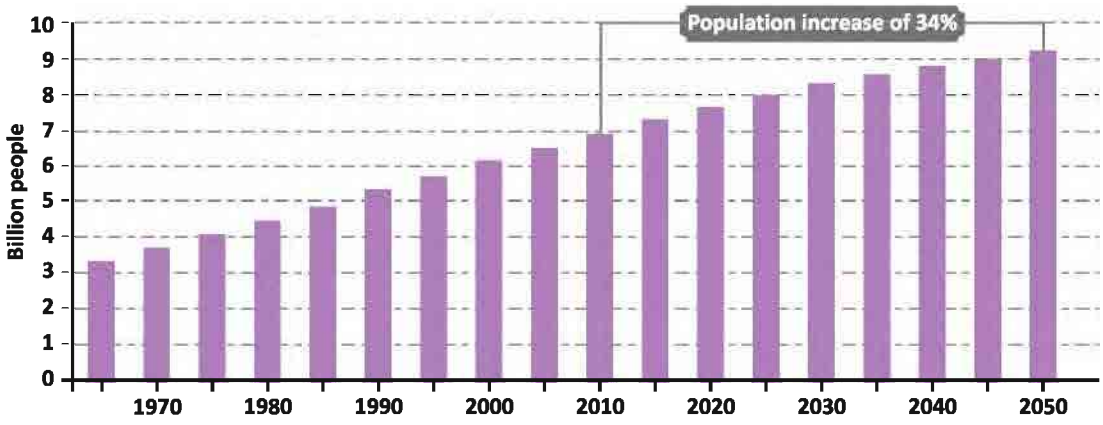


Figure 5.2 The predicted growth of world population [5]

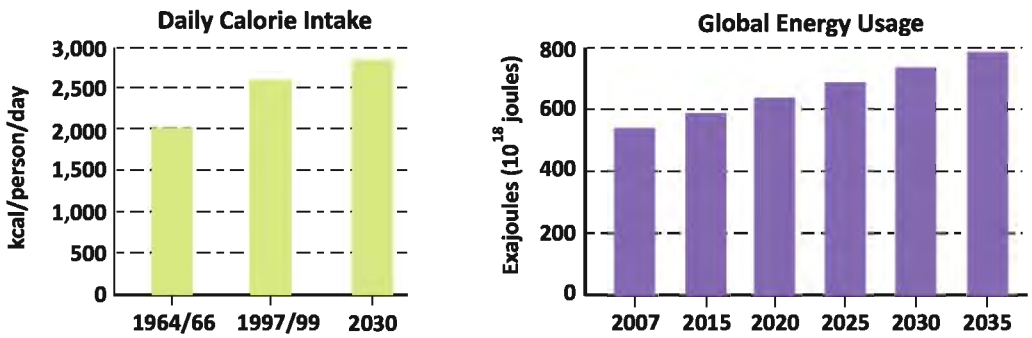


Figure 5.3 Increase in average global daily intake of calories and energy usage [5]

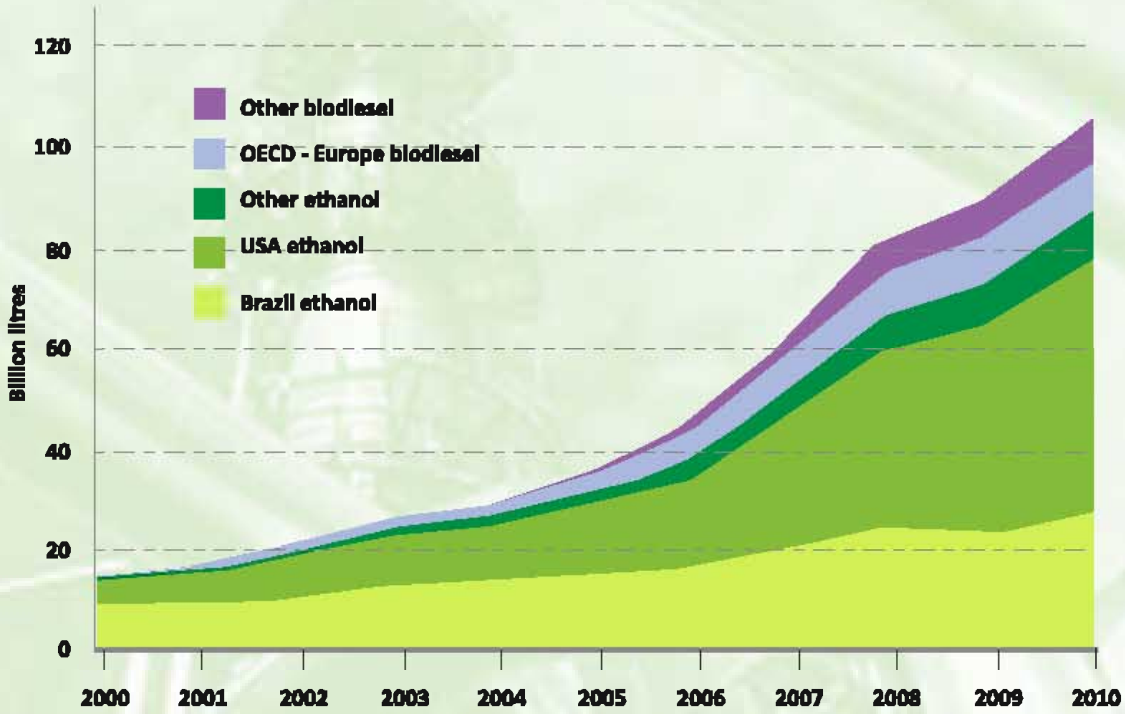


Figure 5.4 Global biofuel production in 2010 [6]

Each variety of biofuel has different land area demands. This has initiated the classic debate about food crops versus biofuels as growth in biofuels would either come from using food crop lands, acquiring new land through deforestation or using existing fallow land.

According to a Nature article by Peter Fairley, the global biofuel (both ethanol and bio-diesel) production was 100 billion litres in 2010 with the USA and Brazil being the top two producers (Figure 5.4, [6]). Each variety of biofuel, has different land area demands (Figure 5.5, [6]). This has initiated the classic debate about food crops versus biofuel as growth in biofuels would either come from using food crop lands, acquiring new land through deforestation or using existing fallow land. The land use patterns for biofuels will also influence fluctuations in food prices. [6]

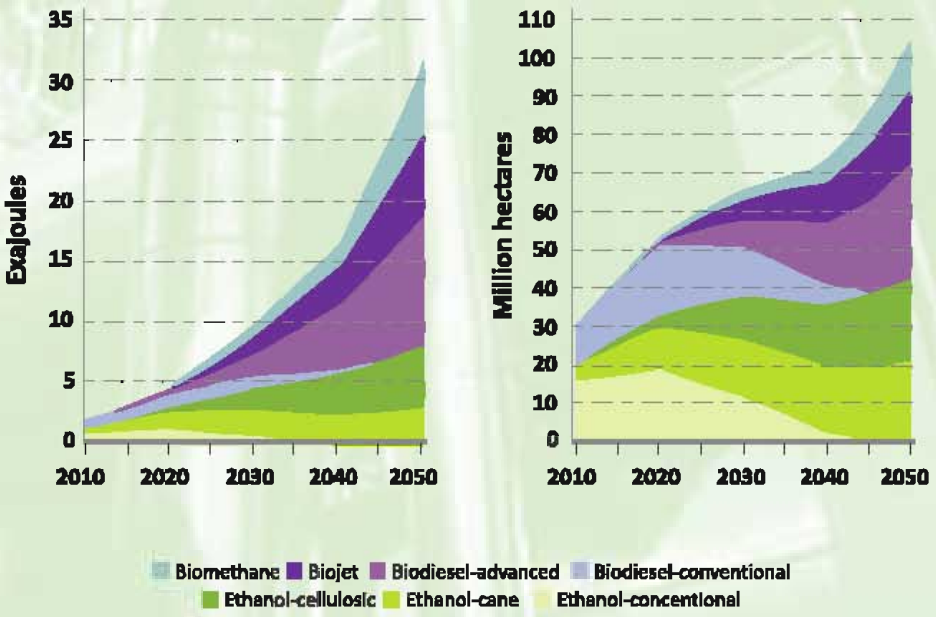


Figure 5.5 Demand for biofuels (left) and resulting land demand (right) [6]

Consequently, this has led to focus on second generation biofuels and increasing productivity by making processes for biofuels production more efficient, scouting for new plant material as an efficient feedstock as well as finding plant species that can be grown in wasteland and fallow land [4, 5, 6].

Bio-energy and biofuel are gaining increased acceptance and popularity across the world and have immense potential as leading alternative resources in the future.

5.1.2 Setting Targets & Providing Subsidies for the Growth of Renewable Bio-Energy: A Global Perspective

Several nations have used targets, subsidies and tariffs to boost the renewable fuels markets, especially biofuels. In May 2011, the International Energy Agency (IEA) produced a roadmap that recommended that the use of biofuel should increase from 2% of global transport fuel in 2011 to 27% by the year 2050 [6]. The IEA report also states that biofuels, if produced sustainably, could replace enough petroleum to reduce 2.1 giga-tonnes of carbon dioxide emissions each year [6].

The USA and the European Union

Biomass fuels supplied around 4% of the total energy used in the USA in 2011 [7]. Of the alternative sources of energy, around 50% of this biomass energy was produced by incinerating wood and other wood products, 40% was from biofuels and the remaining 10% from municipal garbage waste with biological origins [8]. The USA by far leads globally in providing tax benefits to renewable energy with subsidies for biofuels amounting to US $7 billion each year compared to US $5 billion from the European Union. The Renewable Fuel Standard by the US Environmental Protection Agency (EPA) has set long term targets that aim to quadruple biofuel use to 36 billion gallons by 2022 [9]. Similarly, the European Union's 2009 Renewable Energy Directive has set a 10% renewable target for transport energy by 2020 [6].

Several nations have used targets, subsidies and tariffs to boost the renewable fuel markets, especially biofuels.

Brazil

Brazil is the second largest producer of biofuels after the USA. Its national scheme called "National Alcohol Program" was envisioned and launched during the oil crisis of the 1970s [10]. The government increased the blending mandate from 5% to 25% in transport vehicles especially in flex fuel vehicles (FFVs). Since its launch, Brazil, besides becoming the second largest producer of biofuels, has also made US $100 billion in foreign exchange savings and accrued other benefits such as an estimated reduction of greenhouse gases (between 1975 and 2005) in the order of 570 million tons [10]. The success of the Brazilian biofuels sector is the outcome of several successful government incentive schemes. These incentives include setting a guaranteed procurement price for ethanol, a 5% tax subsidy on FFVs (thus increasing the sales of these vehicles), capital subsidies, retaining government control over ethanol stocks to guarantee supply and making the sale of ethanol mandatory at all fuel pumps, thereby increasing access [10]. Based on these policy initiatives Brazil had built 400 ethanol production plants by 2008 [10].

China

China is the world's third largest producer of bioethanol and has a 10% ethanol blending target for 2020. It provides various incentives such as US $2 billion in subsidies to renewable energy as well as R&D support and low interest loans [9].

5.1.3 Industrial Biotechnology R&D for Advanced Research: Establishing Collaborative Institutions for Renewable Bio-Energy

The USA government's Department of Energy has established three research institutes to focus on R&D in bioenergy development and translation into viable products to reduce energy dependency on petro-oil [11]. These centres are:

- The Joint BioEenergy Institute (JBEI) at Emeryville, California, which is led by Lawrence Berkeley Science Laboratory.
- The BioEnergy Science Center (BESC), which is led by Oak Ridge National Laboratory in Oak Ridge, Tennessee.
- The Great Lakes Bioenergy Research Center, which is led by the University of Wisconsin.

The final goal for establishing these centres is not only to understand biological mechanisms for biofuel production but to develop and use them to produce advanced biofuels in mass scale. These centres have many partners, including several industry partners [11]. For example, JBEI has Amyris, Boeing, BP, DuPont, GM, Novozymes and LS9 as its industry partners [12].

Similarly the Energy Biosciences Institute at University of Berkeley is funded by British Petroleum (BP). The USA's national funding agencies such as the National Science Foundation (NSF) has a "catalysis and biocatalysis programme" that fosters research and development on biomass conversion into fuels.

In the USA and Europe several innovative firms and research organizations are focussed on R&D in advanced biofuels by using novel methods of synthetic biology as well as green chemistry

In the USA and Europe several innovative firms and research organizations are focussed on R&D in advanced biofuels by using novel methods of synthetic biology as well as green chemistry. Current strategies include finding efficient methods for production of cellulosic ethanol, biodiesel and butanol from diverse sources such as agriculture, forestry and algal feedstocks.

Some of the firms in this area are Amyris, Dyadic and Iogen. Amyris, located in Emeryville, USA, uses a synthetic biology platform to re-engineer strains of yeast and other organisms to convert sugarcane as feedstock for biofuel generation.

Dyadic, based in Florida, has developed a modified fungus that can digest lignocelluloses [13]. Wood is also a historical source for bioenergy through incineration, however scientists at the University of California have studied 47 varieties of poplar tree to find out species that are more amenable for extraction of sugars from lignin and hence be a biofuel feed stock [5, 13]. Iogen, a synthetic biology firm that is partly owned by Shell, has developed an enzyme from the fungus Trichoderma reesei (jungle rot) to extract nutrients from trees by digesting lignin. Other feed stocks such as switch-grass (Panicum virgatum) and perennial grass (Micanthus) are being explored because these use less water and store nutrients in their roots [5]. Other interesting projects for using wood as a feed stock has led scientists in York, UK to understand the mechanism through which marine crustacean wood borer Linmoria quadripunctata (known as gribble) dissolves wood in its gut through different mixtures of cellulases [13].

Firms and organizations are also exploring ways to manipulate algae (both micro and macro algae) to produce biofuels. In the USA, the Department of Energy has created a research consortium to advance biofuels production through algal feed stocks [14]. It is estimated that algae could yield 61,000 litres of biofuels compared to the yield value of 400 litres from crops such as soya and canola [14]. There are several other advantages of algae as they can be grown in artificial ponds and lakes (that are unsuitable for agriculture) or in closed photobioreactors. They do also have some disadvantages like the need for fresh water resources (in case of freshwater algae) and the need to be located near an artificial carbon dioxide source (such as coal fired power plants) to rapidly fix carbon dioxide [14].

Large firms, such as Boeing and Exxon Mobil have also initiated R&D projects to seek better varieties of algae as a source for biofuels production. Boeing for example has established the Algal Biomass Organisation to foster algal derived jet fuel, while Exxon Mobil has invested US $300 million in a project partnering with Synthetic Genomics at California to produce oil from algal sources [14].

Sapphire Energy has developed what it calls a "green crude", or algae derived fuel, that it claims is more compatible with existing petroleum infrastructure than first and second generation biofuels, such as bioethanol, which is known to have corrosive properties and hence is difficult to transport via existing pipelines [14, 15].

Firms are circumventing many of the problems faced from first generation algal derived biofuels by manipulating the production process. For example Solazyme (a California based firm) does not allow algal cultures to have any sunlight and adds sugars, thereby forcing the cells to convert sugars directly into oil. The US Department of Defence has given a contract to Solazyme to supply close to 600,000 litres of algal derived fuel [14].

Different biofuels have different energy content and butanol is also being explored as a biofuels. Figure 5.6 gives the energy density of different biofuels and illustrates that butanol and iso-butanol have greater energy density than ethanol [16].

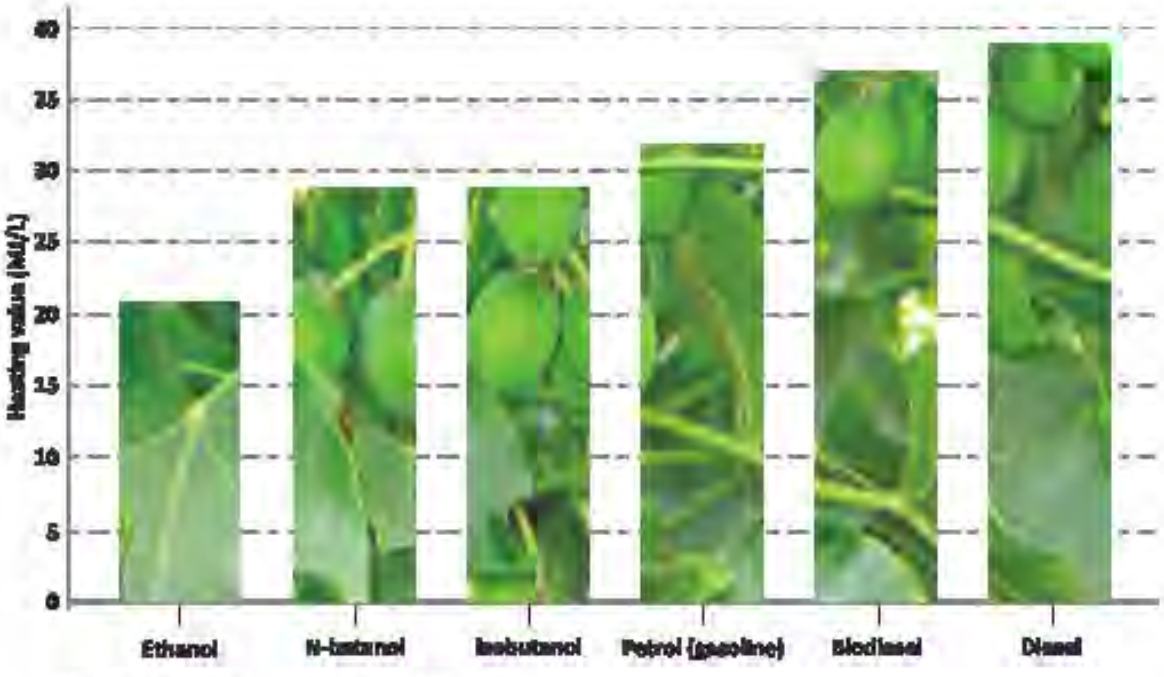


Figure 5.6 Energy density of different fuels [16].

Scientists are exploring ways to extract butanol or iso-butanol from engineered bacteria such as Closterdium, Treponema denticola and Ralstonia eutropha. Firms such as Green Biologics (UK) and Butamax Advanced Biofuels (a joint venture between BP and DuPont) are at various stages of setting up demonstration plants for butanol and iso-butanol production [16].

Firms such as LS9 and Joules Unlimited are exploring using Cyanobacteria as a feedstock for producing hydrocarbons instead of ethanol or butanol. LS9 is a synthetic bio-catalysis firm that uses several feedstocks to extract biofuels. It has identified genes in Cyanobacteria that can directly produce alkanes and has plans for commercial production [16].

Joules Unlimited, founded by leading synthetic biologist, George Church, has genetically modified Cyanobacteria that can generate complex hydrocarbons which are akin to petrochemicals [14]. The company has set up a pilot plant in Texas and reckons that its production processes will yield 140,000 litres per hectare per year [14].

Another technology that is being investigated is the derivation of biofuels through chemical means from plant matter. For example, gamma valectrone (GVL) is derived via chemical process, using sulphuric acid, from various kinds of plant matter (corn stover which is a post harvest leftover corn material, sawgrass and wood). GVL can be used as a blend with petrochemicals such as petrol and can be further processed to yield hydrocarbons [16].

The growth of the biofuels industry is going to continue in the next ten years as both public and private organisations focus on innovative synthetic biology and metabolic engineering methods to bring cost effective biofuels and contribute to global bio-based economies

Several bio-refineries are being built across the USA, Europe and Brazil. The Italian chemical firm Gruppo Mossi & Ghisolfi initiated a 50 million litre per year ethanol production unit at Turin, Italy and will use enzymes supplied by Novozymes to extract biofuels from straw feedstocks [6]. Similarly, Mascoma at New Hampshire, USA and Coskata at Illinois, USA have plans to build 150 million litres and 208 million litres of cellulosic ethanol plants, respectively [6]. BP too is building a 136 million litres capacity ethanol refinery with a US $400 million investment in the UK [5].

The growth of the biofuels industry is going to continue in the next ten years as both international public and private organizations focus on innovative synthetic biology and metabolic engineering methods to bring cost effective biofuels and contribute to global bio-based economies. Developing nations such as India can use this opportunity to capitalize and expand their industrial biotech sector and become a bio-economy.

5.1.4 Global Bioremediation

As advancements in the industrial biotechnology sector increase, there is a growing need to effectively treat industrial pollutants (heavy metals, chemical run offs) so that they do not pose a hazardous threat to the surrounding environment and eco-system. Thus, bio-remediation techniques are also emerging as focus areas in this space, as they provide eco-friendly alternatives for the degradation of toxic industrial wastes. Biosensor technologies can also effectively detect and measure industrial pollutants and are an important component of bioremediation strategies.

In Europe, for example, several lakes have been treated using methods such as cleaning, aeration and addition of microbial cultures to restore natural environmental conditions. Furthermore, as global trade increases and movement of crude oil gains pace, bioremediation techniques will be needed for oil spills and restore soil damaged by mining and extraction of minerals. Hence, bio-remediation techniques also have significant potential for future growth in this sector.

5.2 Indian Bio-Industrial Landscape

While the global market for industrial enzymes is valued at US $3.74 billion [1], India's contribution to this sector is not that significant. Hence, it needs to develop a rigorous growth strategy for the future.

The Indian bio-industrial segment, valued at US $130.4 million in FY 2010-2011, contributed 3.63% of the total revenue generated by the biotech industry in India. The sector is growing at a rate of 10.98% for 2010-2011 as compared to the previous year. The revenue growth of this sector in India in the past few years is shown in Figure 5.7 below. The industrial biotech sector is predicted to steadily rise at a compound and annual growth rate of 15% till 2015 [17].

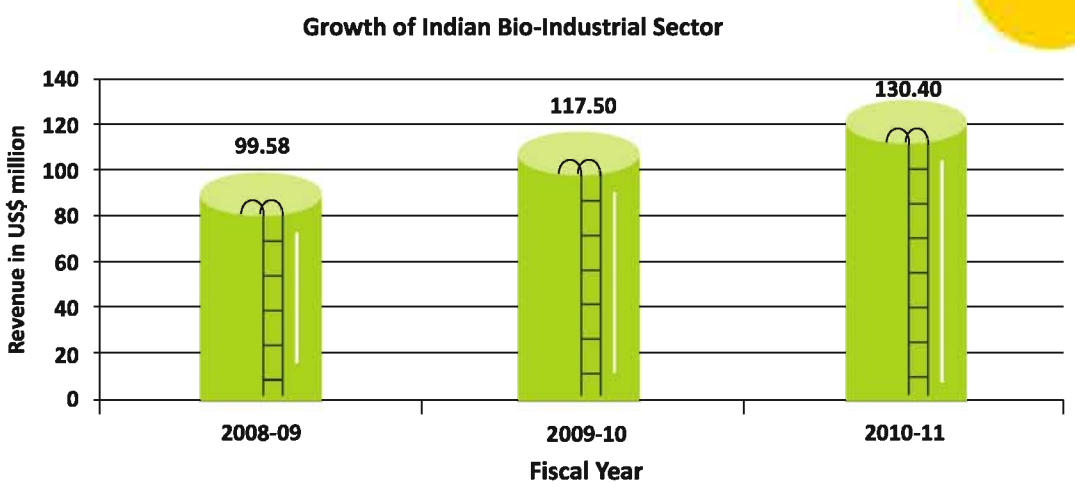


Figure 5.7 Growth of the Indian bio-industrial sector [17]

The key Indian players in this segment include Novozymes, contributing 50% of the total market share, followed by Advanced Enzymes, Rossari Biotech, Richcore, Zytex and Maps India. In this export-oriented industry, the major markets include US and Europe, China and other Asian countries (Figure 5.8, [17]).

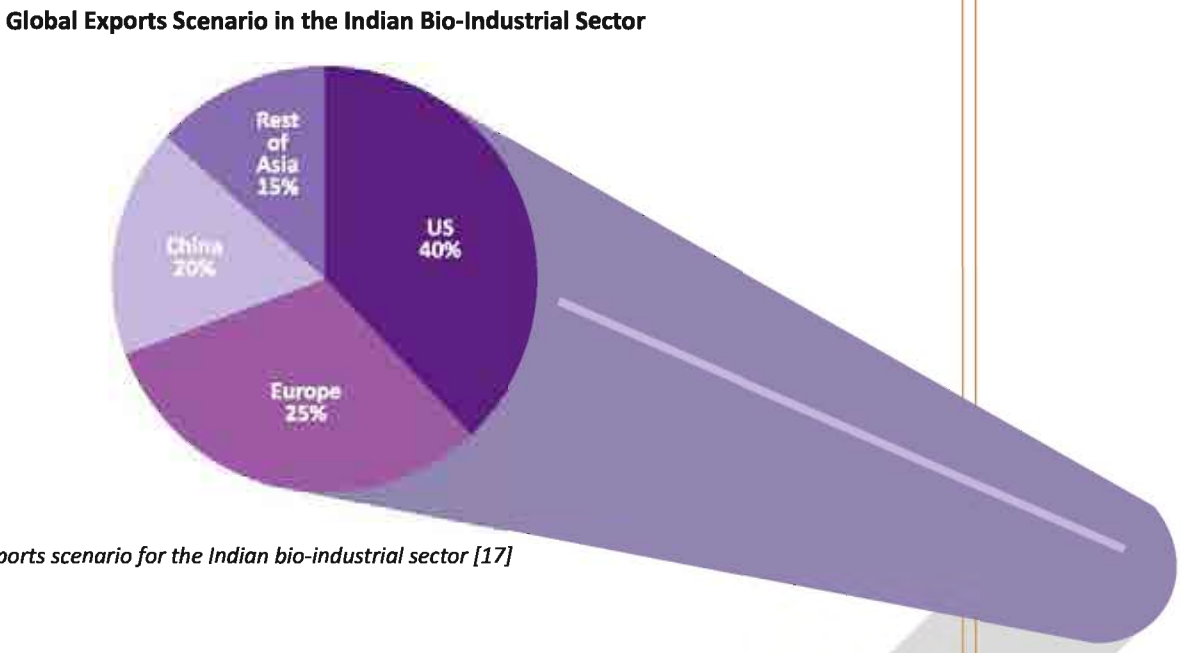


Figure 5.8 Global exports scenario for the Indian bio-industrial sector [17]

While multinational corporations dominate this industry in India, the emergence of new domestic players like Sea6 Energy is predicted to drive the future of this segment in India.

Developments in the Indian sub-sectors of the bio-industrial space are detailed in the following segments.

5.2.1 Enzymes

As the Indian middle class economy is rising steadily, there is a growing tendency towards increased spending on food, drugs, textiles and leather products, which is fueling the growth of this sector.

DBT is funding innovative projects in this sector, for example in 2011 MAPS Enzymes received funding through DBT's Small Business Innovation Research Initiative (SBIRI) for affordable production of Phytase enzyme [18]. This funding will enable the varied use of Phytase for dietary supplements, animal feeds and food processing purposes [18].

Novozymes, the biggest player in this sector is rapidly expanding its presence in India by developing the enzymes sector for the food, beverages and home-care market. They are primarily looking towards growing their research and business market for industrial enzymes in India [19].

As the enzymes industry is largely export-driven, more companies are capitalizing on opportunities abroad. For example, Advanced Enzymes established direct export in more than 59 countries across the globe and soon plan to set up their subsidiaries in European and Chinese markets [20].

Biotech companies in this space are also gradually shifting their focus towards the manufacture of cellulosic enzymes that aid the production of bio-fuels. Novozymes, for instance, are undertaking initiatives to utilize Indian bio-mass resources for the production of second generation bio-fuels such as bio-ethanol [21].

Praj Industries, based in Pune, focuses on providing a wide range of bio-industrial solutions from developing ligno-cellulosic ethanol technology to green chemistry programs. It has been operating one of the world's largest pilot plants since 2009 and has plans for establishing a 100 tonnes per day pilot plant. Similarly, Maps Enzymes partnered with the National Institute of Interdisciplinary Science & Technology (NIIST), Thiruvananthapuram, to manufacture two cellulosic enzymes, P Janthinellum and Beta Glucosidase, for biofuel production [23]. Adding to the advancements in this space, Reliance Life Sciences have also developed enzyme-based technology for the production of bio-butanol from biomass [24].

These developments in the biofuels sector have led to increased opportunities and paved the way for India to develop and utilize alternative energy resources for a sustainable bio-economy in the future. Some of the bio-energy initiatives are discussed in the following segment.

5.2.2 Bio-Energy Resources

Bio-energy in India could be derived from incinerating biomass from agricultural produce, agricultural waste, forestry products or from production of biofuels using agricultural products (sugarcane, sweet sorghum and sugar beet), jatropa plantation, neem forestry or algal resources.

India was the fourth largest energy consumer in 2009 and her demands in this space have been rising constantly. Coal and oil account for the major energy sources and renewable sources such as biomass and agricultural waste constitute 24% of the energy consumption in India (Figure 5.9, [25]).

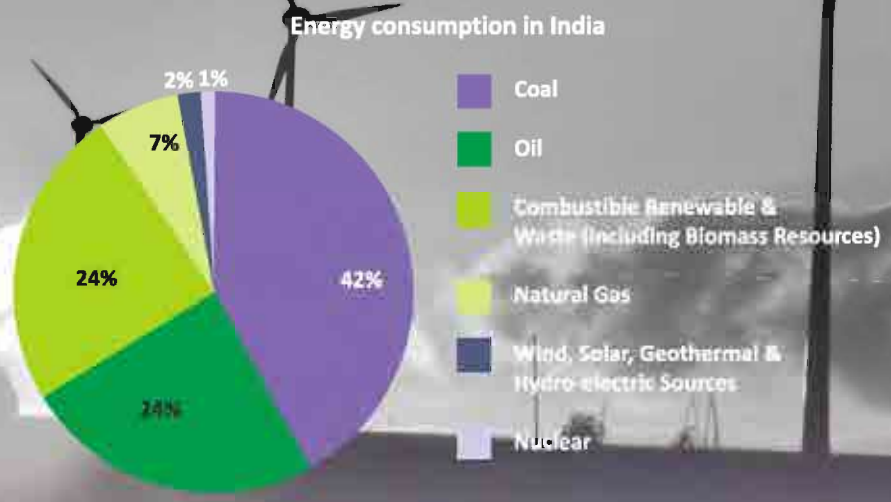


Figure 5.9 Energy consumption in India (2009), [25]

While coal, oil and gas dominate the Indian energy sector, biomass is still a prevalent energy resource in the rural parts of India. Hence, there are emerging initiatives to promote complete utilization of biomass re-sources in rural parts to efficiently meet their energy demands. For instance, the Biomass Energy for Rural India (BERI) Project is an US $8.62 million project sponsored by the Global Environment Facility (GEF) through the United Nations Development Programme (UNDP), India Canada Environment Facility (ICEF), Government of India and Government of Karnataka. This project is aimed at providing socio-economic and environmental benefits at both domestic as well as international levels [26].

Biomass can provide significant cost advantages for producing bio-energy as its capital cost per MW of energy ranges from US $1.04-1.25 million as against a cost of US $3.54-4.58 million for conventional resources [27]. India currently has a biomass excess of around 150 million tonnes that can generate 16 giga watts of power. Utilizing the potential in this space, India already has established 3,000 MW of biomass-based power generation capacities and the Ministry of New and Renewable Energy intends to increase this capacity two-fold during the 12th Five Year Plan [28].

Moreover, as India produces 300 million tons of sugarcane every year [29], bagasse could also be used to produce butanol on a large scale. The Energy Research Institute (TERI) and Bharat Petroleum have initiated a joint venture to produce bio-butanol from sugarcane biomass. This project has obtained the Biotechnology Industry Partnership Programme (BIPP) funding from the DBT [29]. Richcore Life Sciences also has several technologies for the production of sugar and bio-ethanol from bio-mass such as molasses [30].

Some of the other biofuel strategies are discussed in the following section.

5.2.3 Biofuel Strategies

In India oil consumption has always been higher than production (Figure 5.10, [31]).

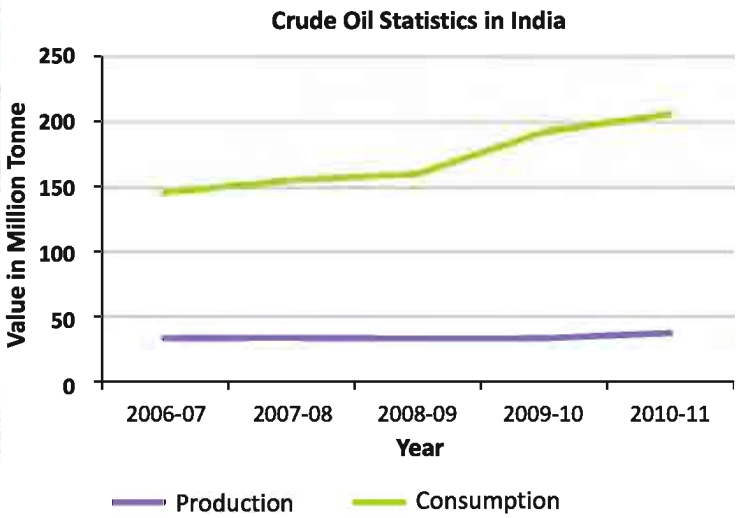


Figure 5.10 Crude oil statistics in India [31]

In order to meet the rising fuel demands and decrease import dependence, novel bio-fuel strategies are emerging as preferred alternatives.

Although the crude oil consumption in India has been rising to a great extent, the production levels have remained relatively flat, leading to an increased reliance on imports. Recent estimates indicate that around 34 percent of the financial budget is allotted to the import of petroleum [32].

In order to meet the rising fuel demands and decrease import dependence, novel bio-fuel strategies are emerging as preferred alternatives. Bio-fuels not only provide cost-effective alternatives, but are also eco-friendly and assist to reduce carbon-dioxide and green house gas emission levels in the atmosphere. The Indian "Biofuel Policy" aims to blend 20% of bio-fuels such as bio-ethanol and bio-diesel with petroleum by the year 2017.

While Brazil has been at the forefront of bio-ethanol production across the globe, India too can emerge as a strong competitor in this space as it is the leading producer of sugar and can use the molasses formed in sugar factories for the manufacture of bio-ethanol. However, infrastructural deficiencies and lack of manufacturing units prevent the large scale production of bio-fuels from molasses.

The GOI policy has been to enable the use of degraded wasteland for non-edible tree plantations such as Jatropa curcas and Pongamia pinnata [10]. According to the Wasteland Atlas of India 2005 the total wasteland in India is 55.37 million Ha out of a total land area of 328.7 million Ha [10]. Out of the 55.37 million ha, the total potential area for future cultivation is 32 million Ha. This estimate however does not take into account other issues such as climatic conditions of those waste lands, their accessibility and ownership [10]. The various types of wasteland in India with potential for cultivation are shown in Figure 5.11 [10].

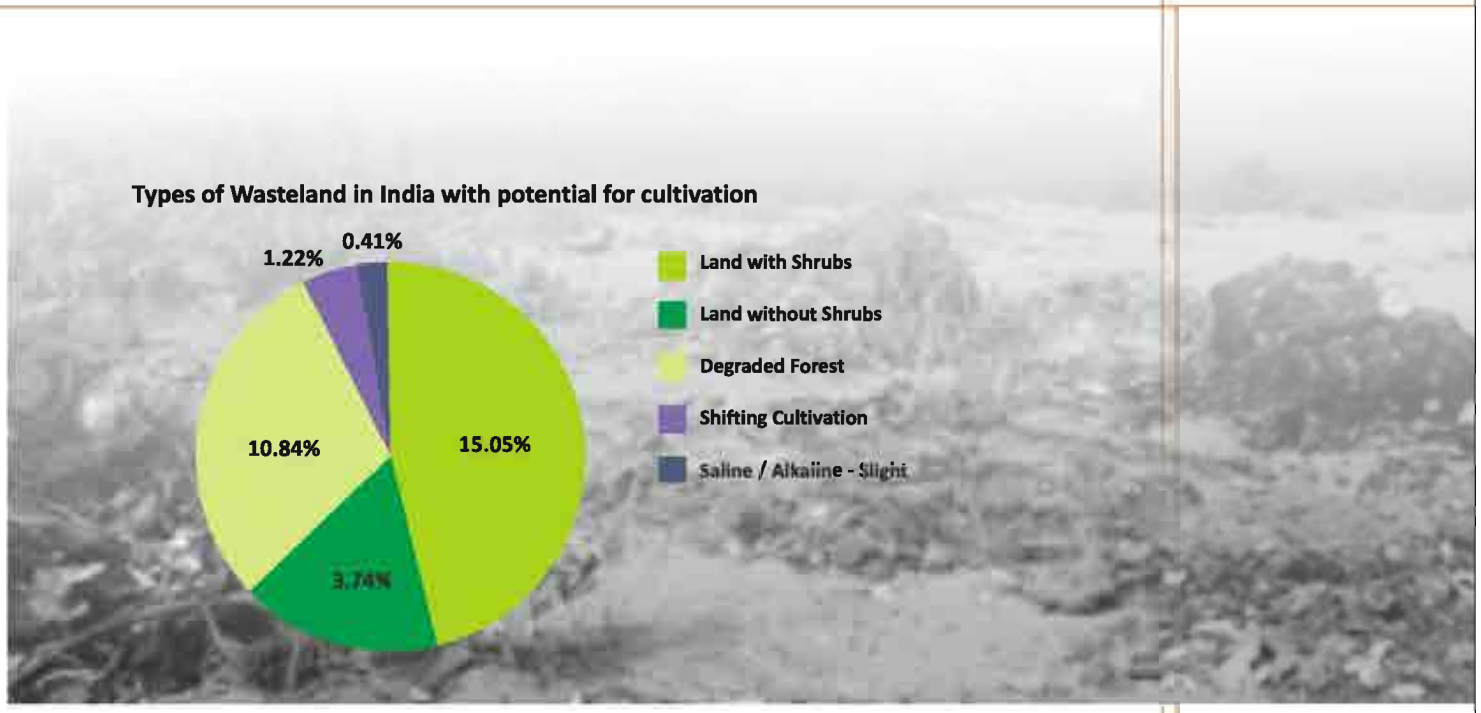


Figure 5.11 Types of wasteland in India with potential for plantation [10]

It has been suggested by the Integrated Energy Policy that 25.71 million kilo litres (KL) of biodiesel can be produced from plantations on 20 million ha of wasteland and 19.65 million kilo litres of bioethanol can be produced through intensive cultivation of over 1.2 million ha [10]. It is estimated that by 2017, India's consumption of diesel in 2017 will be 87 million tons and to meet the 20% blending target, India will need to produce 21.3 million kilo litres of biodiesel [10, 38].

Biodiesel is another emerging alternative in this space. While the use of Jatropa for bio-diesel production is currently declining due to low availability and yield of seeds under harsh conditions, long gestation period and generation of toxic oil-cakes, other non-edible resources such as algae, shrubs and oilseeds are gaining increased acceptance in India. Among such options, algal resources seem to be to the most promising fuel alternative for the future.

5.2.4 Algal Resources

Since cultivation of algae requires non-agricultural land, they are soon gaining importance as the preferred alternative biofuel resources. Other advantages of algal resources include their low requirement of land space, fast reproduction cycles, their ability to grow under varied environmental conditions and their capacity to be cultured in places with brackish, saline and waste water. Thus algal resources can be effectively cultured on a large scale for production of bio-ethanol and bio-diesel.

Figure 5.12 shows the per capita available arable land area across different countries and geographies [33]. India's potential for growing land based biofuels will only come to fruition if either wastelands are used or forests and pasture or existing cropland areas are used to grow biofuels crops. Each of the scenarios, except for the use of wastelands, will have negative impact on food security. Firms such as Sea6 Energy have therefore started focusing on the algal route to develop biofuels especially macro algae such as seaweeds.

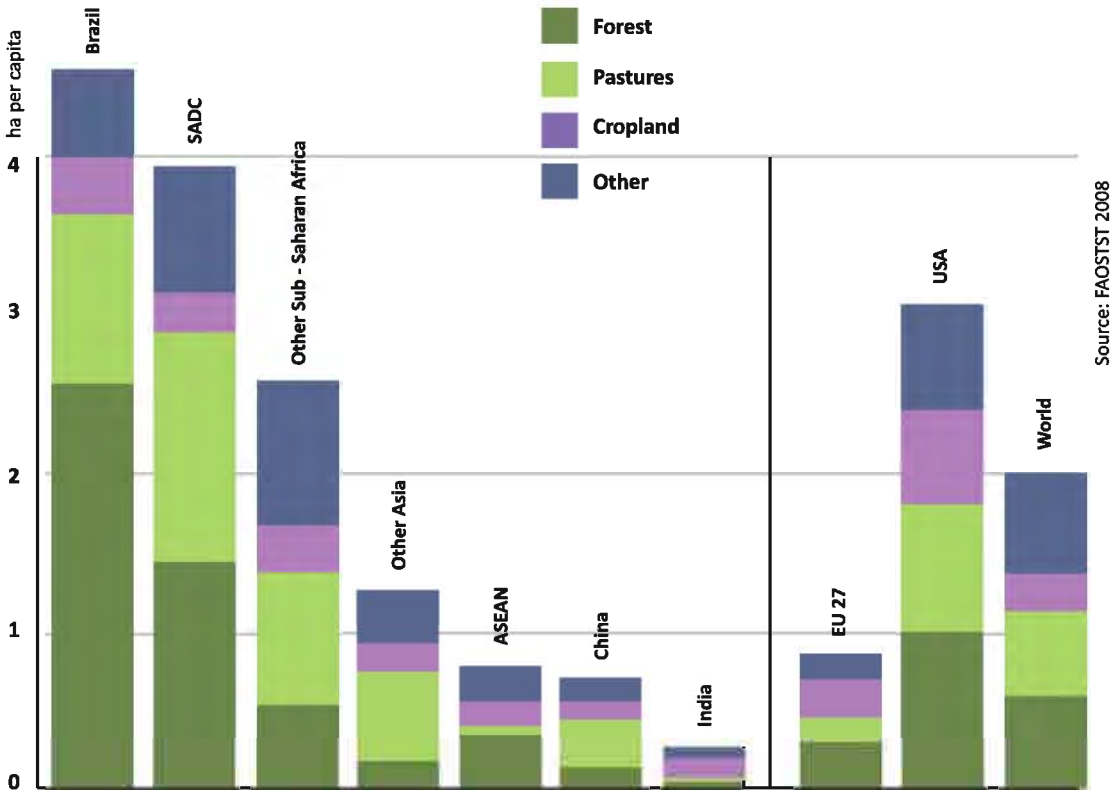


Figure 5.12 The amount of land available per capita [33]

Algal resources can be broadly classified into two types, comprising mainly of micro-algal and macro algal reserves. Micro-algae can either be cultivated using an open system, which requires algal cultivation on a flat open land with continuous supply of water or through closed systems inside transparent containers that are supplied with culture mediums. However, both systems face their own share of hurdles The open systems require continuous water supply and extreme conditions are required to maintain a monoculture to avoid competition from the naturally growing algal strains. On the other hand, the closed systems require high technical skill for construction and also consume high energy for mixing of cultures with the medium. Moreover, the algal species that can be grown in closed systems are relatively limited. Macro-algae mainly comprise of sea-weeds and can be grown at sea-shores, but are currently less advanced as against the land based methods (Figure 5.13).

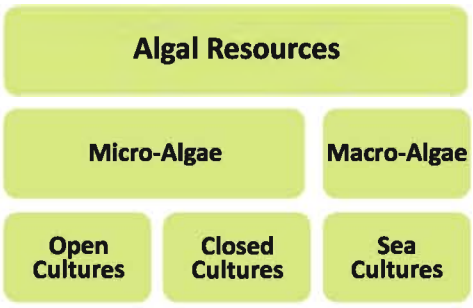


Figure 5.13 Culture techniques for algal resources

While micro-algae are expensive to grow, as they require fresh water and nutrients culture for development; macro-algae cultures are relatively less expensive because they can be grown in sea water with no additional nutrient costs.

As macro-algae emerge as the new and preferred alternative resource for bio-fuel, more companies are looking to expand in this space. Sea6 Energy, established in July 2010, is one such venture which aims to utilize the potential of sea-weeds to produce biofuels. Sea6 Energy has already developed its own off-shore farming system for red sea-weeds (as they are highly productive) and is currently researching micro-organisms that can breakdown the plant (dry red sea weeds contain 50% of their weight as carbohydrates) to monosaccharide sugars [34]. They have partnered with Novozymes to develop enzymes that can work in salt water systems.

Recent advances in genetic engineering techniques and development of bio-refineries will enable the effective utilization of algal biofuels in an economical and sustainable manner over the coming years.

As industries in the bio-technology domain continue to grow and expand, it is also very essential to examine the hazardous toxic effluents generated by them and discover techniques to dispose of them in an eco-friendly manner. The next segment discusses bioremediation methods in India and how it can help in disposing industry waste without harming the surrounding environment.

5.2.5 Bioremediation in India

Bioremediation essentially involves the use of micro-organisms to degrade toxic waste products to less hazardous substances in the environment.

Industrialization and extractive industries such as iron ore and coal mining have increasingly affected the environment in an adverse manner by generating organic as well as inorganic pollutants. This has eventually become a serious hazard to the ecosystems and in turn to all its inhabitants. It is therefore essential to develop novel strategies to de-contaminate the environment and ensure long term sustenance of a balanced ecosystem. As industrial pollutants continue to be a growing a menace for the environment, bioremediation techniques are emerging as potential solutions to address these issues.

In order to address growing environmental concerns in this space; The Energy and Resources Institute (TERI) developed the "Oilzapper" technology that could clean up toxic spills and dispose oily sludge in an eco-friendly manner. In 2011, TERI used this technique to clean the Mumbai shoreline that was contaminated by the oil-spill caused by the accident of MSC Chitra and MV Khalijia 3 in August 2010 with a success rate of 90 percent [35].

Another method called "Oilivorous–S" was developed by Indian Oil Corporation's R&D centre in Faridabad and TERI to treat oily sludge. Currently, leading corporations like Indian Oil, Bharat Petroleum, Hindustan Petroleum, and Oil and Natural Gas Corporation are using Oilzapper and Oilovorous-S technologies to treat and dispose oil pollutants in India [35].

Firms such as Richcore and Praj also have developed methods to effectively treat waste water and effluents with the aid of enzymatic and biological technologies [36, 37]. Richcore is helping the Indian conglomerate ITC, as well as a Dubai based firm AquaChemie in treatment of industrial effluents through its proprietary enzyme technology which saves costs upto 30% and increases water recyclability. It is looking afield to Chile, Japan and Brazil for providing waste water treatment solutions.

Apart from the environmental challenges, there are several hurdles that are currently faced by the Indian bio-industrial sector. Some of the major impediments are discussed in the following segment.

5.3 Challenges and Future Prospects

India is a severely energy deficient nation and energy is the primary driver for the world's economies. A World Bank Report in 2010 stated that if India were to maintain its current GDP growth rate of 8-9% she will need to meet its growing energy demand and it is widely estimated that India's demand will increase three to four folds from its current energy consumption level.

India is a net importer of fossil fuels and the import of crude oil in the last 10 years has grown more than 2.5 times from 57.8 million tons (when India spent US $9.21 billion) in 1999-2000 to close to 140 million tons costing US $75.6 billion [10]. Both petrol and diesel consumption are also set to rise in the coming decade, thus increasing India's dependence on imports [10].

It is reported that in the next 25 years India's consumption of electricity with grow at a rate of 7.4% and that India needs to generate at least five times more electricity to be able to meet future demands. Presently India derives almost 60% of power from coal. Future demand will therefore put pressures on environmental sustainability.

Moreover, the lack of investment in the R&D sector has resulted in very few manufacturing units in India. As a result, domestic companies are usually dependent on enzyme imports and this subsequently decreases their profit margins to a significant extent.

India produces about 100-150 million tonnes of surplus agricultural and forest residues, which can be utilized to produce bio-fuels and bio-chemicals

Looking ahead, it is estimated that if the national biofuel programme becomes successful, it has the potential to create 18 million jobs and hence will significantly improve the future of the Indian bio-economy.

These circumstances necessitate India to strategize for a planned reduction in our dependence on fossil fuels through biofuels as well as bioenergy initiatives.

5.4 Recommendations for Bioindustrial sector

As previously mentioned, that while countries like the USA, Denmark and others in Europe have made significant progress in this sector, India yet has to realize its full potential to innovate in this space The major recommendations for the bio-industrial sector are outlined in the next section.

5.4.1 Deployment of novel technologies for bioenergy through biomass

India produces about 100-150 million tonnes of surplus agricultural and forest residues which can be utilized to produce biofuels and biochemicals. This can help produce about 25-35 million tonnes of biofuels which can replace a significant amount of India's current and future energy demands. In addition, the feedstock available can also be used to produce biochemicals which can replace existing petrochemicals. GOI should support R&D as well as commercialization of biofuel feedstock production and support efficient production engineering methods.

GOI should provide mechanisms and funding for industry led consortia and programs to develop and deploy new technologies for the production of biofuels and biochemicals from biomass using biochemical, pyrolytic, catalytic, and thermo-chemical routes. Technologies such as biomass gasification or combustion face several biomass related barriers such as poor understanding of moisture analysis and drying methods and sizing techniques for cutters. There are also other gasifier engine related barriers such as life-cycle operation issues, as there are not many protocols for maintenance and design.

Currently, the efforts promoted by the government are conducted at national labs and universities who have historically not demonstrated the ability to develop and deploy commercially viable technology. Development and deployment of such technologies involves substantial risk and GOI can provide mechanisms which will enable risk mitigation for industries.

GOI also should focus on updating the "Biomass Atlas" which should incorporate changes in land use and agricultural patterns as well as giving information on wasteland and forest cover [10, 38]. The biomass potential from wasteland including economic viability studies for plantation, collection and extraction should be conducted. These data should be monitored continuously and made accessible to the private sector [38].

5.4.2 Create a dedicated Biofuel and Bioenergy Fund of US $100 million

A dedicated fund of US $100 million for R&D including commercialization of biofuel and biomass energy solutions needs to be created through joint efforts from DBT, DST and Ministry of Agriculture. This fund could be modeled along the lines of SBIR that promotes partnerships amongst industry-academia, coal based powerplants & oil refineries and-renewable energy firms.

5.4.3 Establish Centers for Bioenergy Research to Conduct Cutting Edge Research and Development

As mentioned before, several leading countries in industrial biotechnology such as the USA have established leading centers for research and development into several aspects of industrial biotechnology such as biofuels and synthetic biology. The USA's Department of Energy, for example, has established three leading centers across the country with joint partnership with industry. These centers are the Joint BioEenergy Institute (at California), the BioEnergy Science Center (at Oak Ridge National Lab), and the Great Lakes Bioenergy Research Center (at Wisconsin).

It is pertinent that India establishes five "Centres for Bioenergy Research" with the mandate to conduct industrially relevant research in frontier areas of industrial biotechnology. These centres could be located in Mumbai (in partnership with ICT), Delhi (in partnership with ICGEB), Chennai (in partnership with IIT-Madras) and at Jadavpur (in partnership with Jadavpur University). The centres should also provide core lab facilities needed specifically by industrial biotech firms which can be offered on a pay-per-use basis.

These centres should partner with industry and conduct research and development to improve yields of several oil seed plants such as Jatropa, develop second generation biofuels and algae as source of biofuels. The centres should partner with industry to engineer microbes that can deliver better yields.

5.4.4 Focus on Supply Chain Issues Concerning Biofuels

The biofuel supply chain from procurement to production and distribution is highly complex. It is important to note that supply chain issues of bioethanol and biodiesel are different and hence need different policy interventions.

Ethanol production via molasses, sweet sorghum and tropical sugar beets should be promoted and their supply chain issues including issues related to fluctuation of seasonal production to distribution should be studied. Similarly the biodiesel industry in India, which is in nascent stage and its supply chain issues have not been studied in detail, should be given impetus. It is crucial to understand the possible bottlenecks that affect the biodiesel supply chain. It is reported that about 32 million Ha of wasteland are required for production of biodiesel to meet the 20% blending target of GOI [10]. GOI support in scaling up of Jatropa cultivation is needed and in this process it is also crucial that the government incentivizes large scale cultivation Jatropa by carefully considering the pricing issues of seeds and biodiesel such that it becomes economically viable for industry to produce biodiesel [10].

One of the concerns of industry has been the lack of smooth movement of raw materials needed for production of biofuels across states in India. The GOI should align policies at the central and state level which promote unhindered movement of raw materials across states [10, 38].

GOI should focus on updating the Biomass Atlas which should incorporate changes in land use and agricultural patterns as well as giving information on wasteland and forest cover

5.4.5 Address Algal Biofuel Strategies

Algae based biofuel generation has many benefits as it does not require use of valuable land which could otherwise be utilized for production of food crops. India needs to focus on policies to promote seawater and nutrient rich industrial waste waters as national resources for the production of renewable biomass to promote the bioeconomy and incentivize algae based green fuel such that it becomes economically viable.

R&D in algae strains that give high yield and in "closed photo-bioreactors" i.e. those that use an array of glass tubes to culture algae instead of open ponds (which lose water via evaporation) should also be promoted. India should encourage 100% FDI in the area of algal biofuels to bring new technologies and promote R&D partnership between various countries.

The GOI should establish a national facility for the collection of potential strains of biofuel algae and other microbes to promote biofuel research as well as establish national algae biomass production test-bed facilities to conduct pilot-scale research (5-10 acres). These could be co-located at power plants (such as NTPC power plants), wastewater treatment facilities and ethanol production plants [10].

The GOI should also focus on macro-algal (seaweed) sources of biofuel production. Use of seaweeds as a source for biomass as well as for biofuel production has several advantages. Unlike plants, seaweeds do not contain lignin and are easier to break down and they have higher biomass productivity than sugarcane. For example a hectare of seaweed cultivation will yield 100 tons of biomass as against 30 tons of sugarcane [23]. The GOI should provide grants to establish demonstration plants for biofuel generation from seaweed.

5.4.6 Support Organizations like TERI to work in Partnerships for Bioremediation

India is a mineral rich country and the mining industry is set to expand in the near future. There is a huge potential for biotechnology in resolving environmental issues especially mitigating pollution from hazardous waste emanating from mining, heavy metal, power and pesticide industries. For example, "oil zapper" developed by TERI is being used by several firms to alleviate oil spills. Several modified microbial agents such as Pseudomonas are being used to solve pollution hazards. GOI should promote bioremediation by supporting organizations in this field. Initiatives should be taken by GOI and other organizations to identify novel micro-organisms and utilize them to control pollution. It should also support start ups in this field.

5.4.7 Promote Global Linkages amongst Indian Organizations (both Public & Private)

GOI can play a critical role in enabling India to take a knowledge and deployment leadership position in industrial biotechnology through global partnerships. Specifically, GOI can provide mechanisms which enable rather than hinder collaborations between Indian entities and foreign entities. Such collaborations are expected to follow the joint development route wherein the Indian entities will create and own intellectual property. Such intellectual property will have relevance to Indian feedstock, conditions and products while also being licensable for application globally. GOI mechanisms must include financial incentives and enhanced formal and informal networking between Indian and global entities.

GOI should identify top ten international organizations that are at the cutting edge of green biotechnology research such as the 'Energy Biosciences Institute' at the University of California, Berkeley. Indian organizations, private industry and start ups should be given funds to collaborate with such institutes across the globe.

5.4.8 Create a Talent Pool for Industrial Biotechnology

Industry recommends that GOI should augment existing courses taught to undergraduates and postgraduates in India. These courses should take into account the rapidly changing technologies in industrial biotechnology whether it is in designing new microbes or technologies that improves processes. This will help India create its own talent pool. The sector needs 10,000 cutting edge researchers in several aspects of industrial biotechnologies.

Moreover GOI should also focus on ancillary training in handling plant machineries and plant maintenance which is also very important. Ancillary training should be provided via ITI training institutes.

5.4.9 Government Support for Establishing "Demonstration Plants" & Scale-Up Projects

GOI should provide incentives to scale up and commercialize new technologies that will create the bio-based company. There should be an exemption from central taxes and duties for the companies involved in large-scale production of biofuels. GOI should also de-risk by giving grants for scale up demonstration plants subject to review of projects, installation capacity and delivery timelines. Matching grants for setting up large scale pilot plants will help private investors to increase capacity.

Further regulatory framework for biofuel research, waste land acquisition, carbon credits, pollution control certification should be harmonized between the Centre and the States and most importantly streamlined.

5.9 References

1.http://www.prweb.com/releases/industrial_enzymes/proteases_carbohydrases/prweb8121185.htm
2.http://www.genencor.com/industries/biofuels/fuel_ethanol_from_biomass_cellulosic_biofuels/
3.http://novozymes.com/en/news/news-archive/Pages/Advanced-biofuels-becoming-reality-with-Novozymes-new-enzyme-technology.aspx
4.http://www.dsm.com/en_US/cworld/public/media/pages/press-releases/01_12_dsm_and_poet_to_make_advanced_biofuels_a_reality_by_2013.jsp
5.Rowe DG (2011) Beyond Food versus Fuel, Nature 474, S6-S8
6.Fairley, P (2011) Next generation biofuels. Nature 474, S2-S5
7.EIA Energy Kids-Biomass http://www.eia.gov/kids/energy.cfm?page=biomass_home-basics-k.cfm
8.http://www.renewablegreenenergypower.com/us-biomass-facts/
9.Robbins, M (2011) Fuelling Politics, Nature, 474, S22-S24
10.Gunatilake, H (2011) India Cross Sectoral Implications of Biofuel Production and Use. Asian Development Bank
11.http://genomicscience.energy.gov/centers/#page=news
12.http://www.jbei.org/for-industry/index.shtml
13.Sanderson, K (2011) A chewy problem, Nature 474, S12-S14
14.Savage, N (2011) The scum solution, Nature, 474, S15-S16
15.http://www.sapphireenergy.com/green-crude/
16.Savage, N (2011) The ideal biofuels, Nature 474, S9-S11
17.ABLE-BioSpectrum Survey, Volume 9, Issue 6, June 2011
18.http://biospectrumindia.ciol.com/content/BioSpecial/11104121.asp
19.http://novozymes.com/en/news/news-archive/Pages/Novozymes-ramping-up-its-presence-in-India.aspx
20.http://biospectrumindia.ciol.com/content/biotalk/11203083.asp
21.http://bioenergy.novozymes.com/en/the-basics/bioethanol/Pages/default.aspx
22.http://www.qteros.com/news-events/news-detail.cfm?id=29
23.http://economictimes.indiatimes.com/news/news-by-industry/healthcare/biotech/biotech/biotech-firms-go-after-smart-enzymes-to-fuel-energy-sector/articleshow/11220703.cms
24.http://www.rellife.com/industrial_biotechnology.html
25.http://www.eia.gov/cabs/india/Full.html
26.http://bioenergyindia.kar.nic.in/pro_detail.htm
27.http://www.bioenergyindia.in/towards_substantil.pdf
28.http://articles.economictimes.indiatimes.com/2011-08-22/news/29915076_1_biomass-plants-power-generation-bio-energy
29.http://biospectrumindia.ciol.com:50080/content/BioSpecial/11203084.asp
30.http://www.richcoreindia.com/energy.php
31.http://petroleum.nic.in/petstat.pdf
32.http://biospectrumindia.ciol.com/content/BioSpecial/11110104.asp
33.Hugo Ahlenius, UNEP/GRID-Arenda http://www.grida.no/graphicslib/detail/the-development-potential-available-land-per-capita-in-land-use-class_1068
34.http://archive.biospectrumasia.com/content/140312OTH18422.asp
35.http://www.teriin.org/index.php?option=com_casestudy&task=details&sid=6
36.http://wastewater.praj.net/biological-treatment.html
37.http://www.richcoreindia.com/water.php
38.Sargsyan G et. al. (2010). Unleashing the Potential of Renewable Energy in India. South Asia Energy Unit. Sustainable Development Department. The World Bank

6 Bioinformatics and Systems Biology: Making Sense of the Data Deluge

Luscombe et. al. (2001) define Bioinformatics as "conceptualizing biology in terms of macromolecules (in the sense of physical-chemistry) and then applying "informatics" techniques (derived from disciplines such as applied maths, computer science, and statistics) to understand and organize the information associated with these molecules, on a large-scale" [1]. Systems Biology is a broader field that encompasses bioinformatics and many have attempted to define systems biology. Kitano (2002) defines it as; "to understand complex biological systems require the integration of experimental and computational research"— in other words a systems biology approach" [2, 3].

Bruggeman and Westerhoff (2007) have classified top down and bottom-up approach to systems biology as follows "discovering how function arises in dynamic interactions, systems biology addresses the missing links between molecules and physiology. Top-down systems biology identifies molecular interaction networks on the basis of correlated molecular behavior observed in genome-wide "omics" studies. Bottom-up systems biology examines the mechanisms through which functional properties arise in the interactions of known components" [4]. The systems biology field encompasses a wide range of studies from single cell to genome wide, involves several -omics (genomics, proteomics, transcriptomics and metabolomics etc) as well as computional approaches such as predictive tools for simulation and network modeling [5].

The technology enablers for bioinformatics and systems biology are platforms like next generation sequencing (NGS), microarray, advances in imaging especially cell and single molecule imaging technologies and modeling software, all of which have triggered a profusion of data- the so called "Data Deluge".

6.1 Global Perspective on "The Data Deluge and the Fourth Paradigm of Science": The Effect of Confluence of Biology & Computational Science

The Human Genome project was a pioneering achievement as an initial attempt to understand the 'code of life' that is scripted into our DNA. This was truly a transnational project that involved several laboratories and which took 13 years to complete at a cost of US $2.7 billion. The technology enabler that made this successful was the rapid rise in nucleotide sequencing technologies which has continued to mirror and even exceed Moore's Law on semiconductor albeit in a different metric (cost of whole genome sequencing or a base pair). The cost of sequencing has continued to fall exponentially and presently a whole genome sequence can be available at less than US $8000. Figures 6.1 & 6.2 [6, 7] show the exponentially falling cost of sequencing.

The cost of sequencing has continued to fall exponentially and presently a whole genome sequence can be available at less than US $8,000

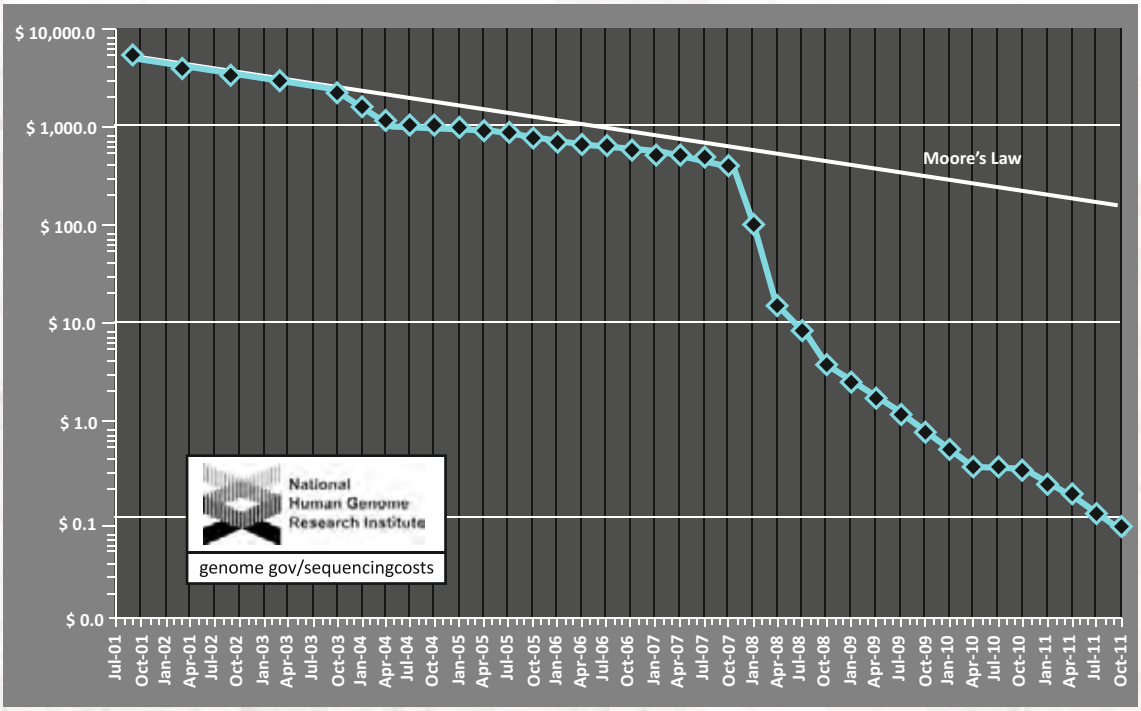


Figure 6.1 Cost per raw megabase of DNA sequence [6]

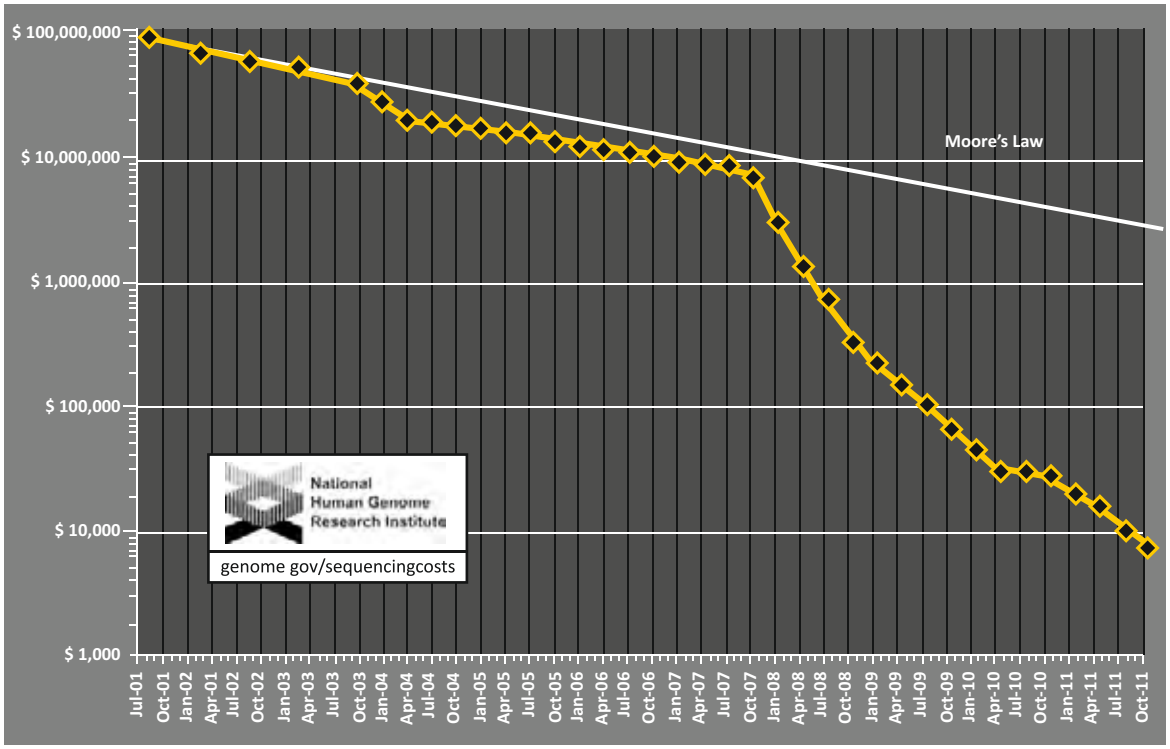


Figure 6.2 The falling cost of genome sequencing [7]

This rapid fall in sequencing cost and new forms of sequencing technologies such as NGS have generated enormous amount of data. For example the number of bases deposited at EMBL from 1982 showed that from 2005 onwards, as the cost of sequencing dived and the speed of the sequencing cycle contracted the number of sequences deposited in EMBL repository grew exponentially (as shown in Figures 6.3 and 6.4, [8]).

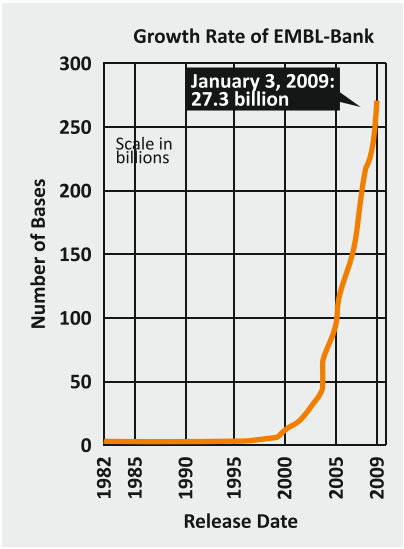


Figure 6.3 Exponential growth in the number of bases deposited in EMBL since 2005 [8]

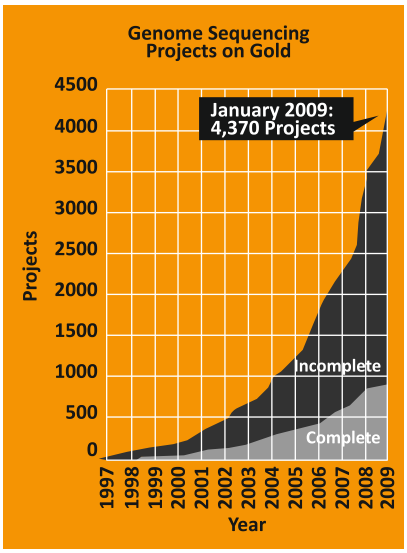


Figure 6.4 The number of genome projects from 1997 [8]

Each sequencing cycle generates terabytes of data that have to be stored, managed and most importantly interpreted intelligibly. Many leading institutes around the world such as the Sanger Institute (UK), BGI Shenzhen (China), and the National Human Genome Research Institute's Large-Scale Genome Sequencing Program in the USA have plans to sequence a minimum of thousand human genomes. Vast amount of data is also being generated through sequencing of many other organisms of plants and animal kingdoms.

Besides the progress in sequencing technologies, other enabling technologies such as NMR studies, imaging technologies that measure single molecule dynamics and cell migrations, imaging technologies used in medicine such as diagnosis and mobile-health technologies are all contributing to the generation of an immense amount of data that is being referred to as the "4th Paradigm of Science" by Microsoft or the "Big Data" by McKinsey & Company [9, 10].

This mix of several technologies for data generation and data analysis is enabling predictive biology especially in pathway analysis, target identification and validation thus reducing the cost of clinical trials and paving the way to personalized medicine.

Biotech firms that are utilizing the advances of sequencing technologies and analysis as their business models are coming in to play. For example firms such as 23andme, deCode genetics and Navigenics are global health genomics firms [11, 12, &13]. Similarly there are several other firms that operate in the pharmagenomics and molecular diagnosis space such as LabCorp, Ingenuity Systems and Exiqon [14, 15, &16].

Each sequencing cycle generates terabytes of data that have to be stored, managed and most importantly interpreted intelligibly

Systems Biology is helping to virtualize many steps in the chain of drug development, thus helping to hasten clinical drug development. Systems analysis of either a disease or an organ is helping the scientific community understand the intricacies of organ homeostasis as well as see possible effects of perturbation of the system. Such predictive technologies therefore help scientists deepen the understanding of disease biology. For instance, the Virtual Vermin Project, a collaborative initiative of the American Diabetes Association and the US biopharma firm Entelos, has developed a virtual, type 1 diabetic mouse model that can be utilized for pre-clinical therapeutic studies. This project was started in 2005 and intends to reduce animal experiments for the initial phases of drug trials [17].

Moving further, global bioinformatics projects, like the 'Europhysiome' initiative to develop a virtual representation of the entire human physiology on a single platform; will also facilitate the development of biomedical research from systems biology perspectives [17].

Another bioinformatics company, 'BioWisdom', now owned by InStem Life Sciences Systems, provides computerized applications to facilitate scientific and healthcare research. For instance, BioWisdom enabled the development of a virtual platform to identify ion channels for pain therapeutics [17].

Global virtualization platforms also aid drug-dosage decisions. Roche, for example, developed computerized models to determine optimal levels of Pegasys (combination drug therapy) for Hepatitis C patients, thereby accelerating clinical research in this area [17].

The US Government has identified Systems and Synthetic biology as one of the priority areas to focus upon in their National Bioeconomy Blueprint. It envisions using systems and synthetic biology to explore new scientific discoveries to treat diseases as well as develop a genomics based homeland security [18].

Bio-IT and Systems Biology acts as an enabler for various biotechnology studies (as summarized in Figure 6.5). Besides health and medicine, systems biology approaches are helping us to sequence and analyze for high yielding crops as well as algae. These technologies also help in our understanding of metabolic pathways that have a role in biotransformation which could lead to the development of agri-biotechnology as well as renewable biofuels (discussed in Chapters 4 and 5).

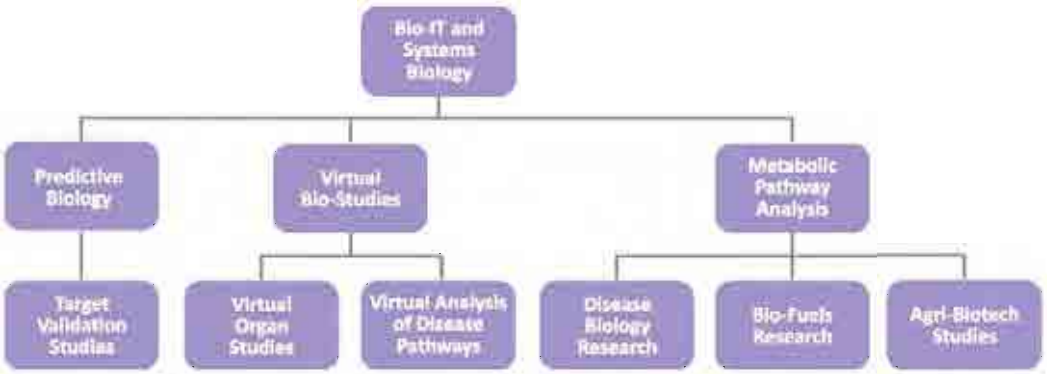


Figure 6.5 Bio-IT & systems biology as enablers for various biological studies

Thus, the global bioinformatics and systems biology sector is poised for rapid advancements in the near future that will facilitate scientific and clinical research and provide easier, cost-effective means to utilize the subsequent healthcare benefits.

6.2 The Indian Bio-IT Scenario

Bioinformatics and systems biology constitutes the smallest segment of the biotechnology industry in India. In FY 2010-11, this sector contributed nearly 2% of the overall biotech industry revenue. As compared to revenues of $48.12 million, in FY 2009-10, this sector touched $50.51 million in FY 2010-11, thereby registering a growth of 5%. There has been a steady rise in the revenues from this sector (as shown in Figure 6.6, [19]) since the past few years.

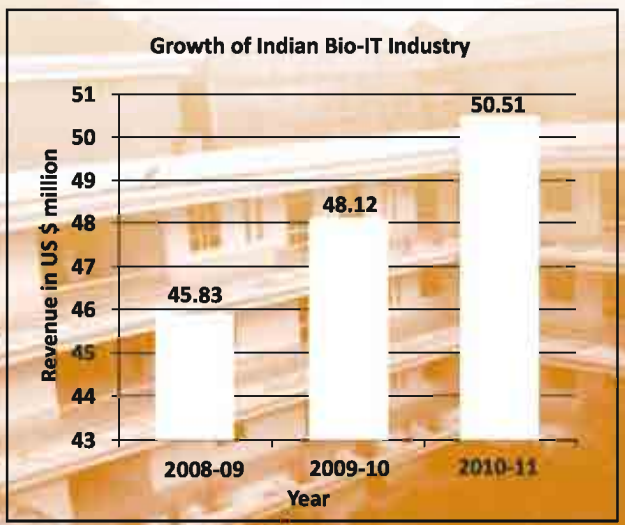


Figure 6.6 Growth of the Indian Bio-IT sector by revenue, [19]

India currently has the potential to leverage its strengths in IT, biology and chemistry by utilizing the multidisciplinary aspects of systems biology and bio-informatics. Moreover, the rising developments in this industry sector predict a major revenue growth for India in the next 5 to 10 years.

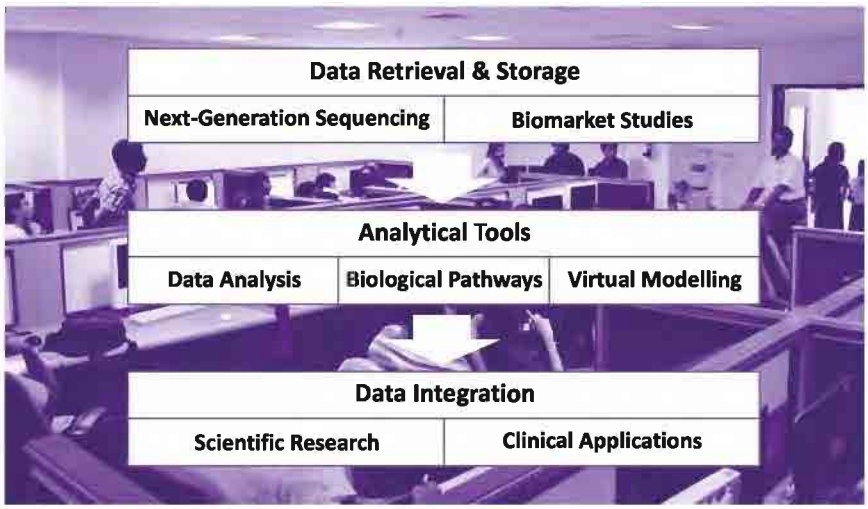


Figure 6.7 Key aspects of Bio-IT and systems biology in India

India currently has the potential to leverage its strengths in IT, biology and chemistry by utilizing the multi-disciplinary aspects of systems biology and bioinformatics

The primary aspects that constitute this industry in India include (Figure 6.7).

- Next Generation Sequencing, Bio-banking, Molecular marker studies
- Data Mining and In-silico analysis (sequencing, microarray, imaging)
- Disease and organ models and perturbation analysis
- Pathway analysis (both disease as well as metabolic pathways)
- Software tool development

The key players in India include Strand Life Sciences, Cellworks, Ocimum Biosolutions, Connexios Life Sciences, vLife, Ganit Labs, Persistent Systems, Molecular Connections, Genotypic, Geschickten Biosciences and several others. Indian IT firms such as Tata Cosultancy Services (TCS), Cognizant and Infosys also maintain relatively small bioinformatics and healthcare sections within their organizations.

While Ocimum Biosolutions and Molecular Connections are services firms, Strand Life Sciences and vLife combine product development as well as services. Connexios and Cellworks focus mainly on discovery research using systems biology tools and have a minimal service component in their business models. Ocimum Biosolutions offers a wide range of services from BioIT consulting, data analysis, LIMS to QT-PCR and biomarker and microarray services.

Strand's product AVADIS® is a data analysis and visualization platform with multiple uses. Based on AVADIS®, Strand developed GeneSpring® an analysis tool for gene expression, genotyping and exon microarrays and includes NLP-derived database of over 1.5 million biological interactions. GeneSpring® is marketed by Agilent Technologies Inc. Strand also built a virtual liver model to analyze and predict drug-induced hepatotoxicity. The virtual liver was developed using a mathematical model of the physiology of a normal rat liver. This advancement thereby enables virtual simulation studies that can eventually reduce animal experimentation to a significant extent [20].

Connexios Life Sciences has focused on disease pathway analysis and has built a network analysis model for Type-II diabetes. The firm using this platform has identified five candidates specific to diabetes many of which are in the lead to hit optimization stage while one molecule is at the pre-clinical stage. Connexios is also focused on identifying candidate molecules for liver disorders and obesity [21].

Cellworks on the other hand uses systems biology approach to find new uses of drugs that are already in the market (re-purposing) and has built immunology and oncology platforms. Using these platforms, has found a couple of candidate molecules for infectious diseases such as TB, chronic diseases such as rheumatoid arthritis, and for cancer such as lung and colorectal cancer [22].

Ganit Labs, which is a public-private partnership among Department of IT (New Delhi), Institute of Bioinformatics and Applied Biotechnology (IBAB) and Strand Life Sciences, is conducting molecular marker studies in oral cancer using NGS. In 2011, they announced the completion of analysis and sequence of the Neem plant's genome- the first de novo sequencing of a eukaryotic organism in India [23]. Other than Ganit, C-CAMP, Genotypic and Xcelris provide NGS sequencing services.

6.2.1 Biomarker Studies in India

Biomarkers are biological indicators of a normal or a pathological condition. They are gaining increased significance in the clinical sector as they can be used to diagnose or predict a disease, stage a pathological condition, monitor disease progression or recurrence, and predict, monitor or select a therapeutic intervention for patients. Biomarkers can also be utilized to study cellular pathways, organ functions and disease pathogenesis. Thus, they have a multitude of applications for both scientific and clinical purposes (Figure 6.8) and hence are gaining increased popularity in the bioinformatics sector.

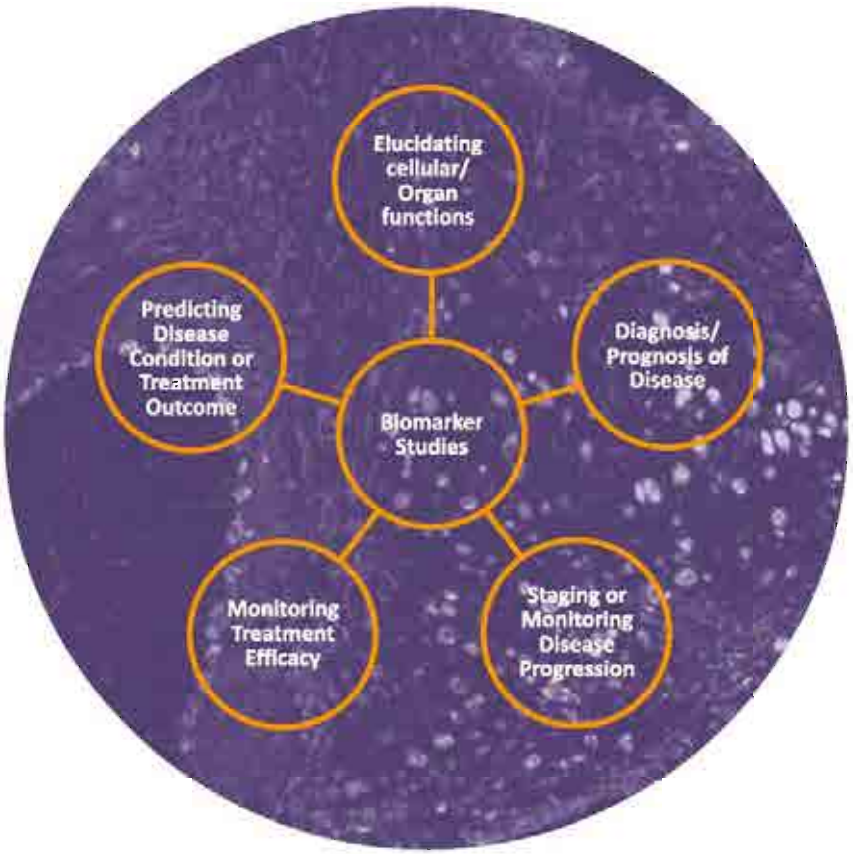


Figure 6.8 Applications of biomarker studies

Advancements in this sector include the collaborative initiative of Clinigene International (a Biocon subsidiary) and Pacific Biomarker to provide specialty biomarkers services in India. This alliance marks a significant progress in the bioinformatics sector for India [24].

Biomarker research at the Mazumdar-Shaw Cancer Center (MSCC) in Bangalore mainly focuses on projects pertaining to the diagnosis, prognosis and therapeutic interventions for head and neck cancer [25]. The National Institute of Biomedical Genomics (NIBMG) is studying the genomic alterations in oral cancer of Indian patients as a part of 'The International Cancer Genome Consortium (ICGC)' project [26]. Similarly, the Advanced Centre for Treatment, Education and Research (a Part of Tata Memorial Hospital) is conducting cancer biomarker studies in breast cancer hepatocellular, cervical and lung cancer.

Strand, Kidwai Memorial Institute of Oncology and the Indian Institute of Science in 2009 jointly conducted a 3 month study to identify potential biomarkers that would assist the prognosis and treatment strategies for breast cancer patients. Strand provided the IT and analysis tools that facilitated this study [27].

The Indian Council for Medical Research (ICMR) announced that it will commence studies on genetic biomarkers for selecting personalized therapeutic interventions for diabetes, cancer, rheumatoid arthritis, epilepsy and infective disorders among several other diseases. ICMR has also started a collaborative programme with DBT to conduct HIV/AIDS research through biomarker studies [28, 29].

Indian biomarker studies are also gaining increased overseas applications. For instance, GVK Biosciences extended their license for the Clinical Biomarker Database (GOBIOM) to USFDA's (US Food and Drug Administration) Biomarker Qualification Group [30]. This USFDA group will use the database to process the qualification of biomarkers. In another association with the Prevention of Organ Failure (PROOF) Center of Excellence in Canada, GVK provided a license to theof GOBIOM database for evaluating the market potential of cardiac, renal and pulmonary disease biomarkers [31].

Table 6.1 below summarizes the Indian research scenario for biomarkers.

Table 6.1 Biomarker research in India

Institutes/Collaborations	Biomarker Research/Study
Clinigine & Pacific Biomarkers	Partnered in 2011 for the study of 'Speciality Biomarkers' [24]
Mazumdar-Shaw Cancer Center (MSCC)	Conducting several biomarker research projects for head and neck cancer [25]
National Institute of Biomedical Genomics (NIBMG)	Studying genetic alterations in Indian oral cancer patients as a part of ICGC project [26]
Strand Life Sciences, Kidwai Memorial Institute of Oncology & Indian Institute of Science	Collaborated in 2009 to study breast cancer biomarkers [27]
Indian Council for Medical Research (ICMR)	Studying biomarkers to facilitate personalized therapy for many diseases [28]
ICMR & DBT	Research on HIV/AIDS biomarkers [29]
GVK Biosciences	Extended GOBIOM to USFDA's Biomarker Qualification Group [30] and to PROOF Center of Excellence in Canada [31]

The increasing investments and collaborations in this sector are indicative of the future potential for biomarker studies. Furthermore, combinatorial and imaging biomarkers are also predicted to emerge as growth drivers for this sector in India.

Moving further, the next step in bioinformatics involves analysis of biological data. Apart from sequencing and biomarker studies, the vast amount of data generated through biological imaging technology, cellular pathway research and virtual organ studies also needs to be analyzed systematically. The computational algorithms that assist the analysis of such data constitute the 'tools for data analyses'.

Figure 6.9 Some developments of the Indian Bio-IT sector [33-37]

The growing interests in pathway studies have facilitated the establishment of several dedicated databases such as 'The Database of Quantitative Cellular Signalling' at the National Centre for Biological Sciences (NCBS), Bangalore [34]. Signalling, metabolic and molecular pathway studies have enabled a deeper comprehension of cellular function and disease pathogenesis, thus subsequently assisting the development of accurate therapeutic interventions.

On the imaging technology front, investments and global collaborations are also set for a steady growth. The Indian Pharmacopoeia Commission (IPC) recently announced that it is seeking partnerships from pharmaceutical and botanical organizations to set up an image and sequence analysis database for herbal plants, thereby potentiating the room for the development in this sector [37].

Global IT companies have also diversified towards data integration in the healthcare and life-sciences sectors. TCS, for instance, have allied with the New Millennium Indian Technology Leadership Initiative (NMITLI) under the Council of Scientific and Industrial Research (CSIR) to facilitate the 'Bio-Suite' software package that comprises computerized algorithms for all drug discovery paradigms. Cognizant, Accenture and IBM Life Sciences also provide clinical data management products among other services in the healthcare sector. Thus, both the public and private sectors are looking towards expansions in this space.

While the investments and collaborative opportunities increase, the challenges for the bioinformatics sector continue to impede its future progress. Therefore, it is essential to address the hindrances in this sector at the earliest to ensure India's steady rise on the global bioinformatics and systems biology platform. The next segment addresses the key challenges of this sector.

6.3 Key Challenges

The primary challenge faced by the bioinformatics sector in India is the lack of infrastructure and standardized data integration platform that will facilitate access to multiple networks through a centralized data source. Moreover, the high volume of data that is fragmented sporadically across varied internet sites makes data integration an increasingly difficult task. This also leads to the redundancy of biological information stored at different virtual repositories.

Another cause for concern in this sector is the deficiency of Bio-IT centres to promote sequencing and multi-disciplinary clinical studies. As a result of this insufficiency, the industry is unable to capitalize the talent pool available in India for the Bio-IT sector. Moreover, access to Bio-IT benefits is extremely limited or mostly absent in the rural areas and is introduced late to the opportunities of informatics.

Lastly, data security challenges also raise concerns regarding the safe and ethical use of personalized data on a public platform. Lack of regulatory paradigms to monitor the access to genomic data can lead to misuse of the information, thereby impeding the development of this sector.

India should establish a Genomic Policy that should identify how to utilize the diversity to enrich the lives of people through health, food and fuel

Thus, these challenges need to be addressed at the earliest in order to secure a stable future in the Indian bio-informatics and systems biology sector.

6.4 Future Prospects

For a developing country like India, which has an agrarian economy, bioinformatics and systems biology will have horizontal application and be play a foundational enabler for variety of segments from biopharma and drug discovery research (reducing cost and time), clinical trial management, in molecular marker discovery for productivity and stress markers for crop improvement and pest management, renewable biofuel generation as well as for biotransformation and other industrial biological applications.

Furthermore, the combination of IT and healthcare data (imaging, remote diagnosis and monitoring of diseases) hold the potential to improve the standard of healthcare services too, for example through management of hospital medical records and decision support. India has a robust IT industry coupled with a strong domestic pharmaceutical market, along with the low cost of infrastructure, which includes the high quality of educational infrastructure and human resources. All this will contribute to India's growing acceptance as a leading global player in the Bio-IT sector and contribute to overall growth of the Indian bioeconomy.

6.5 Recommendations

India could leverage its strengths in IT, biology and chemistry by utilizing the multidisciplinary aspects of systems biology and bioinformatics that include several applications in protein research, speeding up drug discovery and pharmacogenomics, advancement in biomolecular sciences, structural biology, and analyzing cellular networks.

6.5.1 Establish a 'Genomic Policy for India'

India has deep genetic diversity in many areas- ethnicities, plant and crop varieties and soil microorganisms. India should establish a "Genomic Policy for the nation" that should identify how to utilize the diversity to enrich the lives of people through health, food and fuel.

- Sequence and characterize India (and developing world) specific diseases and focus on biomarker studies for rapid identification as well as treatment for a whole host of infectious and chronic diseases.
- Sequence and characterize economically beneficial plants, animal and microbial species. This would not only help in conservation of the country's rich diversity but in safeguarding India against bio-piracy.

• Bring in genomics based measures that will rapidly identify bio-security threats by as harmful microbes which could cause pandemics or that have been either manipulated or engineered for causing human harm.
• Bring in policies for DNA databases that will be generated once personalized medicines takes off in the next 5-7 years

Such large scale sequencing projects will have positive spill-over effects:
A. Large scale sequencing projects will lead to annotation and characterization of large number of India specific paradigms (be it in disease or diversity). This will help in delivering personalized medicine solutions to patients, find new drug molecules from India's rich repository of traditional knowledge and help protect several endangered species that may have economic benefit.
B. They will build capacity in SMEs within this sector as well as increase the pool of biological data skilled people.
C. Generation of India specific biomarkers for diseases, plant productivity and stress resistant markers which will have an impact in providing food and health security.
D. Will create training and employment opportunities for a large number of biotechnology graduates.

6.5.2 Resolve Data Security Concerns
Unsecured biological data on public-domain servers can adversely affect public interests and raise ethical issues. For instance, the misuse of personalized genomic or other publicly available bioinformatics data by insurance companies can adversely affect an individual's health coverage benefits. Thus, it is very important to establish centralized regulatory paradigms that control public as well as private access to personalized biological data for ethical and security reasons. This should be initiated at the earliest to secure a stable future for Bio-IT growth in India.

It is very important to establish centralized regulatory paradigms that control public as well as private access to personalized biological data for ethical and security reasons

6.5.3 Establish Five Bio-IT Centres & Develop Standardized Integrative Platforms for Bio-IT
A huge amount of new information is being gathered by researchers, the fall in cost of sequencing is leading to rapid analyses of the human genome and biological molecules, thus creating huge pools of data that will increasingly play an important role in drug discovery and personalized medicine. Considerable amount of data is also being generated from clinical trials and from electronic medical records. More sophisticated approaches are required for compiling, integrating and analyzing these data. India has existing strengths in IT and chemistry and it should build upon the growing strengths in biology by establishing five multidisciplinary "Centre for Bio-IT" (or Centre for Computational Biology) to study and analyze genomes, understand cellular and molecular pathways and tissue analyses that will help in personalized medicine, animal husbandry, improved crops and wildlife conservation. A budget of US $10 million per Centre over five years is needed to establish the five "Centre for Bio-IT". Once established, the centres should be professionally managed to work closely with industry in providing access to next generation sequencing facilities as well as other related services. The Centre for Bio-IT should also have data storage and retrieval facilities that provide for a secure environment.

6.5.4 Encourage India's Renowned IT Industry to Focus on Systems Biology
GOI should create a taskforce consisting of IT industry leaders as well as biotechnology industry experts (from industry, Government and academia) to chart out a roadmap on leveraging India's IT prowess and exploring what role Indian IT firms can play in enabling this sector.

6.5.5 Establish Courses in Systems Biology and "Big Data" Management
A recent report by McKinsey & Company highlighted that India lags far behind the USA and China in having proper human resources who can understand, analyze and manipulate 'big data' across all sectors including healthcare [10]. Generally in India, lifescience (including biotechnology) courses lack quantitative data courses (except for a small component of statistics) with the result that many lifescience students in India lack basic understanding of using computational methodologies. India therefore should encourage courses in quantitative analysis in biology. GOI should establish 150 fellowships in the area of systems biology especially in postdoctoral and early lectureship positions.

6.6 References

1. Luscombe et. al. (2001) What is Bioinformatics. A proposed definition and overview of the field. Method Inform. Med., 40, 346-358
2. Kitano H (2002), Overview Systems Biology, Nature, 420, 206-210
3. http://blogs.nature.com/sevenstones/2007/07/what_is_systems_biology_3.html
4. Bruggeman FJ and Westerhoff HV (2007) The nature of systems biology, Trends in Microbiology, 15, 45-50
5. http://blogs.nature.com/sevenstones/2007/07/what_is_systems_biology_3.html
6. http://www.genome.gov/images/content/cost_per_megabase.jpg
7. http://www.genome.gov/images/content/cost_per_genome.jpg
8. Christopher Southan and Graham Cameron (2009) Beyond the Tsunami: Developing the Infrastructure to Deal with Lifescience Data in "The Fourth Paradigm: Data Intensive Scientific Discovery", Edited by Tony Hey, Stewart Tansley and Kristin Tollie. Microsoft Research
9. The Fourth Paradigm: Data Intensive Scientific Discovery", Edited by Tony Hey, Stewart Tansley and Kristin Tollie. Microsoft Research
10. Big Data:The next Frontier for Innovation, Competition and Productivity. McKinsey & Company (2011)
11. https://www.23andme.com/
12. www.decode.com
13. www.navigenics.com
14. http://www.ingenuity.com/
15. https://www.labcorp.com/wps/portal/
16. www.exiqon.com
17. Pharma 2020: Virtual R&D which path will you take? PwC (2008)
18. National Biotechnology Blueprint. The White House, 2012
19. ABLE-BioSpectrum Survey, Volume 9, Issue 6, June 2011
20. http://www.strandls.com/
21. http://www.connexios.com/
22. http://www.cellworksgroup.com/
23. http://www.ganitlabs.in/
24. http://www.clinigeneintl.com/docs/PR_21122011_clinigene.pdf
25. http://mscc.in/ResearchSections.aspx?secid=5
26. http://www.nibmg.ac.in/icgc_india_purpose.php
27. http://www.strandls.com/viewnews.php?param=5&param1=55
28. http://pharmabiz.com/NewsDetails.aspx?aid=66602&sid=1
29. http://pharmabiz.com/NewsDetails.aspx?aid=66874&sid=1
30. http://biospectrumindia.ciol.com/cgi-bin/printer.asp?id=127226
31. http://biospectrumindia.ciol.com:50080/cgi-bin/printer.asp?id=130416
32. http://www3.ocimumbio.com/bio-research-design-execution/services/sequencing/
33. http://www.strandls.com/viewnews.php?param=5&param1=68
34. http://doqcs.ncbs.res.in/
35. http://www.strandls.com/VirtualLiver
36. http://www.cellworksgroup.com/overview.php
37. http://pharmabiz.com/NewsDetails.aspx?aid=61395&sid=1

7 Conclusion – Creating the Indian Bioeconomy

"Ideas don't last long, something must be done with them" Santiago Ramon y Cajal (1852-1934). Spanish Nobel Laureate, histologist, physician and pathologist

7.1 The Future Ahead

The 1980s were a time when India took several steps in S&T policy that are bearing fruits today. This was the time when the GOI became one of the first governments in the world to establish a separate department to focus on building biotechnology capacity and innovation in India, the Department of Biotechnology (DBT) in 1986. Indian biotechnology has grown over the last three decades built upon the foundations laid by DBT, as well as from the support provided by a host of other organizations such as DST, ICMR, ICAR and CSIR. Mirroring the public support for this sector, the private industry has grown in strength from a nascent stage in 1980s to a mid-maturity level in 2000s with revenues of US $4 billion in 2011 and likely to reach US$ 5 billion in 2012.

The Indian economy that was liberalized in the early 1990s has now become a trillion US dollar economy and the current winds of change will propel India to become one of the leading economies of the world by 2030s and possibly one of the top three economies by 2050. The policy imperative to make biotechnology one of the main engines of this growth is building upon its current strengths such that India becomes a bioeconomy and a global destination for innovations in biotechnology. The combined potential for biotechnology and healthcare could be as large as US $100 billion by 2025. The sector should grow to a level where it can provide solutions to long term and short term challenges that India and the world will face; be it in food, fuel or healthcare. In the next decade, immense opportunities lie in biosimilars, vaccine and biotech manufacturing, stem cells, diagnostics and devices, systems biology, m-health, agribiotech and green energy from biological sources. Each of these fields will contribute significantly to the creation of a vibrant bioeconomy.

To achieve this goal India needs a concerted effort from the GOI, private industry and academia. The entrepreneurial energy in this sector should be harnessed and channeled to build the Indian bioeconomy.

To achieve this goal India needs a concerted effort from the GOI, private industry and academia. The entrepreneurial energy in this sector should be harnessed and channeled to build the Indian bioeconomy

The roadmap to become a fully fledged bioeconomy involves creating a world class regulatory system (that is robust, transparent, streamlined, accountable and with predictable time lines), infrastructure that involves cutting edge translational centres as well as dedicated corridors of special economic zones, a vibrant university system, a conducive tax and fiscal environment, fostering an entrepreneurial class through targeted funding linked to metrics for success and enabling a collaborative environment for Indian organizations to partner both with indigenous as well as international organisations.

The coming decade will be crucial for building upon and shaping the biotechnology industry from its current position of strength to a world class global centre for innovation. The ground has been laid for the sector to leap to the next level. The initiation of institutions such as BIRAC, including its funding and support schemes, will go a long way to help this sector grow.

The report has outlined the steps that GOI needs to take in the near to medium term for fashioning a bioeconomy. Fulfilling the vision will need political will, sustained focus, commitment, capital and partnership model of operation.


India's Biotechnology Road Map
Targeted Funding
Translational Centres
Vibrant University System
Special Economic Zones
World Class Regulatory Systems
Conducive Tax & Fiscal Environment

List of Abbreviations

ABLE - Association of Biotech Led Enterprises
ACIP - Accelerated Crop Improvement Programme
ACTREC - Advanced Centre for Treatment, Research and Education in Cancer
AIIMS - All India Institute of Medical Sciences
AML - Acute Myeloid Leukaemia
ATMP - Advanced Therapeutic Medical Products
AYUSH - Ayurveda, Yoga, Unani, Siddha and Homeopathy
BA/BE - Bio-Availability/Bio-Equivalence
BBSRC - Biotechnology and Biological Sciences Research Council
BESC - BioEnergy Science Center
BMT - Bone Marrow Transplantation
B-O-T - Build-Operate-Transfer Model
BP - British Petroleum
Bt - Bacillus thuringiensis
CAGR - Compound and Annual Growth Rate
CBBTDEC - Cellular Biology Based Therapeutic Drug Evaluation Committee
C-CAMP - Centre for Cellular and Molecular Platforms
CCMB - Center for Cellular and Molecular Biology
CDRH - Center for Devices and Radiological Health
CDSCO - Central Drugs Standard Control Organization
CIRM - California Institute for Regenerative Medicine
CIRM - California Institute of Regenerative Medicine
CMC - Christian Medical College
CML - Chronic Myeloid Leukaemia
CMO - Contract Manufacturing Organization
COPD - Chronic Obstructive Pulmonary Disease
CPCSEA - Committee for the Purpose of Control and Supervision of Experiments on Animals
CRAMS - Contract Research and Manufacturing Services
CRO - Clinical Research Organization
CSIR - Council of Scientific and Industrial Research
CSO - Central Statistical Office
CT - Clinical Trials
CTO - Clinical Trials Organisation
CTRI - Clinical Trials Registry of India
DBT - Department of Biotechnology
DCGI - Drug Controller-General of India
DGFT - Directorate General of Foreign Trade
DRDO - Defence Research and Development Organisation
DST - Department of Science and Technology
EMEA - Europe, Middle East and Africa
EO - Executive Order
EPA - Environment Protection Agency
EPO - Erythropoietin
EPSRC - Engineering and Physical Sciences Research Council
EU - European Union
FAO - Food and Agriculture Organization
FDA - Food and Drug Administration
FFVs - Flex Fuel Vehicles
FY - Fiscal Year
GACP - Good Agricultural and Collection Practices
GAP - Good Agricultural Practices
GCSF - Granulocyte Colony Stimulating Factor

GDP - Gross Domestic Product
GEAC - Genetic Engineering Approval Committee
GLP - Good Laboratory Practices
GM - Genetically Modified
GMOs - Genetically Modified Organisms
GMP - Good Manufacturing Practices
GOBIOM - GVK Biosciences extended their license for the Clinical Biomarker Database
GOI - Government of India
GTP - Golden Triangle Partnership
GVAP - Global Vaccine Action Plan
HCV - Hepatitis C Virus
hESC - Hematopoietic Embryonic Stem Cell
HIV - Human Immunodeficiency Virus
I SPY 2 TRIAL - Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis 2
IAEC - Institutional Animal Ethics Committee
IARI - Indian Agricultural Research Institute
ICAR - Indian Council of Agricultural Research
ICMR - Indian Council for Medical Research
ICPS - International Consortium for Polynucleotide Synthetics
ICRISAT - International Crops Research Institute for the Semi-Arid Tropics
IC-SCRT - Institutional Committee-Stem Cell Research Therapy
IfM - Institute for Manufacturing
iGEM - The international Genetically Engineered Machines competition
IGIB - Institute of Genomics and Integrative Biology
IISc - Indian Institute of Science
IIT - Indian Institute of Technology
IND - Investigational New Drug
IPC - Indian Pharmacopoeia Commission
iPST - Induced-Pluripotent Stem Cell Technology
IRMA - Imatinib Resistance Mutation Analysis
IT - Information Technology
IVD - In-vitro Diagnostic
IVF - In-Vitro Fertilization
JBEI - Joint BioEenergy Institute
JNCASR - Jawaharlal Nehru Centre for Advance Scientific Research
LMOs - Living Modified Organisms
LVPEI - LV Prasad Eye Institute
MAS - Molecular Assisted Selection
MAT - Marker Trait Associations
m-Health - Mobile Health
MIT - Massachusetts Institute of Technology
MNC - Multinational Corporation
MoD - Ministry of Defence
MoEF - Ministry of Environment and Forests
MSCC - Mazumdar-Shaw Cancer Centre
NAC-SCRT - National Apex Committee for Stem Cell Research and Therapy
NBRC - National Brain Research Centre
NCBS - National Center for Biological Sciences
NCCS - National Centre for Cellular Sciences
NCL - National Chemical Laboratory
NDAC - New Drug Advisory Committee
NGS - Next Generation Sequencing

NIAID - National Institute of Allergy and Infectious Disease
NIBMG - National Institute of Biomedical Genomics
NIH - National Institutes of Health
NIIST - National Institute of Interdisciplinary Science & Technology
NIT - National Institutes of Technology
NME - New Molecular Entity
NMITLI - New Millennium Indian Technology Leadership Initiative
NOC - No Objection Certificate
NRHM - National Rural Health Mission
NRTN - National Rural Telemedicine Network
NSABB - National Science Advisory Board for Biosecurity
NSF - National Science Foundation
OLS - Office of Lifesciences
PGIMER - Post Graduate Institute of Medical Education & Research
PPACA - Patient Protection and Affordable Care Act
PPP - Public Private Partnership
PROOF - Prevention of Organ Failure
PwC - PricewaterhouseCoopers
QTL - Quantitative Trait Loci
R&D - Research and Development
RGCB - Rajiv Gandhi Centre for Biotechnology
RM - Regenerative Medicine
SAARC - South Asian Association for Regional Cooperation
SBIRI - Small Business Innovation Research Initiative
SBSTTA - Subsdiary Body on Scientific, Technical, and Technological Advice
SCNT - Somatic Cell Nucleus Transfer
SGI - Synthetic Genomics Incorporation
SGPIMS - Sanjay Gandhi Postgraduate Institute of Medical Sciences
TCM - Traditional Chinese Medicine
TERI - The Energy and Resources Institute
TESSY - Towards a European Strategy for Synthetic Biology
TMC - Tata Memorial Centre
UAS - University of Agricultural Sciences
UK - United Kingdom
UNICEF - United Nations Children's Fund
USA/US - United States of America
USD - United States Dollar
VGCP - Vaccine Grand Challenge Programme
WHO - World Health Organization

Acknowledgements
We would like to acknowledge and thank Department of Biotechnology (DBT) and BIRAC for the support provided to write this high level report.

We would like to express our gratitude for the input and help that we received from the following experts who generously donated their time, effort and insights for this project:

Anand Anandkumar, *Managing Director & Chairman*, Cellworks
Ajay Bharadwaj, *CEO*, Anthem Biosciences
Achin Gupta, *Director* - Strategic Planning Established Pharmaceuticals, Abbott (Formerly Senior VP, Glenmark Pharmaceuticals)
Arun Chandavarkar, *Chief Operating Officer,* Biocon
Balu Sarma, *President and Chief Technology Officer,* Praj Matrix
Bharathi Sriram, *Vice President R&D,* Gangagen
Binay Panda, *Head,* Ganit Labs
BN Manohar, *President and CEO,* Stempeutics
Chandrasekhar Nair, *Director,* Bigtec Labs
Devashish Ohri, *Managing Director- South Asia,* Life Technologies
Gayatri Saberwal, *Faculty,* Institute of Bioinformatics and Applied Biotechnology
Harish Iyer, *CEO,* Shantha Biotechnics
K K Narayanan, *Managing Director,* Metahelix Life Sciences
Krathish Bopanna, *President and Executive Director,* Semler Research Centre
K V Subramaniam, *President and CEO,* Reliance Life Sciences
Maria Kammerer, *Specialist-Marketing Communications,* Strand Life Sciences,
Nandita Chandavarkar, *Director Operations,* ABLE
Narayanan Suresh, *Group Editor,* BioSpectrum and Technology Review India
Pawan Dhar, *Professor & Director Centre for Biodesign,* Symbiosis International University
P M Murali, *Hon. President,* ABLE and *MD & CEO,* Evolva
Pramod Chaudhari, *Executive Chairman,* Praj Industries
Premnath Venugopalan, *Head,* NCL Innovations
Rajesh Rai, *CEO,* India Innovation Fund
Ramaswamy S, *Professor and Dean* Institute of Stem Cell Biology and Regenerative Medicine (inSTEM) & *CEO,* Centre for Cellular and Molecular Platforms (C-CAMP)
Satya Prakash Dash, *Chief Operating Officer,* ABLE
Shrikumar Suryanarayan, *Hon. Director General,* ABLE and *Chairman,* Sea6 Energy
Shirshendu Mukherjee, *Senior Strategic Advisor India,* Wellcome Trust
Shyam Suryanarayanan, *CEO,* C-Drive
Supreet Deshpande, *CEO,* VLife Sciences
Subir Basak, *President,* Global Drug Discovery Services, Jubilant Life Sciences (Formerly *CEO and Chief Commercial Officer,* Celestial Biologicals)
Subramani Ramachandrappa, *Chairman and Managing Director,* Richcore Lifesciences
Vijay Chandru, *Chairman & CEO,* Strand Lifesciences
Vandana Iyer, *Research Writer,* ABLE

The views expressed herein are personal and do not reflect the views of the organisations represented by the individual concerned.

The report also drew upon the discussions and insights from various ABLE platform events over the last two years such as High Level Policy Conclave (2011), Bangalore INDIA BIO (2011, 2012), BIOIndia Partnering (2011) and other ABLE workshops and meetings (2010-2012). We would like to thank the expert panelists who participated and provided insights during the platform meetings.

ABLE would also like to thank the following experts:

Abhijeeth Chandrasekaran, *Clinical Scientist,* RxMD
Amit Sharma, *Co-founder,* Consure
Anand Sivaraman, *Director,* Remidio Innovative Solutions
Anuradha Acharya, *Founder & CEO,* Ocimum Biosolutions
Chandra Viswanathan, *Head Regenerative Medicine,* Reliance Life Sciences
D A Prasanna, *Chairman & Founder,* Ecron Acunova
David Gill, *MD,* St. John's Innovation Centre, Cambridge
D Balasubramanian, *Director of Research,* LV Prasad Eye Institute
Deepanwita Chattopadhyay, *MD & CEO,* IKP Knowledge Park
Dhananjay Dendukuri, *CEO & Co-founder,* Achira Labs
Dhananjay Patankar, *VP-Biologics,* Syngene
G S Krishnan, *Regional President,* Novozymes South Asia
G Padmanabhan, *NASI-Platinum Jubilee Chair Hon. Professor,* IISc
Gyanendra Shukla, *Director Corporate Affairs and Cotton Traits,* Monsanto
Jignesh Bhate, *Founder & CEO,* Molecular Connections
Kalyanasundaram Subramanian, *Chief Scientific Officer,* Strand Life Sciences
K Chandrasekhar, *CEO,* Forus
Kiran Mazumdar-Shaw, *CMD,* Biocon
M Ramasami, *MD,* Rasi Seeds
Moni Abraham Kuriakose, *Professor & Director Surgical Oncology,* Mazumdar-Shaw Cancer Centre
Myshkin Ingawale, *Co-founder,* Biosense Technologies
Nitin Deshmukh, *CEO,* Kotak Private Equity
Partha Majumder, *Director,* National Institute of Biomedical Genomics
P. S. Dravid, JK Agrigenetics
Pushpendra Gupta, *Emeritus Professor,* Meerut University
Rajiv Vasudevan, *CEO,* AyurVAID
Raju Barwale, *MD,* Mahyco
Rashmi Barbhaiya, *CEO & MD,* Advinus
Ravi Kumar, *MD,* Xcyton Diagnostics
S Nandakumar, *CEO,* Perfint
Senthil Chinnasamy, Aban Infrastructure
Sudip Gupta, *Professor Medical Oncology,* Tata Memorial Hospital/Centre
Sujay Shetty, *Partner*, Pharma Life Sciences, PricewaterhouseCoopers
Sunil Bhaskaran, *MD & CEO,* Indus Biotech
Sunita Sreedharan, *CEO,* SKS Law Associates
Suri Venkatachalam, *Founder & CEO,* Connexios Lifesciences
Syed Shams Yazdani, *Group Leader,* ICGEB
Taslimarif Saiyed, *Director & COO,* Centre for Cellular & Molecular Platforms
Tim Minshall, *Senior Lecturer,* Inst. for Manufacturing, University of Cambridge
Utkarsh Palnitkar, *Executive Director,* Centrum Capital
Venkita Subbulakshmi, Chromous Biotech
Vinay Konaje, *Founder & Director,* Navya Biologicals
Vis Niranjan, *President & Founder,* RxMD

Appendix 1

The exchange rates for US dollar (USD) to Indian Rupees (INR) has fluctuated over the period of 2011 & 2012. The conversion rate used in this report is US$1= INR48

http://www.indexmundi.com/xrates/graph.aspx?c1=INR&c2=USD&days=365

About ABLE

ABLE – Association of Biotechnology Led Enterprises - www.ableindia.in is a national forum that represents the Indian Biotechnology Sector. It was launched in April 2003 after industry leaders felt the need for an exclusive forum to represent the sector.

The primary objective of ABLE is to accelerate the pace of growth of the Biotechnology Industry in India, through partnering with the Government of India in their Biotechnology initiatives to deliver optimal policies and create a positive regulatory environment, encouraging entrepreneurship and investment in the sector, providing a platform for domestic and overseas companies to explore collaborations and partnerships, forging stronger links between academia and industry and showcasing the strengths of the Indian biotech sector.

ABLE thus catalyses a symbiotic interface between the industry, the government, academic and research institutes and domestic and international investors.

Today, ABLE has over 270 members representing all verticals of the sector like agri-biotech, bio-pharma, industrial biotech and clean tech, -omics, bio-services, investment banks and Venture Capital firms, law firms, leading research & academic institutes and equipment suppliers.

More details about ABLE: www.ableindia.in

Disclaimer

This document is provided by Association of Biotechnology Led Enterprises (ABLE) for general guidance only and does not constitute the provision of legal advice, accounting services, investment advice or professional consulting of any kind. The information provided herein should not be used as a substitute for consultation with professional tax, accounting, legal or other competent advisers. Before making any decision or taking any action, you should consult a professional adviser who has been provided with all pertinent facts relevant to your particular situation.

The information provided as is, with no assurance or guarantee of completeness, accuracy, or timeliness of the information and without warranty of any kind, express, or implied, including but not limited to warranties of performance, merchantability and fitness for a particular purpose.

This document is prepared on the basis of information obtained from key industry players, trade associations, government agencies, trade publications and various industry sources specifically mentioned in the document. It contains certain examples extracted from third party documentation and so, being removed from the context of the original third party documents, should be read with this in mind. The copyright in such third-party materials remains with the third parties concerned.

While due care has been taken to ensure accuracy of the information contained in this document, no warranty express or implied, is being made, or will be made, by ABLE as regards the accuracy and adequacy of the information contained in this document. No responsibility is being accepted, or will be accepted, by ABLE, for any consequences, including loss of profits, that may arise as a result of errors or omissions in this document. This document is only intended to be a general guide and professional advice should be sought before taking any action on any matter.

Department of Biotechnology,
Ministry of Science and Technology
Government of India,
New Delhi, India

and

Association of Biotechnology Led Enterprises,
Bangalore, India

ABLE Association of Biotechnology Led Enterprises

The collective face of the Indian Biotech Industry

ABLE Secretariat
123/C, 16th Main Road, 5th Cross, 4th Block,
Koramangala, Bangalore - 560 034 INDIA
Telefax:: +91-80-25633853/41636853
www.ableindia.in

Creative: Cariapa Design Associates · *Printed at:* Black, White & Color